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Toxoplasmosis and its Significance in Public Health: A Review

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Abstract

Toxoplasmosis is an obligate intracellular protozoon that infects warm-blooded animals and humans, causing multiple manifestations. It can cause serious ocular disease, even in immune competent people, as well as abortions and encephalitis in domestic and wild animals. It can also result in fatal encephalitis in immunosuppressed individuals; if first contracted during pregnancy, it can result in miscarriage or congenital defects in the new-born. The parasite then penetrates the intestinal epithelial barrier and spreads from the lamina propria to a wide range of other organs in the body. The disease has a complex epidemiology and is spread by consumption of oocysts that are shed in the faeces of definitive feline hosts and contaminate water, soil, and crops, or by consumption of intracellular cysts in undercooked meat from intermediate hosts. Congenital infection is mostly diagnosed through laboratory testing, such as PCR and serologic assays, which also helps with the confirmation diagnosis of toxoplasmic encephalitis and ocular toxoplasmosis. For prevention and control, programs on the parasite and avoiding contact with infectious stages; biosecurity and sanitation to ensure the safety of food and water; chemo- and immunotherapeutic to control active infections and disease; prophylactic measures to prevent the infection of livestock and the formation of cysts in meat; and vaccines to prevent oocyst shedding by permanent feline hosts.

Keywords: *T. gondii,* bradyzoite, oocysts, tachyzoite, protozoa, immunocompetent, immunosuppressed.

Acronyms and Abbreviations: T. *Gondii* *Toxoplasma Gondii*; **CNS** Central Nervous System; **IG** Immune Globulin; **ELISA** Enzyme Linked Sorbent Assay; **IFA** Immune Florescence Assay; **LD50** Lethal dose 50; **Th1** T-helper 1; **TE** *Toxoplasma Encephalitis*; **CT** *Congenital Toxoplasmosis*; **OT** Ocular Toxoplasmosis; **DAT** Direct Agglutination test; **MAT** Modified Agglutination test; **PCR** Polymerase Chain Reaction; **HAAT** Highly Active Antiviral Therapy; **USDA** United State Department of Agriculture.

Introduction

The protozoan parasite Toxoplasmosis which infects all warm-blooded vertebrates and poses a serious threat to both human and animal health is the source of the infection known as toxoplasmosis [1].

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Human T. *gondii* infection is one of the most important public health problems that affects one-third of the human population [2, 3].

T. *gondii* has developed a number of potential transmission pathways both within and between various host species. It is facultatively heteroxenous. Eating raw meat contaminated with tissue cysts or accidentally ingesting contaminated food, water, or soil can both cause humans to contract the infection [4]. It also accesses to the host's body through several principal pathways, including: vertical transmission, organ transplantation, and blood transfusion [5].

In humans, infection is often asymptomatic due to efficient immunological regulation; but, in situations of acute infection or reactivation of latent infection in those with impaired immune systems, serious illness can develop [6]. Pregnant women and immunocompromised individuals (cancer, transplant and AIDS patients) comprise the two important risk groups for toxoplasmosis [7].

The clinical manifestations of toxoplasmosis are influenced by the parasite strain type, host genetic background and host immune status, among other factors [8, 9]. If Toxoplasma predilection is the brain and eye, poor prognosis and complications such as glaucoma, chorioretinitis, retinal detachment, brain abscess and encephalitis can occur during acute or recrudescent infection. The most common pathologies associated with infection in immunocompromised individuals or neonates include ocular toxoplasmosis and infection of the central nervous system (CNS) [10].

When an organism infects a host, the sporozoites that are housed in two sporocysts inside the oocysts are released, causing an infection to spread to the enterocytes of both intermediate and final hosts. The three infectious phases of T. *gondii* life cycle are tachyzoites, bradyzoites (in tissue cysts), and sporozoites (in oocysts). Although the exact process for tachyzoites to change into bradyzoites is still unknown, it appears that tissue cyst development begins when the parasite enters the cell and a characteristic vacuole form. There is a decrease in the number of dividing organisms after around three months. Tissue cysts can range in size (5-70 mm) and can contain a few to hundreds of bradyzoites [11]. Toxoplasmosis is diagnosed using a variety of techniques, most frequently serological ones. For the identification of Toxoplasma-specific antibodies, serology-based diagnostic methods like the enzyme-linked immunosorbent test (ELISA) and indirect immunofluorescence assay (IFA) are regarded as the gold standard (IgG or IgM) [1].

There isn't much information available in Ethiopia on congenital toxoplasmosis in children or seroprevalence statistics in pregnant women. Less than one-third of Ethiopia's estimated 1 million HIV-positive people are expected to be getting highly potent antiviral medication. Numerous opportunistic illnesses, such as toxoplasmosis, might cause thousands of people to die if a cautious T. *gondii* seroprevalence of 50% is used. However, precise numbers are unavailable, and the majority of serological surveys are outdated. According to serological studies, up to 79% of sheep and goats contain T. *gondii* antibodies. However, no data are available about toxoplasmosis-related livestock losses or the presence of viable T. *gondii* in any host in Ethiopia [12]. There is no approved treatment for clinical toxoplasmosis in cats. Sulphonamides, trimethoprim, pyrimethamine, and clindamycin, either alone or in combination, have been used to treat cats with clinical toxoplasmosis, with varying results [13]. The recommended treatment in cases of human cerebral toxoplasmosis is pyrimethamine and sulfadiazine (plus folinic acid) [14].

For prevention and control the following practices should be considered includes practicing good hygiene (e.g., hand washing after soil contact, washing fruits and vegetables that are eaten raw), freezing meat at 12 8°C for 24 hours [15]. Moreover, and/or cooking meat until an internal temperature of 66 8°C is reached, and not drinking untreated water [14].It is also recommended to keep cats indoors, feed them commercially prepared diets, and clean their litter boxes daily, because it takes at least one day for the organisms to sporulate and become infectious after being shed [16]. Recommendations specifically for pregnant women include wearing gloves when

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gardening or being in contact with soil or sand, followed by thorough hand-washing [17]. It may be ideal to minimize zoonotic transmission of toxoplasmosis in the absence of a viable human vaccination, and this must be done by restricting exposure to oocysts or tissue cysts. It is clear that Ethiopia lacks a centralized facility for guidance, information on mechanisms of transmission, and information on the presence of viable T. *gondii* in edible meats and T. *gondii* oocysts in the environment.

Objectives Readers should be able to know upon completion of this review:

- Describe the etiology, epidemiology, history, and risk factors of toxoplasmosis.
- Identify the clinical signs and symptoms of toxoplasmosis in immunocompetent, immunocompromised, and pregnant individuals.
- Talk about the treatments and circumstances that are utilized to manage and prevent illness in immunocompromised individuals and pregnant women.

Toxoplasmosis and It's Public Health Significance

History/Background of disease

The condition currently known as toxoplasmosis, which is caused by the parasite Toxoplasma *gondii*, was originally identified in 1908 in the mouse Ctenodactylusgundi in Tunisia [18, 19] and in the domestic rabbit (Oryctolaguscuniculus) in Brazil by [20]. It is an amazing coincidence that both teams of researchers first suspected that this illness originated in lab animals and was caused by Leishmania. Toxoplasma *gondii* was the name given to the parasite by [19]. Congenital toxoplasmosis was probably first recognized in Brazil in 1927 by Carlos Bastos Magarinos [21] who performed an autopsy on a 2-day-old girl in Rio de Janeiro. [21], named the parasite *Encephalitozoonchagasi*. In retrospect the lesions and the morphology of the parasite are indicative of toxoplasmosis. The first detailed scientific study was studies of viruses [22].They demonstrated that Toxoplasma was an obligate intracellular parasite that could be transmitted to lab animals by brain homogeneity injections intracranial, subcutaneously, and intraperitoneally. Congenital toxoplasmosis's first documented case was recorded by [23]. In Turkey in 1970's first isolated viable T. gondii from a dog [24], and from a child [25, 26].

Etiology and Parasite Life Cycle

The life cycle of T. gondii may be split into feline and non-feline infections, which correspond with sexual and asexual replication, respectively. Oocysts produced by parasite replication in the gut of feline family members are shed in the feces and proceed through sporulation. [27]. When consumed by animals, oocysts carrying sporozoites become infectious and give birth to the tachyzoite stage. Tachyzoites are the Toxoplasma stage that multiplies quickly and may invade all nucleated cells in the body. Tachyzoite replication results in cell death and rapid spread to other cells. The clinical signs of infection are brought on by a robust inflammatory response. When the host immune system exerts pressure, tachyzoites change into bradyzoites. For the duration of the host's life, this type of the parasite, which reproduces slowly, lives inside cysts that are mostly found in the skeletal muscle and the brain. In immunocompromised patients, tachyzoites that were once bradyzoites can be freed from cysts and reactivate [28, 29]. T. gondii is an obligate intracellular protozoan parasite that exists in nature in 3 forms: [30].T. gondii has a complex life cycle consisting of three stages:

1. Tachyzoite; The kind of the bacterium that causes congenital infection is called a tachyzoite. Cell invasion causes an immediate inflammatory response and the death of parasitized cells. This particular parasite invades and multiplies inside of cells during the acute stage of infection. It may be detected in all organs, but is most prevalent in the heart, liver, spleen, lymph nodes, and central nervous system muscle. Human placental lesions are often minute, however animal reports of massive necrosis [31, 32].Tachyzoites of T. gondii have been found in the bodily fluids of a

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number of intermediate hosts, including sheep, goats, cows, and camels, including saliva, sputum, urine, tears, and semen [33]. Tachyzoites are sensitive to proteolytic enzymes and are usually destroyed by gastric digestion.

2. **Bradyzoite**; The term "bradyzoite" was proposed by [34], to describe the stage encysted in tissues. Bradyzoites are also called cystozoites [35]. Proposed that cysts should be called tissue cysts to avoid confusion with oocysts and pseudocysts. According to [36], cysts can also develop, but to a lesser extent, in any visceral organs, such as lungs, liver, and kidneys. Professional groups such as slaughter house workers, butchers and hunters may also become infected during evisceration and handling of meat. Bradyzoites of T. *gondii* are more resistant to digestive enzymes (i.e., pepsin and trypsin) than tachyzoites [37, 38]. Therefore, ingestion of viable tissue cysts by a non-immune host will usually result in an infection with T. *gondii.* Tissue cysts of T. *gondii* are relatively resistant to changes in temperature and that remain infectious in refrigerated (1-4°C) carcasses or minced meat for up to three weeks [39]. This is usually longer than the meat remains suitable for human consumption. Heating to 67°C or higher is a safe way to kill tissue cysts [40]. Some studies have suggested that tissue cysts are killed by commercial procedures of curing with salt, sucrose or low temperature smoking [41].

3. **Sporozoite**; Environmentally sourced sporulated T. *gondii* oocysts have the potential to infect people and animals used for food. It's possible that diseased domestic cats or wild cats are to blame for the oocyst contamination of the environment. Oocysts can sporulate and become contagious within a day in an environment with enough aeration, humidity, and warmth, however sporulation may take longer in an environment with low levels of oxygen. Environment-resistance in T. *gondii* sporulated oocysts is high. They can withstand brief periods of dryness and cold, and they may live up to 18 months in damp sand or soil without losing their infectiousness. As a result of their great im-permeability and strong resistance to disinfectants [33].

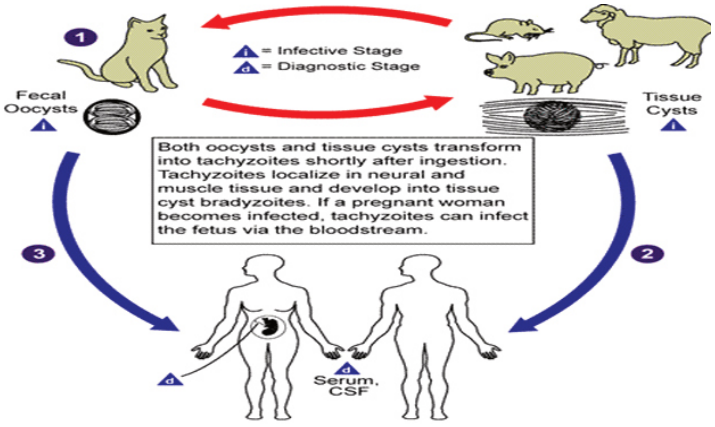

Figure 1. Life cycle of *T. Gondii;* Source CDC

Epidemiology

Prevalence

In Human

In this work, Rostami and colleagues estimated the worldwide and regional IgG seroprevalence of Toxoplasma *gondii*. Seroprevalence in the adult population was actually estimated to be between 20 and 40% in the UK and the USA, 50 to 80% in Central Europe, South and Central America, and West Africa, 4 to 39% in South East Asia, China, and Korea, 11-28% in Scandinavia, and 30% in Australia [42]. Additionally, findings from a thorough assessment of Toxoplasma *gondii* seroprevalence data revealed that seropositivity rates throughout the world ranged from less than 10% to over 90% [43]. The prevalence increases with age and does not differ greatly between males and females [6]. The infection is also more prevalent in warm and humid climates [44]. Importantly, the prevalence of infection clearly depends on the quality of water resources and hygiene. Some human epidemics have arisen as a result of the ingestion of insufficiently treated water [45]. The infection is also more common in those consuming undercooked meat [44]. The seroprevalence of T. *gondii* infection in pregnant women has been examined in different parts of the world and is estimated to range between 14% and 77% in regions with moderate to high rates of prevalence, uninfected pregnant women are at

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considerable risk of acquiring a primary infection and transmitting it to the foetus [6].

In Animals

Using a random effects model, the pooled worldwide seroprevalence of *T. gondi* was calculated to be 35% (95% CI: 32-38%) in domestic cats and 59% (95% CI: 56-63%) in wild felids, respectively. The *T. gondi* seropositivity in domestic cats was 52% (95% CI: 15-89%) and 51% (95% CI: 20-81%), respectively, in Australia and Africa, where the seroprevalence was greater.

Asia was expected to have the lowest seroprevalence at 27% (95% CI: 24-30%). *T. gondi* seroprevalence rates in wild felids were 74% (95% CI: 62-83%), 67% (95% CI: 23-111%), 67% (95% CI: 58-75%), and 66% (95% CI: 41-91%) in Africa, Asia, Europe, and South America. [46].

Prevalence in Conventional Meat Animals and Animal Products

1. Swine meat (Pork); Due to swine's increased vulnerability to T. *gondii* infection, pork has a higher chance of contracting the parasite compared to beef and fowl [47]. Only one case of an outbreak after consumption of under-cooked pork has been reported [48]. Due to the development of intensive farming, severe confinement housing, stringent biosecurity rules, improved rodent control, and proper carcass disposal have become standard farm management practices. In many nations, the virus has all but disappeared. Because of this, hog flesh is no longer a significant source of illness as it formerly was. But it's important to keep in mind the current trend toward “organic animal raising" or "animal-friendly farming," since it may cause pig infections to recur [49]. Recent trends in consumer habits, in fact, indicate a shift toward consumption of animal-friendly or organic pigs, which include increased exposure of the pig to the environment, and this, will lead to an increased risk of T. *gondii* in products from such animals [50].

2. Sheep (Lamb, mutton,) and goat meat; the presence of sporulated oocysts in the environment increases the risk of infection in animals kept on pastures, such as sheep and goats. In many parts of the world, such animals have high seropositivity rates. The USDA classifies sheep that are <, 1 year old and without permanent teeth as lambs [51].

Mutton is defined as meat from older sheep. Only lamb is killed for human consumption in the United States, whereas mutton is used to make pet food or is exported to other nations. Numerous case-control studies have shown that eating undercooked lamb meat is a significant risk factor. It is conceivable that the flesh of seropositive sheep contains a significant number of tissue cysts. [14], since sheep and lambs are frequently housed in pastures; the environment is contaminated with sporulated oocysts, which increases the risk of infection for these animals. Goat milk and flesh are widely consumed across the world [52].

3. Bovine meat (Beef); some case–control studies have demonstrated that consumption of under-cooked beef is a risk factor for T. *gondii* in humans [53]. Although seroprevalence in cattle is very high (antibodies are detected in up to 92% of cattle and up to 20% of buffaloes) tissue cysts are found only rarely in beef or buffalo meat [2]. Cattle are considered poor hosts for T. *gondii*; there have been no confirmed cases of T. *gondii*–induced abortion in cattle [54]. *Neosporacaninum*, a parasite morphologically similar to T. *gondii*, is the major cause of abortion in cattle [55].

4. Poultry meat; According to the USDA, chicken (in particular broiler chickens) and turkey are the most popular meats in the United States. Chicken is considered one of the most important hosts in the epidemiology of T. *gondii* infection [54]. Chicken age and husbandry methods are associated with the prevalence of T. *gondii* infection. Older chickens are more likely to be infected with T. *gondii* due to longer exposure to environmental oocysts. The parasite has been detected in meat from up to 80% seropositive chickens [56, 57]. And T. *gondii* is expected to be detected more commonly in free range chickens as opposed to intensively housed chickens [58, 54]. Parasite studies in muscle samples (breast) constantly give negative results

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even in the presence of seropositivity, in animals originating from intensive farming [59]. In contrast to indoor chickens, the prevalence of T. *gondii* in free-range chickens is much higher [54]. Infection in free range chickens has been used as an indicator of environmental oocyst contamination because these chickens roam freely and obtain food directly from the ground [60].

5. Horse meat; in recent research conducted in Italy, 90% of meat samples had parasites [61]. Horse flesh is consumed raw in various nations, which may have a significant impact on the spread of T. *gondii* [61].

6. Milk; Tachyzoites of T. *gondii* have been detected in the milk of several intermediate hosts, including sheep, goats, and cows [2]. Acute toxoplasmosis in humans has only been associated with consumption of unpasteurized goat's milk [62]. A recent report on how sheep can eliminate T. *gondii* in their milk is of interest [63]. In the past, it has often been thought that the risk of acquiring an infection with T. *gondii* by drinking cow's milk, if any, is minimal, but it cannot be excluded that any type of milk is a potential source of infection if consumed raw [2].

7. Eggs; There are discrepant findings in literature regarding the presence of T. *gondii* in eggs of poultry [54]. An early study reported that T. *gondii* tachyzoites may be isolated from raw chicken eggs laid by hens with experimentally induced infection [64], whereas other studies demonstrated very low level or absence of viable organisms in eggs laid by hens experimentally infected. Raw hen eggs are therefore unlikely to be a source of infection for humans [54].

8. Water and contaminated food and soil; several studies have confirmed a link between toxoplasmosis outbreaks and water contamination with oocysts [65, 6]. Sources other than meat and water have been identified: contact with soil eating unwashed raw vegetables or fruit and geophagia in preschool-aged children [53].

Risk factors for *T. gondi*

Many factors associated with toxoplasmosis for which preventive measures must be implemented. In-depth knowledge of associated risk factors is therefore needed to prevent, or at least reduce, the transmission of CT and to open new avenues of research. The availability of data on toxoplasmosis risk factors would enable health educators, public health practitioners and clinicians to plan appropriate screening and counselling [66].

1. Age; The prevalence of toxoplasmosis increases with age [67, 68]. A significant difference in T. *gondii* antibodies was observed between adults (28.3%) and children (18.7%) in Taiwan, Increased seroprevalence with age is a predictable result due to the increased duration of risk of exposure to T. *gondii*. The increasing seroprevalence with age highlights the continuing need to educate women of childbearing age about the risk factors for toxoplasmosis [69].

2. Gender; No significant differences in the prevalence of T. *gondii* serum antibodies have been found between males and females [70]. However, the increased risk of seropositivity in males reported in one study was attributed to less attention being paid to cleanliness in food preparation and eating [71].

3. Geography; the influence of climate on the survival of Toxoplasma oocysts in the environment has been established [72, 73]. However, minor differences in eating habits and husbandry practices of domestic animals across geographical regions within the country may influence exposure to infection. A related study in Chile demonstrated a progressive increase of the seroprevalence of toxoplasmosis from the higher altitude to the lower altitude regions of the country, and this phenomenon probably related to geographical conditions and the type of meat consumed [69].

4. Pregnancy; Cell-mediated immunity plays the main role in host resistance to T. *gondii* infection, and a Th1 cytokine profile is necessary for protection and control of infection. Production of progesterone

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during pregnancy leads to down regulation of cellular immune functions, and therefore increases the risk of T. *gondii* infection in pregnant women [24].

5. Immunodeficiency; The correlation between severity of T. *gondii* infection and the immune status of the infected person are well recognized. While toxoplasmosis in immunocompetent adolescents or adults is generally asymptomatic, it causes significant morbidity and mortality among immuno compromised individuals. Immunosuppression is caused by acquired immunodeficiency syndrome or therapies for malignancies, transplants or lymphoproliferative disorders [74, 75].

6. Exposure to cats; a link between feline T. *gondii* infections and an increased risk of human infections via soil contact as a possible mode of transmission. In reality, the possible risk factor for infection from cleaning contaminated cat litter trays in relation to kitchen cleanliness. These findings showed that a large source of T. *gondii* infection in humans may come from infected cats. However, other researchers did not discover a significant link between cat ownership and T. *gondii* infection [76]. The oocysts do not seem to stick to the cat's fur as roundworm eggs might. While grooming, cats may remove any oocysts on the fur before they become infective, and these oocysts are often buried in soil along with cat faeces [76].

7. Contaminated food; convincing epidemiological evidence that tissue cysts in contaminated meat are the primary human source of T. *gondii* infection [77]. T. *gondii* was even detected in one out of 67 ready-to-eat cured meat samples in the UK.

8. Drinking untreated water; In Victoria, British Columbia, Canada, the first and biggest toxoplasmosis epidemic connected to a public water source was identified in 1995. It was assumed that T. *gondii* oocysts were spread via cat faeces into a surface water reservoir [77].

Parthenogenesis and Clinical Symptom

T. gondi is a cosmopolitan protozoon [78] with no host specificity in the asexual stage (it can parasitize all mammals, including humans and felids), whereas in the sexual stage it is specific to felids where it becomes localized in the intestine. Toxoplasma can become systemic via the blood stream and localize in vital organs, muscle tissue, and the nervous system. Toxoplasma *gondii* tachyzoites invade nucleated host cells by active penetration [79. and in inactivated cells, the parasites establish a non fusogenic vacuole [80], within which they replicate by endodyogeny [81]. Ultimately, tachyzoites will enter the circulation and disseminate to secondary tissues. T. *gondii* induces a strong inflammatory response from the host, which plays a critical role in controlling the infection and reducing parasite burden [82]. After the acute stage of the infection, the tachyzoites differentiate back into bradyzoites and establish a chronic infection in a large variety of tissues [83]. Tissue cysts harbouring bradyzoites persist for the lifetime of the host, and the bradyzoites are characterized as multiplying very slowly and having a quiescent metabolic program [84].

T. *gondii* isolates comprise four major lineages of strains: types I, II, III and the recently identified haplotype 12 strains. In mice, the type I strain is the most virulent (LD100 = 1). The type II strain is commonly associated with human disease, the type III strain with disease in livestock, and the type 12 strains with wild animals. Notably, differences in the dissemination of these strains in infected mice correlate with disease pathogenesis and virulence. The type I strain exhibits a highly migratory phenotype, which may contribute to its invasiveness in the infected host [5].

In Humans

Humans acquire their infections from ingestion of oocyst-contaminated soil and water, from tissue cysts in undercooked meat, by transplantation, blood transfusion, laboratory accidents, or congenitally [14]. Most people infected after births were asymptomatic; however, some may develop fever, malaise, and lymphadenopathy. Congenital toxoplasmosis often results in debilitating ocular disease, causing (among other manifestations) retinochoroitis and anterior uveitis [85]. Prenatal infection is the direct

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consequence of a primary infection of the mother during pregnancy. Congenital toxoplasmosis ranges from sub-clinical forms to extremely serious cases leading to fetal or neonatal death. In these cases, the central nervous system and the eyes are constantly infected, whereas other organs such as the liver, spleen, kidneys, and lungs are rarely involved. Infections in the first stages of pregnancy can bring about abortion, death, or serious fetal damage, such as retinochoroiditis, endocranial calcification, hydrocephaly, and microcephaly [86]. In the later stages of pregnancy, on the other hand, T. *gondii* infections are sub-clinical, even though retinochoroiditis and neurological disorders are sometimes found [87].

Ocular toxoplasmosis is a consequence of prenatal infection only in one-third of cases and it is considered a probable consequence of postnatal infections [88]. The severity of ocular lesions depends on the length of infection and inflammatory intensity. The clinical picture presents necrotizing retinitis with variations in lesion size, number, and aspect. Lesions can be either monolateral or bilateral, with re-activation occurring in 80% of cases. More rarely, but not less serious, are the manifestations of anterior uveitis, and inflammation of sclera and papilla [89].

In Other Animals

1. In Cats; Feline infections are typically subclinical; congenitally infected kittens are the most likely to have clinical signs of infection, but previously clinically healthy adult cats may also be affected [16, 14]. Common symptoms of T. *gondii* infection in cats can include fever, ocular inflammation, anorexia, lethargy, abdominal discomfort and neurologic abnormalities [16]. Most infected cats are asymptomatic, whereas clinical toxoplasmosis is mostly manifested in pneumonia, and in cats that subsequently died the most common signs were sensory depression and anorexia [11]. Other consequences of the infection are hepatitis, pancreatic necrosis, myositis, myocarditis, uveitis, dermatitis, and encephalitis with the worst lesions being in kittens with congenital infections [90, 91]. Analogously with humans, cats with immune deficiency syndrome are found to have a predisposition to systemic toxoplasmosis [92]. In cases of complicated ocular disease or nervous system symptoms, it is always opportune to include a laboratory test for Toxoplasma [92]. Ocular infections give rise to retinochoroiditis, uveitis with mydriasis, and photophobia leading to blindness. When checking for clinical signs of the nervous system, the veterinarian should take note of any altered motor coordination: signs of hyperesthesia, behavioral changes (e.g., moving in circles with ears lowered, typical signs of fear or aggressiveness), difficulty in mastication or swallowing, epileptic type convulsions, and urinary incontinence [92], cases of myocarditis and encephalitis have been reported [14].

2. Pigs; Clinical signs of the infection are rare in pigs but can cause premature births and pneumonia. Rare cite nervous system clinical signs (tremors and ataxia), coughing, diarrhea, and a 50% mortality rate, as well as still born and premature births, and neonatal deaths [52] [after 14 days of diarrhoea, revealed signs of lymphadenitis, pneumonia, enchepalitis, and necrotizing enteritis, and tachyzoites were detected in all lesions [93]. Most infections are actually sub-clinical or feature non pathognomonic signs such as hyperthermia, anorexia, and tachypnea [94].

3. Cattle; There have been no confirmed cases of clinical toxoplasmosis in cattle and probably many cases of abortion were attributed to T. *gondii* before the discovery that Neosporacaninum can provoke abortions in cattle [35].

4. Poultry; Reported clinical cases are very rare with the most recent describing nervous system symptoms in free-range chickens in a family run farm [59]. The autopsy on one animal showed necrosis, perivascular lymphocyte cuffs, and gliosis as well as tissue cysts and tachyzoites in the lesions [59].

5. Sheep and goats; the prevalence of T. *gondii* in adult sheep and lambs is high and the parasite is known to cause abortions and neonatal mortality in sheep [95]. Lambs that survive congenital infections grow

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regularly and are therefore can be a source of infection for humans. In goats, apart from abortions and neonatal mortality, clinical signs may be present and the parasite can be found in organs and tissue (mainly liver, kidneys, and brain) [35].

6. Horses; Even though infection is possible in horses [61], the complete absence of reported evident clinical disease must be mentioned.

Transmission

In Animals

Cats and wild felids are essential to the persistence of T. *gondii* in hosts such as grazing animals (e.g., sheep and deer) because they serve as the sole source of the infectious oocysts that contaminate the environment.

At the same time, it is only in the feline host that sexual multiplication of this parasite takes place, so cats serve as the only site wherein genetic recombination and re-assortment of this parasite can occur. Different isolates of T. *gondii* from around the world, with isolates being placed mainly in one of three genetic strains, Type I, II, and III [27].

Toxoplasma infection can be transmitted by the ingestion of oocysts shed into the environment from cat feces which may contaminate water, soil, and vegetables, or also by viable tissue cysts found in raw or undercooked meat of intermediate hosts. Oocysts are highly infectious to herbivores and bradyzoites to cats. Infections caused through the ingestion of oocysts are considered more severe clinically in intermediate hosts than those related through the ingestion of tissue cysts [96].

In Human

Toxoplasmosis can be transmitted to humans by three principal routes. First, humans can eat raw or inadequately cooked infected meat (especially pork, mutton, and wild game meat [51] or eat uncooked foods that have come in contact with infected meat. Second, humans can inadvertently ingest oocysts that cats have passed in their feces, either in a cat litter box or in soil (e.g., soil from gardening or unwashed fruits or vegetables). Third, a woman can transmit the infection to her unborn fetus trans placentally. Women infected with T. *gondii* before conception, with rare exception [97], do not transmit the infection to their fetuses. Women infected with T. *gondii* during pregnancy can transmit the infection across the placenta to their fetuses. When the mother is infected in the first trimester of pregnancy, abortion or stillbirth can occur. When mothers acquired their first infection in the second or third trimester, only 15% and 5% of children presented with a subclinical infection form at birth [98]. The risk of congenital disease is lowest (10–25%) when acute maternal infection occurs during the first trimester and highest (60–90%) when acute maternal infection occurs during the third trimester. In adults, the incubation period ranges from 10 to 23 days from ingestion of undercooked meat, and from 5 to 20 days from ingestion of oocysts from cat feces [99, 100,101].

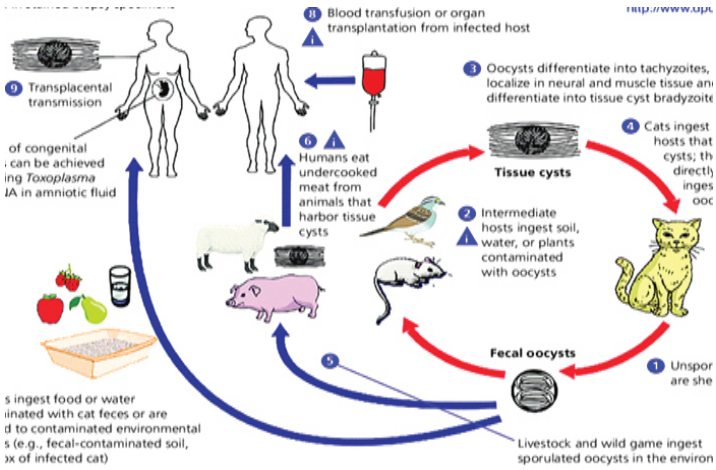

Figure 2. Transmission cycle of toxoplasmosis; Sources CDC

Diagnosis

A diagnosis of toxoplasmosis can be established by the isolation of T. *gondii* from blood or body fluids, demonstration of the parasite in tissues; detection of specific nucleic acids with DNA probes, or by carrying out serologic tests in order to detect T. *gondii*-specific immunoglobulins synthesized by the host in response to infection. Currently, routine diagnosis of toxoplasmosis relies mainly on the use of various serological tests to detect specific antibodies in the serum samples of infected patients:

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1. **Sabin–Feldman dye test:** Development of a novel serologic test, the dye test, in 1948 by Albert Sabin and Harry Feldman was perhaps the greatest advancement in the field of toxoplasmosis [102]. The dye test is highly sensitive and specific with no evidence for false results in humans. The ability to identify T. *gondii* infections based on a simple serological test opened the door for extensive epidemiological studies on the incidence of infection. It became clear that T. *gondii* infections are widely prevalent in humans in many countries.

2. **Detection of IgM antibodies:** The first proposed the usefulness of the detection of IgM antibodies in cord blood or infant serum for the diagnosis of congenital toxoplasmosis because IgM antibodies do not cross the placenta, whereas IgG antibodies do [103]. Modified the indirect fluorescent antibody test and the ELISA [104]. To detect IgM in cord blood they developed a modification of IgM-ELISA, combining it with the agglutination test (IgM-ISAGA) to eliminate the necessity for an enzyme conjugate. Although IgM tests are not perfect, they have proved useful for screening programs [105, 106].

3. **Direct agglutination test (DAT):** The development of a simple DAT has aided tremendously in the serological diagnosis of toxoplasmosis in humans and other animals. In this test no special equipment or conjugates are needed. This test was initially developed by [107] and improved by [108], and [109] and, who called it the modified agglutination test (MAT). The MAT has been used extensively for the diagnosis of toxoplasmosis in animals. The sensitivity and specificity of MAT has been validated by comparing serologic data and isolation of the parasite from naturally and experimentally infected pigs [110, 111].

4. **Detection of Toxoplasma *gondii* DNA:** The first reported detection of T. *gondii* DNA from a single tachyzoite using the B1 gene in a polymerase chain reaction (PCR). Several subsequent PCR tests have been developed using different gene targets. Overall, this technique has proven very useful in the diagnosis of clinical toxoplasmosis [112].

Treatment

Generally, in immunocompetent patients' treatment is usually unnecessary since the infection is subclinical and the immune response is able to control it. However, in immunocompromised patients (including HIV and other risk groups), the patients need to be treated and monitored since toxoplasmosis is a major cause of death among AIDS patients [11]. In these patients, the recommended treatment is a combination of two drugs, pyrimethamine (25–100 mg daily) and trisulfapyrimidines (2–6 g daily), administered for 1 month where this combination acts by inhibiting the enzyme, dihydrofolatereductase, of T. *gondii* preventing the synthesis of DNA and proteins.

Untreated acute toxoplasmosis among pregnant women can lead to infection of the fetus via transplacental transmission [113]. At first examination, new-borns affected by congenital infection may seem normal; however, serious sequellae, such as neurological impairment and blindness, can develop within a few years later [101,114, 30].

There is no approved treatment for clinical toxoplasmosis in cats. Sulphonamides, trimethoprim, pyrimethamine, and clindamycin, either alone or in combination, have been used to treat cats with clinical toxoplasmosis, with varying results [13]. Ponazuril, an approved treatment for equine protozoalmyeloencephalitis caused by *Sarcocystisneurona* in horses, is excellent in treating acute toxoplasmosis in mice and should be evaluated in domestic cats [17, 13]. The recommended treatment in cases of human cerebral toxoplasmosis is pyrimethamine and sulfadiazine (plus folinic acid) [14].

Toxoplasmosis in Ethiopia

In Humans

Ethiopia is the second-most populous nation in the horn of Africa, with over 82 million inhabitants, and a high rate of AIDS. The finding of 93.3% seroprevalence of T. *gondii* antibodies in HIV patients by [115] is notable. Although clinical toxoplasmosis has been suspected in many HIV-infected patients treated with highly active

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antiviral therapy (HAART), and immune reconstitution [116]. There is no histologically verified cases of toxoplasmosis in HIV-infected or immunocompetent persons in Ethiopia because histological diagnosis has not been pursued [12]. Limited data indicate a high seroprevalence of T. *gondii* antibodies in humans in Ethiopia. Seroprevalence varied from 47–96% with high rates in 97 children (aged 14–18 years) from leprosy families (85.5%) and from 427 blood donors (50–92%). This high prevalence in blood donors is important because toxoplasmosis can be transmitted by blood transfusion, especially in immunosuppressed persons or during acute infection [12]. In Ethiopia Out of the 360, 128 (35.6%) pregnant women were found to be positive for antibodies specific to T. *gondii*. Furthermore, 117 (32.5%) women were positive only for IgG, and 11 (3.1%) were positive both for IgM and IgG antibodies [117].

Toxoplasmosis in other animals in Ethiopia

There are no records of clinical toxoplasmosis in other species. Despite being more than ten years old, serological investigations show that sheep and goats have a significant incidence of T. *gondii* antibodies. Recently, [118] reported 74.9% seroprevalence in 641 goats from central and southern regions of Ethiopia. Seroprevalence in cattle was low [119]. To our knowledge, there is no report of isolation of viable T. *gondii* from animals (or humans) in Ethiopia [120].

Host	Prevalence %	Study Area
Goat	19.74	CE
Sheep	34.66	CE
Sheep and goat	74.88	CSE
Camel	48.57	CE
Chicken	38.4	CE
Pig	32.09	CE
Cat	91.67	CE
Human	90	CE
Human	81.09	SE
Human	78.92	NE
Human	88.24	SE
Sheep, goat	26.09	SE

Table 1. Summary of prevalence in Ethiopia. CE, Central Ethiopia; CSE, Central and Southern Ethiopia; NE, Northern Ethiopia; nr, not reported; SE, Southern Ethiopia; WCSE, Western, Central and Southern Ethiopia

Control and Prevention of Infection in Animals and Humans

Toxoplasmosis prevention by zoonotic transmission control, which requires restricting exposure to oocysts or tissue cysts, may be the best strategy in the absence of a human vaccine that is effective. The main goal of toxoplasmosis prevention is to prevent human exposure to the parasite through health education. Many nations have implemented educational initiatives meant to lower the prevalence of congenital toxoplasmosis [120].

Hygiene Measures

To achieve this, suggestions include maintaining proper cleanliness (such as washing hands after using the restroom and washing fruits and vegetables eaten raw).

Another suggestion is to freeze meat at 12 °C for 24 hours [15], and avoiding untreated water consumption, cooking meat until it reaches an internal temperature of 66 °C, and other measures [14]. Due to the fact that it takes at least a day for the organisms to sporulate and become contagious after being shed, it is also advised to keep cats indoors, give them commercially prepared diets, and clean their litter boxes every day [16]. Pregnant women are advised to thoroughly wash their hands after handling dirt or sand and to use gloves when gardening or otherwise coming into contact with those materials [17]. Additionally, if at all feasible, pregnant women should refrain from changing cat litter. To prevent oocyst consumption, owners should also be counselled to keep their dogs away from the litter box [121].

Vaccination for the Control of Toxoplasmosis

The development of vaccinations to stop feline oocyst

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shedding is still continuing, mostly using live vaccines. There are certain drawbacks, including as its short shelf life and the possibility of infection for anyone handling the vaccinations [122]. Toxovax1 (S48 strain), a live vaccination that was first created for use in sheep, prevents T. gondi from developing sexually in cats. Therefore, the parasite strain is recognized by the immune system, but cats are unable to manufacture oocysts [123]. This vaccination is applied to sheep to lessen the growth of tissue cysts. Given that initial infection confers lifetime immunity to the parasite, the development of an effective T. gondi vaccine appears to be a feasible objective [124].

Studies on a T. *gondii* vaccination in humans have not been reported. However, there is a lengthy list of experimental vaccines that have recently undergone testing in mouse models, including The only commercial vaccination against T. *gondii* available today is based on an attenuated strain intended to prevent abortion in sheep and is not deemed acceptable for administration to people due to significant safety and regulatory difficulties related with a possible reversion to fully virulent parasites [125]. Recent studies have focused on developing more effective adjuvant systems, discovering better ways to display and transport immunogenic antigens to the immune system, and boosting the effectiveness of vaccinations by combining these antigens with their T-cell epitopes [124].

Conclusion & Recommendation

Consumer knowledge of the hazardous foodborne protozoan disease toxoplasmosis is limited. Congenital toxoplasmosis, which is transferred vertically to the newborn, is one of the worst side effects of primary T. gondi infection. During pregnancy, it could be difficult to identify primary T. gondi infection. Ethiopia lacks a centralized center for diagnostic confirmation and counseling, and there is less information available on the mechanisms of transmission, the possibility that edible things may contain viable T. *gondii*, and the prevalence of T. *gondii* oocysts in the environment. The only way to lower the risk is via prevention, and efforts are currently being made to provide an effective vaccine. Despite the possibility of reducing the risk by practicing great general hygiene, the development of effective vaccines remains a high priority for public health. The recommendations were as follows in light of this conclusion:

- Food should be prepared at safe temperatures… Pork, ground meat, and wild game should be cooked to 160 °F (71.11 degree Celsius) before consuming, whereas roasts and steaks made of beef, lamb, and veal should be cooked to at least 145 °F (62.78 degree Celsius). To make sure the meat is done all the way through, whole fowl should be cooked to 180 °F (82.22 degree Celsius) in the thigh.
- Before consuming, fruits and vegetables should be properly cleaned or peeled.
- Cutting boards, dishes, countertops, utensils, and hands should be cleaned with hot water with soapy
- Pregnant women should be wearing gloves when gardening, hands should be properly cleansed after working in the garden or coming into touch with sand or soil, and people who are immunosuppressed should receive education on infection prevention.
- The prevention of T. *gondii* infection in people and animals requires educational initiatives.

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