



## Relevant aspects of human toxoplasmosis

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### Abstract

Considering the great importance that the infection by *Toxoplasma gondii* has in public health, the aim of this article was to demonstrate some aspects about this disease in human being. This parasite can cause several behavioral changes and many cases of reactivation of this disease are associated with Acquired Immunodeficiency Syndrome – AIDS. Major cases of human infections by *T. gondii* are asymptomatic and the main clinical manifestation in the acute phase of this zoonosis is lymphadenopathy, usually in the cervical area. There may also be fever, night sweats, myalgia, maculopapular rash lymphocytic atypia and chorioretinitis. The congenital and/or acquired chronic latent cerebral toxoplasmosis play an important role in the development of some types of neurodegeneration, like Alzheimer disease and Down Syndrome. Humans and animals should not consume raw or undercooked meat, unpasteurized or not boiled dairy products, water without being treated and poorly washed fruits and vegetables. Educational programs focused on reducing *T. gondii* environmental contamination are essential for the congenital infection control. Due to the severity of this kind of infection and its sequel, it is critical that those responsible for the community's health establish prevention programs to avoid such a situation, obtaining results in the medium and long term, and particularly preserving the involved population's welfare. A lack or incomplete prenatal treatment was identified as an important risk factor for congenital toxoplasmosis, reinforcing the need of improvement of prenatal care. In this study was demonstrated the importance of implementing prevention programs to guide pregnant women to prevent the infection. Preventive measures like information and health education; screening of pregnant women and infants; limiting harm from risk behaviour; treatment of risk cases and vaccination are recommended. Serum monitoring throughout pregnancy, so as to detect cases of maternal seroconversion allowing for early maternal treatment is also basic. Some countries have adopted control programs of human toxoplasmosis, however, this issue should be of world attention, considering its relevant aspects of public health, requiring the establishment of community education campaigns and monitoring of pregnant women in the pre and neonatal, especially in a preventive action to reduce the pathogenic effects of this disease.

**Keywords:** *Toxoplasma gondii*, public health, parasitic control, congenital infection

### Introduction

*Toxoplasma gondii* has great importance in public health. Women in initial stages of gestation may undergo miscarriage, premature birth, neonatal death and even the classical Sabin's Triad, characterized by retinochoroiditis, cerebral calcifications, hydrocephaly or microcephaly [1,2].

This parasite can cause behavioral changes [3] and during pregnancy cases of antenatal depression and anxiety have been related [4-7].

Many cases of reactivation of this disease are associated with Acquired Immunodeficiency Syndrome - AIDS, including pregnant women [8], especially with brain abscess manifestation [9-11].

Educational programs focused on reducing *T. gondii* environ-

mental contamination are essential for the congenital infection control [7,12,13].

### Human toxoplasmosis

Major cases of human infections by *T. gondii* are asymptomatic and the main clinical manifestation in the acute phase of this zoonosis is lymphadenopathy, usually in the cervical area. There may also be fever, night sweats, myalgia, maculopapular rash lymphocytic atypia [14] and also chorioretinitis [11].

In primary infection of immunocompetent patients, microgranulomas with no necrosis of giant cells, in cases of cervical lymphadenopathy, can be observed.

In hosts with immune deficiency, neonates and the ones infected by the protozoan during intrauterine life, the findings

may include necrotizing meningoencephalitis and systemic aggravation. Lymphadenopathy-type Piringger Kuchinka and encephalitis were particularly evident [15].

The continued *T. gondii* tachyzoites proliferation and tissue destruction can occur in fetal brain even when there is a marked maternal immune response including maternal IgG [16].

Patients with autism spectrum disorders (ASD) and with chronic toxoplasmosis have persistent neuroinflammation, hypercytokinemia with hypermetabolism associated with enhanced lipid peroxidation, and extreme changes in the weight resulting in obesity [17].

The congenital and/or acquired chronic latent cerebral toxoplasmosis play an important role in the development of some types of neurodegeneration, like Alzheimer disease and Down Syndrome [18].

The intermediate hosts, humans and animals, can acquire the disease by eating raw or undercooked meat, infected with tissue cysts, as well by the consumption of raw vegetables and water contaminated with oocysts [19]. Tachyzoites of *T. gondii* can be acquired by consuming unpasteurized milk, eggs, blood transfusion, semen, organ transplantation, laboratory accidents with biological material and by transplacental via [14,19-24].

In its cycle, the protozoan shows two evolutionary forms in the intermediate host: tachyzoites, structures of rapid multiplication present in organic fluids in the acute phase, and bradyzoites, confined in tissue cysts, especially in the central nervous system and muscles, in the chronic infection. Oocysts, the final product of sexual reproduction, are formed only in the digestive tract of felids, definitive hosts that shed the oocysts with their feces, where by means of sporogony they become infective and extremely resistant to environmental conditions [19,25-27].

The cats are probably the main sources of environmental contamination, because, when infected, they release large quantities of oocysts, allowing the continuity of the parasite biological cycle [23]. Our research group noticed that *T. gondii* oocysts are widely distributed on the soil of elementary public schools in our region, likely constituting the main contamination source for these children [12]. It was observed that cat owners in a cohort of middle-aged UK women do not have an increased risk of brain cancer, when compared with non-cat owners [28].

Cases of enhanced maternal-fetal transmission of *T. gondii* infection of HIV-infected women chronically infected were described, which may have important public health consequences, considering the increasing frequency of HIV-infection observed among human being around the world [8].

The prevalence of 3599 samples of the National Health Survey 2000 (NHS-2000) and 2916 of the National Health and Nutrition Survey 2006 (NHNS-2006) serum banks, obtained from 1-98 year old subjects of both genders and all states of Mexico was studied. Anti-*T. gondii* IgG antibodies were

determined by ELISA and confirmed by western blot. National crude prevalence was 60.1% and 62.6% for NHS-2000 and NHNS-2006, respectively [29].

All soldiers before being deployed in jungle operations should be tested for *T. gondii* antibodies and to receive adequate health information about the routine use of personnel filters to purify their water for consumption [13].

The tachyzoite, reaches the fetus by transplacental via, causing different levels of damage severity, depending on the virulence and/or lineage, on the strain of the mother's immune response capacity and on the gestational period that the woman presents, that can result, even, in fetal death or severe clinical manifestations. Toxoplasmosis may manifest months or even years later in children born with this parasitosis and in these cases the most common manifestations are retinocorioidite, cerebral calcifications, neuropathies and microcephaly [4].

Studies demonstrated that chorioretinitis affected 18.9% of children suffering from congenital toxoplasmosis despite antenatal and neonatal screening associated with early treatment. Long-standing follow-up is needed because the first lesion can occur as late as 12 years after birth. Late lesions were less often macular but nevertheless caused sometimes visual impairment [6].

The demonstration of the occurrence of human toxoplasmosis associated to the milk ingestion from proven infected goats, is particularly important in rural and peri-urban areas where these animals are raised for the purpose of production of milk for domestic consumption [30].

Contamination of municipal water reservoirs with a significant amount of *T. gondii* oocysts can lead to epidemics, as recorded in Canada, in 1995, or trigger outbreaks like the one reported in 2001, in Santa Isabel do Ivaí, Paraná State, Brazil [31,32,33].

### Control of human toxoplasmosis

Humans and animals should not consume raw or undercooked meat, unpasteurized or not boiled dairy products, water without being treated and poorly washed fruits and vegetables [34]. Meat products from ovine and swine are more contaminated with this parasite cysts, and these are rarely found in bovine [9,14].

Monitoring of *Toxoplasma* infection in animals destined for human consumption is a great challenge for human toxoplasmosis prevention. In Spain, some people eat horse meat and it was observed that many horses from various regions of the country are serologically positive for toxoplasmosis [35]. It was showed the impossibility of any serological test asserting the absence of *T. gondii* in meat and guarantee that undercooked lamb can be consumed without risk for people [36,37].

As daily routine, the cleaning of catteries, with fecal material removal is indicated, since, in dependence on the environmental conditions, the *T. gondii* oocysts eliminated

by cats require at least 24 hours to sporulate and become infectious. It is also important to cover or encircle sand tanks for children recreation, especially when they are not in use, to prevent the cats access [12,33].

Dishes and utensils should be washed with hot water after contact with unwashed fruits, vegetables, unpasteurized milk and seafood. Pregnant women and immunosuppressed individuals need to wear gloves to get contact with the soil or dumps, avoiding possible touches in cat feces [34].

A lack or incomplete prenatal treatment was identified as an important risk factor for congenital toxoplasmosis, reinforcing the need of improvement of prenatal care in Brazil [5]. A 2009 survey in the United States showed that 87.7% counsel patients about how to prevent toxoplasmosis [38].

In our studies, were interviewed 85 teachers about toxoplasmosis and 67.06% (57/85) did not know about this issue. Interviews were made with 30 teachers of 18 educators from local elementary schools in Brazil and 28.33% did not know anything about the topic [32]. One hundred and thirty four elderly people, from the institutions, were interviewed and 86.57% (116/134) were ignorant of the dissemination ways [39]. There is a need of implanting programs of control against human toxoplasmosis [39-43].

It's important to reinforce the importance of sanitation control in industrial restaurants and also demonstrate the need for improvement in quality control regarding vegetables at risk for *T. gondii* oocyst contamination [44].

Strategies to work on muscle fluids offers a great potential for toxoplasmosis studies on farm animals, especially for large scale control studies. We cannot yet offer any serological test asserting the absence of *Toxoplasma* in meat and offering the guarantee that undercooked lamb can be consumed without posing an unacceptable risk for people at risk and freezing the meat remains necessary [36,37].

Prenatal screening is performed in Austria, France and Slovenia and neonatal screening in the New England states of the USA, parts of Brazil, Denmark and Ireland, but on-demand examination for *T. gondii* antibodies are widely practiced in many European countries [45].

Since 1975, in Austria, serological monitoring of pregnant negative women until the third month of pregnancy it is mandatory, and for suspected cases, treatment is performed until four months of pregnancy with spiramycin and piimetamina associated with sulfadiazine after three months and three weeks [45,46].

In France, since 1978, *T. gondii* tests were established in seronegative women. However, control measures are not standardized in this country, and so there are divergence between treatment protocols and diagnostic interpretation of infection [47].

In some American states, only serological monitoring of newborns for *Toxoplasma* IgM has been preconized, without prenatal intervention [48]. The Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults

and Adolescents, produced by Centers for Disease Control and Prevention, National Institutes of Health, and HIV Medicine Association of the Infectious Diseases Society of America, contains detailed recommendation [49,50].

Considering the high prevalence of HIV infection in the Kyrgyz Republic, personalized medical orientation as well as treatment and prevention of *T. gondii* infection are recommended, with special attention to health education for those with lower economic and social status and less access to information [51].

In Spain, due to the low incidence of toxoplasmosis in pregnant women, there is no proper disease control recommendation from health authorities, however, detailed control program has been preconized by the Spanish Society of Pediatric Infectious Diseases for the diagnosis and treatment of congenital toxoplasmosis [52].

Early detection with repeated serological examination and the treatment of pregnant women can reduce the risk of infection by *T. gondii* as observed in India [53].

Pregnant women in Al Hasas, Saudi Arabia, are substantially vulnerable to toxoplasmosis infection because have no sufficient knowledge for primary prevention of congenital toxoplasmosis [54].

The most commonly therapy is the combination of pyrimethamine and sulfadiazine and folinic acid [55]. In Germany, spiramycin is given until the 16th week of pregnancy, followed by at least 4 weeks of combination therapy with pyrimethamine, sulfadiazine, and folinic acid independent of the infection stage of the fetus and this treatment program was efficient in minimize transplacental parasitic transmission [56].

As future perspectives, vaccines development studies against *T. gondii* have demonstrated that heterologous DNA priming and recombinant adenovirus boost strategy may provide protective immunity against *T. gondii* infection [57] and multiantigenic DNA antigen pGRA7-ROP1 was more effective in stimulating host protective immune responses than separately injected single antigens, and that IL-12 serves as a good DNA adjuvant [58].

It was possible to show the importance of implementing prevention programs to guide pregnant women to prevent the infection. Preventive measures like information and health education; screening of pregnant women and infants; limiting harm from risk behaviour; treatment of risk cases and vaccination are recommended [38]. Serum monitoring throughout pregnancy, so as detect cases of maternal seroconversion allowing for early maternal treatment is also basic [7,10].

## Conclusions

Some countries have adopted control programs of human toxoplasmosis, however, this issue should be of world attention, considering its relevant aspects of public health, requiring the establishment of community education campaigns and

monitoring of pregnant women in the pre and neonatal, especially in a preventive action to reduce the pathogenic effects of this disease.

### List of abbreviations

AIDS: Acquired Immunodeficiency Syndrome

*T. gondii*: *Toxoplasma gondii*

HIV: Human Immunodeficiency virus

### Competing interests

The authors declare that they have no competing interests.

### Authors' contributions

Authors' contributions	KDSB	ALBG	ALV	LVSM	JCP	JAS	JFG	AJC
Research concept and design	√	√	√	--	--	--	--	--
Collection and/or assembly of data	√	√	√	√	√	√	√	√
Data analysis and interpretation	√	√	√	√	√	√	√	√
Writing the article	√	√	√	√	√	√	√	√
Critical revision of the article	√	√	√	--	--	--	--	--
Final approval of article	--	--	--	--	--	--	--	--
Statistical analysis	--	--	--	--	--	--	--	--

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