Review Article

CONGENITAL TAXOPLASMOSIS CHALENGES AND PROzSPECT: A REVIEW

Abstract

Recent research have indicated that screening and treatment for toxoplasmosis during gestation result in a decrease of vertical transmission and clinical sequelae. Early treatment was associated with reduced infection with *T. gondi*. Thus, laboratory diagnostic methods should aim for early identification of infants with congenital toxoplasmosis. Detecting the infection early and beginning proper treatment immediately may help prevent some of the severe health outcomes associated with the condition. The most commonly used and accepted laboratory method for the diagnosis of Congenital Toxoplasmosis during gestation is the use of PCR in amniotic fluid, and a positive test result is diagnostic of Congenital Toxoplasmosis . In the postnatal period, the gold standard to establish a diagnosis of Congenital Toxoplasmosis is the persistence of *Toxoplasma* IgG by 12 months of age. In addition, in-depth epidemiological studies are needed to inform the design of regional strategies and to guide implementation of control programs involving both the medical and veterinary sectors.

INTRODUCTION

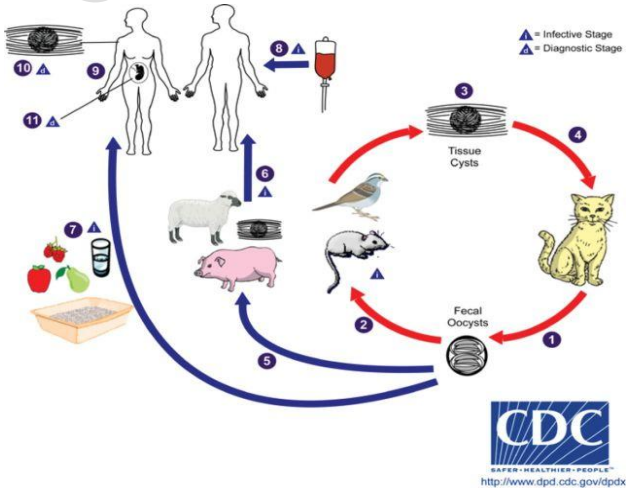
Toxoplasma gondii belong the kingdom Protista and sub-kingdom protozoa. It is a zoonotic parasite that can infect nearly all warm blooded animals including humans [1, 2]. It is an intra-cellular parasite that causes toxoplasmosis. *T. gondii* belongs to the of phylum Apicomplexa that was first identified and isolated in African rodent "*Ctenodactylus gundii*" in 1908 by Nicolle and

Manceaux at Pasteur institute of Tunis[3, 5)]. In humans, *T. gondii* is one of the most common parasites in developed countries. Serological studies estimate that 10–90% of the global population has been exposed to and may be chronically infected with *T. gondii*, although infection rates differ significantly from country to country depending on environmental or socioeconomic factors and geographic locations [4, 5]. For example, previous estimates have shown the highest prevalence of persons infected to be in France, at 84% [6, 7]. In Nigeria seroprevalence of human toxoplasmosis is estimated at 32% [8]. Although mild, flu-like symptoms occasionally occur during the first few weeks following exposure, infection with *T. gondii* produces no readily observable symptoms in healthy human adult [7]. This asymptomatic state of infection is referred to as a latent infection and has recently been associated with numerous subtle adverse or pathological behavioral alterations in humans [2]. In infants, HIV/AIDS patients, and others with weakened immunity, infection may cause a serious and occasionally fatal illness; *T. gondii* has been shown to alter the behavior of infected rodents in ways that increase the rodents' chances of being preyed upon by felines. Support for this "manipulation hypothesis" stems from studies showing *T. gondii*-infected rats have a decreased aversion to cat urine [8, 28]. Because cats are the only hosts within which *T. gondii* can sexually reproduce to complete and begin its lifecycle, such behavioral manipulations are thought to be evolutionary adaptations that increase the parasite's reproductive success [9, 11]. The rats would not shy away from areas where cats live and would also be less able to escape should a cat try to prey on them. The primary mechanisms of *T. gondii*–induced behavioral changes in rodents is now known to occur through epigenetic re-modeling in neurons which govern the associated behaviors; for example, it modifies epigenetic methylation to cause hypomethylation of arginine vasopressin-related genes in the medial amygdala to greatly

decrease predator aversion [10, 27]. Widespread histone-lysine acetylation in cortical astrocytes appears to be another epigenetic mechanism employed by *T. gondii*. Differences in aversion to cat urine are observed between non-infected and infected humans and sex differences within these groups were apparent, too [11]. A number of studies have suggested that subtle behavioral or personality changes may occur in infected humans, and infection with the parasite has recently been associated with a number of neurological disorders particularly schizophrenia and bipolar disorder [11] The major target group of the parasite includes immunocompromised patients (e.g. AIDS, cancer, organ transplantation) and fetus bearing pregnant women where it develops toxoplasmic encephalitis, myocarditis, chorioretinitis and abnormal fetal brain development or stillbirths respectively [12, 2, 8]. Other studies have found schizophrenia, depression, anxiety and other mental diseases are more common in people with toxoplasmosis, and there is also evidence to suggest infection by the parasite is linked to more extroverted, aggressive and risk-taking behavior.[13]

LIFE CYCLE OF *TAXOPLASMA GONDII*

Infection by the intracellular apicomplexan parasite Toxoplasma gondii affects an estimated 25–30% of humans worldwide [14, 19], making this zoonotic parasite one of the most widespread human pathogens in the world. When a feline definitive host consumes a tissue cyst (containing bradyzoites), bradyzoites convert into merozoites inside intestinal epithelial cells. Following a brief period of rapid population growth in the intestinal epithelium, merozoites convert into the noninfectious sexual stages of the parasite to undergo sexual



reproduction, eventually resulting in zygote-containing oocysts [15, 32]. Infected felids excrete up to several hundred million environmentally resistant oocysts with their feces, which can infect any warm-

Fig. 1. Life cycle Of *Taxoplasma gondii*

blooded animal upon ingestion. There, *T. gondii* reproduces asexually via two distinct life cycle stages, the fast growing tachyzoite and the slower reproducing bradyzoite stage [16, 14]. The latter forms cysts in various host tissues, which may be consumed by carnivores or omnivores. Cysts usually range in size between five (5) and fifty (50) µm in diameter, (with 50 µm being about two-thirds the width of the average human hair). Following ingestion, bradyzoites are released from the tissue and transformed into tachyzoites which are actively dividing and infect other host cells. Inside host cells, the tachyzoites replicate inside specialized vacuoles (called the parasitophorous vacuoles) created during parasitic entry into the cell [17, 6, 11].

Tachyzoites multiply inside this vacuole until the host cell dies and ruptures, releasing and spreading the tachyzoites via the bloodstream to all organs and tissues of the body, including the brain [18, 19]. Human infection may be acquired by ingestion of undercooked meat containing *T gondii* cysts, ingestion of oocysts from hands, food, soil, or water contaminated with feline feaces, organ transplantation or blood transfusion from infected donors, trans-placental transmission from an infected mother to fetus [20, 9]. The two major routes of transmission of *Toxoplasma* to humans are oral and congenital [12, 10]. In humans, ingesting either the tissue cyst or the oocyst results in the rupture of the cyst wall which releases sporozoites that invade the intestinal epithelium, disseminate throughout the body, and multiply intracellularly. The host cell dies and releases tachyzoites, which invade adjacent cells and

continue the process [21, 26, 12]. The tachyzoites are pressured by the host's immune response to transform into bradyzoites and form tissue cysts, most commonly in skeletal, muscle, myocardium, and brain etc. These cysts may remain throughout the life of the host [22, 13]. Clinical disease may occur if the host becomes immune-suppressed and the cysts rupture, releasing the parasites [14, 15]. The sexual life cycle is initiated when a member of the feline family ingest oocyst from or tissues that are infected with bradyzoite cyst. The cycle is limited to the feline intestine and result in the shedding of oocyst in the cat feaces [23]. The oocyst sporulate in the soil for five days and become infective and can survive in the environment for up to one year. Any warm blooded animals that ingest this cyst become a host for the asexual life cycle [24, 16]. Upon ingestion of tissue cyst in raw undercooked meat from an infected host, the bradyzoites infect the intestinal epithelium of the host and differentiate back to tachyzoites to complete the life cycle [25, 17].

CONGENITAL TRANSMISSION

Congenital infection occurs predominantly after primary infection of a pregnant woman [26, 24]. The incidence of congenital toxoplasmosis varies with the trimester during which maternal infection was acquired. For untreated women, the transmission rate is approximately 25 percent in the first trimester, 54 percent in the second trimester, and 65 percent in the third trimester [27, 18]. Although the mother will generally not notice any symptoms, the infection may spread to the baby before birth or in the process of labour and delivery [28]. Babies with toxoplasmosis are often born too early and can have a variety of health problems affecting the eyes, nervous system, skin, and ears. For some babies with toxoplasmosis, detecting the infection early and beginning proper treatment immediately may help prevent some of the severe health outcomes associated with the condition [29]. Although the precise mechanism of movement of the parasite

across the human placental is not fully understood, recent studies may offer new insights. Human placental studies suggest that the extravillous trophoblasts (EVT) that anchor the placenta to the uterus are much more vulnerable to infection than are the syncytiotrophoblasts that are bathed in maternal blood [30, 19]. Studies in animals have shown that initial infection occurs in the uterus [31, 19]. Thus, it is likely that after primary infection a woman becomes parasitemic, leading to intracellular infection in the uterus, which then gradually leads to EVT infection, as the tachyzoites move from cell to cell, with eventual infection of the fetus [19]. It is also possible that direct movement of tachyzoite infected maternal leukocytes to or across the placenta contributes to the infection of the fetus [32]. Apart from toxoplasmosis in immuno-compromised individuals, congenital toxoplasmosis is the most serious manifestation of infection, resulting from the vertical transmission of *T. gondii* transplacentally from a parasitemic mother to her offspring [33, 34]. The severity of disease depends on the gestational age at transmission [11]. Ophthalmologic and neurologic disabilities are the most important consequences of infection and can be present even when the congenital infection is asymptomatic [35, 2].

The fetus, newborn, and young infant with congenital toxoplasmosis are at risk of infection-associated complications, particularly retinal disease that can occur into adulthood [36]. Hosts who are immunocompromised, especially those with defects in cellular immunity such as AIDS, are also at increased risk for severe disease [37, 4]. Congenital toxoplasmosis is a preventable disease. Prepregnancy screening accompanied by serial titers and appropriate counseling in women with initial negative titers may minimize cases.

PATHOGENESIS

In humans, clinical disease is normally limited either to immune-compromised individuals or to congenital disease resulting from an acute infection of the expectant mother [38, 17]. Toxoplasmosis can be categorized into 4 groups: (i) acquired in the immunocompetent patient; (ii) acquired or reactivated in the immunodeficient patient; (iii) Ocular; and (iv) Congenital. Diagnosis and treatment may be different for each clinical category [29]. Acquired infection with *Toxoplasma* in immunocompetent individuals is generally an asymptomatic infection [39]. However, 10%–20% of patients with acute infection may develop cervical lymphadenopathy or a flu-like illness [40, 1]. The clinical course is benign and self-limited; symptoms usually resolve within weeks to months. Recent data have suggested an association between *T gondii* infection and various neurologic or psychiatric syndromes, including schizophrenia, Alzheimer disease, and even suicide [33]. These findings are intriguing but require further study to validate.

Immunodeficient patients often have central nervous system (CNS) disease but may have myocarditis or pneumonitis [41]. In patients with acquired immune deficiency syndrome, toxoplasmic encephalitis is the most common cause of intracerebral mass lesions and is thought to be due to reactivation of chronic infection [42, 8]. Toxoplasmosis in patients being treated with immunosuppressive drugs may be due to either newly acquired or reactivated latent infection Ocular toxoplasmosis, an important cause of chorioretinitis in the United States, may be the result of congenital or acquired infection [43, 44]. Congenitally infected patients can be asymptomatic until the second or third decade of life, when lesions develop in the eye presumably due to cyst rupture and subsequent release of tachyzoites and bradyzoites [45, 17]. Chorioretinitis is more often bilateral (30%–80%) in congenitally infected individuals than in individuals with acute acquired *T gondii* infection [46]. Further defining the interaction of human immunity, timing of infection, and parasite genotype is an important area of ongoing research in

158 understanding ocular toxoplasmosis [47, 4]. Congenital toxoplasmosis has a wide spectrum of
159 clinical manifestations, but it is subclinical in approximately 75% of infected newborns [48, 29].
160 The severity of clinical disease in congenitally infected infants is related inversely to the
161 gestational age at the time of primary maternal infection—with first-trimester maternal infection
162 leading to more severe manifestations [49]. When clinically apparent, it may mimic other
163 diseases of the newborn. In a proportion of cases, spontaneous abortion, prematurity, or stillbirth
164 may result. Involvement of the CNS is a hallmark of congenital *Toxoplasma* infection [23]. The
165 presence of chorioretinitis, intracranial calcifications, and hydrocephalus is considered the classic
166 triad of congenital toxoplasmosis [50]. Fever, hydrocephalus or microcephaly,
167 hepatosplenomegaly, jaundice, convulsions, chorioretinitis (often bilateral), cerebral
168 calcifications, and abnormal cerebrospinal fluid are the classic features of severe congenital
169 toxoplasmosis [51, 15]. Other occasional findings included rash (maculopapular, petechial, or
170 both), myocarditis, pneumonitis and respiratory distress, hearing defects, an erythroblastosis-like
171 picture, thrombocytopenia, lymphocytosis, monocytosis, and nephrotic syndrome [29]. Some
172 infected children without overt disease as neonates may escape serious sequelae of the infection;
173 however, a significant number (14 to 85%) develop chorioretinitis, strabismus, blindness,
174 hydrocephalus or microcephaly, cerebral calcifications, developmental delay, epilepsy, or
175 deafness months or years later [52, 29]. Current treatment regimens work primarily against the
176 actively dividing tachyzoite form of *T gondii* year and often initiated before birth—seem to be
177 associated with substantially less frequent and severe sequelae. Further refining the optimal
178 treatment regimen is an area requiring further research, especially as newer drugs (azithromycin,
179 atovoquone, etc) with activity against the various stages of months after delivery can
180 significantly ameliorate subsequent neurologic damage in infected children [19]. The severity of

congenital infections depends on the stage of pregnancy when the acute infection occurred, and spontaneous abortions or neurological disorders such as blindness and mental retardation can result [39, 12]. In the past two decades, there has been a dramatic increase in the number of immune-compromised individuals and thus a concomitant increase in severe toxoplasmosis [42]. Within this latter patient group, *Toxoplasmosis* is a frequent cause of intracerebral focal lesions resulting in toxoplasmic encephalitis [53, 21]. If left untreated, toxoplasmic encephalitis can be fatal, and thus this disease represents an important concern in the AIDS community [28]. Although the current drug therapy (sulfonamide and pyrimethamine will effectively kill the tachyzoite stage, such treatment does not remove the chronic bradyzoite stage, and thus long-term therapy is needed [23]. The toxic side effects of these drugs, combined with their inability to eliminate the infection, makes the need for safer and more effective treatments critical [37]. In recent studies, researchers have begun to appreciate that differences in [15] reactivation and disease severity may be explained in part by different genotypes of *T gondii*, of which there are 3 occurring in different parts of the world. These studies are important because they may explain conflicting reports from different regions of the world on the relative public health importance of screening and treatment for congenital disease [29]. Further research is needed to define the role of *T gondii* genotypes and the interplay with human innate immunity, particularly in the developing fetus and newborn infant. One study on transmission across the human placenta showed a trend towards increased transmission by 1 genotype; however, the differences were not statistically significant [29].

Initially, a *T. gondii* infection stimulates production of IL-2 and Interferon- γ (IFN-γ) by the innate immune system [19]. Continuous IFN-γ production is necessary for control of both acute and chronic *T. gondii* infection [21]. These two cytokines elicit a CD4+ and CD8+ T-cell

mediated immune response [9, 35]. Thus, T-cells play a central role in immunity against *Toxoplasma* infection. T-cells recognize *Toxoplasma* antigens that are presented to them by the body's own Major Histocompatibility Complex (MHC) molecules. The specific genetic sequence of a given MHC molecule differs dramatically between individuals, which is why these molecules are involved in transplant rejection. Individuals carrying certain genetic sequences of MHC molecules are much more likely to be infected with *Toxoplasma* [17]. One study of >1600 individuals found that Toxoplasma infection was especially common among people who expressed certain MHC alleles (HLA-B*08:01, HLA-C*04:01, HLA-DRB 03:01, HLA-DQA*05:01 and HLA-DQB*02:01) [26]. IL-12 is produced during *T. gondii* infection to activate natural killer (NK) [15]. Tryptophan is an essential amino acid for *T. gondii,* which it scavenges from host cells. IFN-γ induces the activation of indole-amine-2, 3-dioxygenase (IDO) and tryptophan-2,3 dioxygenase (TDO), two enzymes that are responsible for the degradation of tryptophan [29]. Immune pressure eventually leads the parasite to form cysts that normally are deposited in the muscles and in the brain of the hosts [17]. The IFN-γ-mediated activation of IDO and TDO is an evolutionary mechanism that serves to starve the parasite, but it can result in depletion of tryptophan in the brain of the host. IDO and TDO degrade tryptophan to N-formylkynurenine and administration of L-kynurenine is capable of inducing depressive-like behaviour in mice [21]. *T. gondii* infection has been demonstrated to increase the levels of kynurenic acid (KYNA) in the brains of infected mice and KYNA has also been demonstrated to be increased in the brain of schizophrenic persons [13]. Low levels of tryptophan and serotonin in the brain were already associated to depression.

EPIDEMIOLOGY

Serologic prevalence data indicate that toxoplasmosis is one of the most common infections of humans throughout the world, and prevalence increases with age [13]. Due to environmental factors impacting the survival of the oocysts, infection is more common in warm climates and at lower altitudes than in cold climates and mountainous regions. Variations in mode of exposure also lead to variations in prevalence. Analysis of National Health and Nutrition Examination and Survey (NHANES) data showed *T. Gondi* seroprevalence had declined in United State-born persons 12–49 years old from 14.1% in 1988–1994 to 9.0% in 1999–2004 [23]. The incidence of congenital toxoplasmosis depends upon the proportion of women entering pregnancy without prior immunity and the rate of exposure to *Toxoplasma* during pregnancy. Estimates of congenital infection in the United States have ranged from 1 in 3000 to 1 in 10 000 live births. In 2014, 42 confirmed congenital toxoplasmosis cases were reported by 20 European Union/EEA countries. This represents a fivefold decrease compared with 2013, which is mainly due to missing data from France [35]. Excluding the French congenital toxoplasmosis data, the number of cases reported in 2014 is comparable to the annual number of cases reported between 2010 and 2014, i.e. an average of 34 cases/year. Two countries reported the majority of cases in 2014, namely Poland (48%) and the United Kingdom (26%) [34]. In India, a prevalence rate of 22.4% (8.8-37.3%) has been reported with an overall IgM positivity of 1.43% [33]. It is estimated that approximately between 56,737 and 176,882 children per year are born in India with a possible risk of congenital toxoplasmosis [18]. The diagnosis of congenital toxoplasmosis can be made by serological methods which are most commonly used. The other methods are parasite isolation by culture and molecular methods. Toxoplasmosis is treatable and transplacental transmission can be prevented by spiramycin, which concentrates in the placenta. However, if infection has done any damage to the fetus or the parasite has passed the placenta, spiramycin cannot reverse the

damage. Prevention remains the best remedy []24. In Morocco the seroprevalence of *T. gondi* in pregnant women ranged between 36.7% and 62.1%, between 2007 and 2017 [31]. As a novel diagnostic tool, the chemiluminescent microparticle immunoassay (CMIA) was used for *T. gondii* antibodies detection among pregnant women in Fes city [17]. Among the risk factors, age was the most commonly reported factor in these studies and the overall conclusion is that the prevalence of *Toxoplasma* infection increases with age [21, 16]. Infection rates also varied according to the locality; reaching 50.6% in Rabat which is higher than 43.3% in Nador (North East), 42.6% in Tetouan (North) and 36.7% in Kenitra (North West) [31]. The authors attributed this difference to the temperate climate of Rabat city, which maintains the biological cycle of *T. gondii* (rapid and complete sporulation). Regular contact with the land (soil, gardening and agricultural activities) was retained as a major risk for *T. gondii* infection in Rabat city [31]. In one study conducted in Rabat and concerning pregnant women, school level and knowledge of toxoplasmosis modes transmission were found to be risk factors ($p < 0.01$), while the consumption of raw meat, contact with cats, and level of hygiene were not significant. Results of toxoplasmosis epidemiological surveys in animals and humans in South-West, North-West, North-East and North-Central Zones of Nigeria have been reported with greater impact on the health of pregnant women and HIV-infected individuals [20, 36]. Meanwhile, studies in states within the South-South and South-East Zones are relatively scanty or non-existent. Overall, the seroprevalence of human toxoplasmosis in Nigeria is estimated at 32% with the following reports for North-West (32%), North-East (22%), North-Central (24%) and South-West (37%) [8]. Information on the genetic diversity of isolates of *T. gondii* in humans and animals including the role of the environment in transmission and maintenance of the disease are highly needed.

DIAGNOSIS

Principles and methods used for the diagnosis of congenital toxoplasmosis: Diagnosis of Congenital Toxoplasmosis in the fetus during gestation; the presence of the parasite in amniotic fluid (DNA amplification, microscopy, or isolation of the organism) and/or fetal tissues (DNA amplification, antigen staining, microscopy, or isolation of the organism is diagnostic of Congenital Toxoplasmosis) [30]. The most commonly used and accepted laboratory method for the diagnosis of Congenital Toxoplasmosis during gestation is the use of PCR in amniotic fluid, and a positive test result is diagnostic of Congenital Toxoplasmosis [5, 7]. In the postnatal period, the gold standard to establish a diagnosis of Congenital Toxoplasmosis is the persistence of *Toxoplasma* IgG by 12 months of age. Conversely, the standard to rule out the diagnosis is the decrease of *Toxoplasma* IgG titers until its disappearance at ≤12 months of age in the absence of treatment [30]. Some me of the diagnostic methods employed for Taxoplasma gondi include the following: In 1948, Sabin and Feldman develop a serological assay called the dye test for conducting serological diagnosis of taxoplasmosis [7]. Immunohistochemical staining of parasites with fluorescent or other types of labelled *T. gondii* antisera can aid in diagnosis. In women it is based on serology by detecting IgG and IgM antibodies [1]. The bradyzoites Tissue cysts are usually spherical, lack septa, and the cyst wall can be stained with a periodic acid Schiff (PAS) staining technique. Diagnosis can be made by finding *T. gondii* in host eissue removed by biopsy or at necropsy [26]. A rapid diagnosis may be made by microscopic examination of impression smears of lesions. *T. gondii* can be diagnosed by means of serology, culture based methods using RPMI 1640 medium, mouse assay and PCR. Ideally, it should be established first whether the mother is immunocompromised or immunocompetent and whether she belongs to one of the following three groups: (i) never infected with *Toxoplasma* and confirmed to remain seronegative 1 month after birth (no risk for Congenital taxoplasmosis), (ii) chronically

infected—mother acquired her infection prior to gestation (no risk for Congenital taxoplasmosis unless she is immunocompromised), or (iii) acutely infected—mother acquired her infection during gestation or within 3 months prior to gestation (at risk for Congenital taxoplasmosis) [33]. For group 3, it is important to establish (or estimate) the month during gestation at which maternal infection was acquired and whether the mother received anti-*Toxoplasma* treatment (and if so, which drugs) since the sensitivity and interpretation of laboratory tests can be largely affected by these variables [9]. For instance, the sensitivity of serological test results in newborns is lower in those born to mothers who acquired their infection early in gestation and/or received anti-toxoplasmosis treatment during gestation than it is in those born to mothers who acquired their infection late in gestation and/or did not receive treatment [9]. Information on the presence of clinical signs in the fetus and newborn may also be helpful in the interpretation and recommendations, for instance, regarding intervals for follow-up testing after birth or indication for additional tests e.g., *Toxoplasma* PCR.

PREVENTION AND CONTROL

The fetus can be prevented from infection by given an infected mother spiramycin (a mycrolide antibiotic that does not cross the placenta [20]. Reduce Risk from Food by cooking food to safe temperatures (74^{O}C). A food thermometer should be used to measure the internal temperature of cooked meat. Peel or wash fruits and vegetables thoroughly before eating.Wash cutting boards, dishes, counters, utensils, and hands with soapy water after contact with raw meat, poultry, seafood, or unwashed fruits or vegetables [2]. People with AIDS who have recovered from acute toxoplasmosis are at high risk of future episodes, because the dormant parasite may be reactivated. To prevent this, an AIDS patient must begin a regimen of preventive drugs and continue to take the medications as long as his or her immune system remains weakened. Cats

are only infectious for a few weeks after ingesting the parasites and kittens are more likely to pass on the infection than older cats [2]. Suggestions on reducing the risk of infection in your cat include: Keep your cat indoors whenever possible [3]. Don't allow the cat to hunt and eat birds or other wildlife. Feed your cat canned or dry foods, instead of raw meat (including kangaroo meat). Oocysts in cat feces take at least a day to sporulate and become infectious after they are shed, so disposing of cat litter daily greatly reduces the chances of infectious oocysts being present in litter [13]. As infectious oocysts from cat feces can spread and survive in the environment for months, humans should wear gloves when gardening or working with soil, and should wash their hands promptly after disposing of cat litter [32]. The same precautions apply to outdoor sandboxes, which should be covered when not in use. Furthermore, pregnant or immunocompromised people are at higher risk of becoming infected or transmitting the parasite to their fetus. Because of this, they should not change or handle cat litter boxes. Ideally, cats should be kept indoors and fed only food that has low to no risk of carrying oocysts, such as commercial cat food or well-cooked table food.

CONCLUSION

Congenital toxoplasmosis is a severe disease that can be treated and prevented [10]. Are there better treatment options available, both for prevention of transmission from an infected pregnant woman to her developing fetus and for the treatment of congenitally infected children? Many of the plants extract have shown activity against related parasites? Is it time to seriously consider universal screening of pregnant women in order to diagnose those who are infected? Do we understand the epidemiology well enough to institute such screening? Can more be done to improve food safety? Perhaps now the time has really come for us to address the issue of congenital toxoplasmosis once and for all. Having better impact data would make it easier to

convince decision makers to invest in toxoplasmosis control and prevention. In addition, more in-depth epidemiological studies are needed to inform the design of regional strategies and to guide implementation of control programs involving both the medical and veterinary sectors.

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