ENVIRONMENTAL EXPOSURE OF PREGNANT WOMEN TO INFECTION WITH *TOXOPLASMA GONDII* – STATE OF THE ART

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**Abstract:** Infection with *T. gondii* is particularly dangerous for pregnant women as it may lead to the transplacental passage of the parasite. Currently, congenital toxoplasmosis is the second most frequent intrauterine infection. The risk of transmission of *T. gondii* to the foetus varies throughout the world and ranges from 0.6–1.7/1,000 of pregnant women. The consequences of congenital toxoplasmosis are multifarious. On the basis of current literature review, the authors discuss the epidemiological and clinical aspects of toxoplasmosis in pregnant women, the influence of climatic and environmental factors that may lead to an increase in *T. gondii* infections in humans, particularly in pregnant women, and the principles of prophylactics against *T. gondii* infections in those women.

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**INTRODUCTION**

Infection with *T. gondii* is widespread all over the world in humans and in animals (rats, dogs, cats, cattle, sheep, hens, pigs, and others). It is estimated that 1/3 of the world population is infected with toxoplasmosis [52]. Most infections are latent (symptomless).

In the human population the frequency of infection varies from 5–90%, according to climate, nutrition style, and sanitary-epidemiological conditions. In Europe, infection with this protozoon is very common. It is accepted that in Poland ca. 60% of the adult population is seropositive. It is also estimated that ca. 70% of cats and more than 10% of pigs are infected, being a permanent reservoir of the pathogen [45]. As the natural reservoir of the pathogen is exceptionally large, it will probably never be effectively eliminated.

Invasion of *T. gondii* usually occurs by ingestion, especially by eating meat containing the viable tissue cysts of the parasite, or food contaminated with the oocysts excreted by a cat – the definite host of the parasite. Iatrogenic infection, e.g. via the blood or transplant tissues, etc., and laboratory infection is also possible. The parasite may also cause vertical infection, penetrating through the placenta into the foetus from the circulation of the primarily infected mother. It was believed until recently that the main source of infection is faeces of the felids – both domestic and wild. Later, a major role in spreading the infection was ascribed to the meat of slaughtered animals, especially to pork. This view has been revised recently as contamination of the environment with the oocysts is becoming increasingly frequent. They can survive in the environment even for many years [16]. In recent years, contamination of waters have also been detected, and consequently – a high prevalence of the infection in animals living in seas and oceans [8, 16, 20]. Contaminated water may also become a source of infection for humans [12]. Infections in humans caused by the oocysts are more serious than those produced by the tissue cysts [16].

Infection with *T. gondii* is particularly dangerous for pregnant women as it may lead to the transplacental passage of the parasite. The consequences of congenital toxoplasmosis are multifarious. *T. gondii* development in a foetus may result in its intrauterine death. Other consequences
that should be emphasized are: hydrocephaly, microcephaly and intracerebral calcifications. In less serious cases, toxoplasmosis manifests itself in the form of mild damage, such as retinitis or chorioiditis. Thus toxoplasmosis is a disease with a varying course and may reveal itself even many years after primary infection [23, 26].

The primary infection in pregnant women is usually symptomless, and the few symptomatic cases are associated with lymphadenopathy, usually in the nodes of the head and neck. In most cases the only infection marker is seroconversion – from negative to positive. The latent infection may be reactivated with a decrease in immunity. Cases of toxoplasmosis reactivation were observed in pregnant women infected with HIV, even when their immunity was relatively slightly impaired by the virus; the consequence of reactivation was the transplacental passage of the parasite and congenital toxoplasmosis in the child [5]. However, even in women with normal immunity, a past toxoplasmosis and the developed immunity do not fully protect against an infection risk in the child, caused either by reactivation of the infection or by superinvasion during pregnancy with a genotypically different strain of the parasite [48]. However, latent toxoplasmosis in women is considered beneficial, as it usually protects pregnant women against acute toxoplasmosis, and their children from the consequences of congenital toxoplasmosis.

Currently, congenital toxoplasmosis is the second most frequent intrauterine infection. The development of possible consequences depends on many factors, among others, on the degree of parasitemia in the mother, the placenta maturity, foetal age and immunological maturity [40]. The risk of transmission of T. gondii to the foetus varies throughout the world and ranges from 0.6–1.7/1,000 of pregnant women [11, 13, 41, 46]. The risk of foetus infection increases along with the duration of pregnancy. In 90% of cases, infection occurs in the last weeks of pregnancy. The risk of developing congenital toxoplasmosis in the foetus decreases along with the pregnancy duration, which suggests that the degree of maturity of the foetus vary significantly affects the onset of possible consequences. This is probably related to the immunity change in pregnant women that may cause immunological suppression. This explains raised sensitivity to T. gondii infection in the third trimester [10, 28]. A significant correlation was found between toxoplasmosis cases and the number of pregnancies in a woman. In multiparae the risk of infection was twice as higher than in nulliparae, although all the infected women had contact with cats, dogs, fleas, cockroaches, rats and/ or soil [4].

The clinical course of the disease in a child with congenital toxoplasmosis is not influenced by whether the mothers showed any clinical symptoms of the disease, or it was entirely symptomless [42]. Until recently, it was believed that antipROTOzoan therapy started during pregnancy largely reduces the percentage of children born with congenital toxoplasmosis. The approach to this question has lately been changing. Cases of congenital infection were found in the newborn of mothers with diagnosed and treated toxoplasmosis in pregnancy. There are authors who argue that the only effective method of reducing the number of toxoplasmosis infections is, along with developing fast and reliable diagnostic tests both for the mother and for the child, to encourage pregnant women to follow hygienic habits and dietary guidelines [40, 44].

Research by Flegr et al. [24, 25] provided a lot of data on physical and mental changes produces by chronic toxoplasmosis in humans, e.g. body mass reduction, a decrease in the intelligence quotient, a lack of concentration, or schizophrenia. A permanent, latent presence of toxoplasmosis in the host organism leads, as is increasingly often found, to another unexpected consequence. It was discovered that T. gondii affects the proportions of sexes in the newborn, causing an increase in the ratio of males to females directly proportional to the titre of anti-Toxoplasma antibodies in the mother [31].

All researchers stress the necessity of serological tests in children in their first year of life, even if they do not show any indicators of the infection. According to Willson, in ca. 85% of the newborns with congenital toxoplasmosis, no clinical symptoms are observed after birth [55].

The prevalence of congenital toxoplasmosis in Europe varies largely and depends on numerous factors, among others, on the socioeconomic situation. A high socioeconomic level makes it possible to introduce countermeasures on a large scale. The countries where preventive activities are systematized include: Austria, Great Britain, and Denmark, where the percentage of toxoplasmosis cases is very low [3, 27, 35]. The incidence of T. gondii infection in pregnant women ranges from 10% in Great Britain to 55% in France and Greece, in many countries, however, a decrease in the number of cases was observed in the last three decades [9]. A drop in the incidence of T. gondii infection does not translate directly into a decreased number of cases during pregnancy. However, a reduction in the incidence in pregnancy would probably lead to a lower number of infections in children.

In Poland, 50% of women at reproductive age acquire T. gondii infection. It is estimated that acute infection during pregnancy occurs in 1–4 cases per 1,000 pregnant women [42]. In the Polish population, women most often give birth between 20–35 year of age. In this age group, because of a high percentage of women without immunity, the risk of infection for the pregnant woman and of a negative influence on the foetus is relatively high.

According to the latest studies, differences in T. gondii prevalence depend, among others, on the climate, cultural differences concerning consumption of raw meat, and an increase in the consumption of the meat of farm animals and frozen meat.

In the last two decades, studies on T. gondii infection risk indicate a significant evolution of views concerning the importance of individual factors in causing the infection. There is still no conclusive proof concerning which
environmental factors should be considered as posing the greatest risk to pregnant women. This fact induced the authors of this review to present the state of the art views on the environmental factors influencing the prevalence of *T. gondii* infection in pregnant women and to indicate the possibilities to counteract infection by primary prevention.

**CLIMATIC FACTORS INFLUENCING INFECTION WITH *T. GONDII***

It is predicted that the global climate warming will produce an increase in *T. gondii* infection in humans in some regions of North-West Europe. The increase caused by the environmental factors will be concurrent with anthropogenic factors, such as urbanization and re-emergence of the parasite as a result of changes in systems of domestic animals husbandry [39].

The climate warming caused by human activity changes the ecological equilibrium, and consequently the incidence of parasitic diseases in their definitive and intermediate hosts, the development and transmission of those diseases [43].

Changes concerning *T. gondii* may be described as follows: 1) virulence of the pathogen will depend on the intensity of environmental changes; 2) due to an increase in precipitation, the excreted oocysts will much easier spread in the environment; 3) climate changes will affect the ecology of definitive or intermediate hosts [39].

Environmental conditions are essential for the survivability of the oocysts. *T. gondii* survivability is high in moist tropical areas and low in dry and hot ones. It is low also in the arctic environment [52]. The prevalence of *T. gondii* oocysts in an environment depends, to a large degree, on the conditions of sporulation. The oocysts mature for 1–5 days and this process requires an appropriate temperature and humidity [37].

Climate changes lead to an increase in temperature, dry summers and wet winters. As the average winter temperature grows, the possibility of effective sporulation of the oocysts also rises. This increase may affect the prevalence of *T. gondii* in intermediate and definitive hosts [39]. A 10-year study of domestic cats in France showed that the emergence of anti-*T. gondii* antibodies depended on the interaction between air temperature and rains. The risk of infection in cats increases when the weather is warm and wet. The authors suggest that this is due to a prolonged survivability of the oocysts in the wet environment [1]. Also, in the USA, the level of antibodies in cats was lower in the windiest regions of the country [53]. Referring the problem to the incidence of infection in humans, Tenter *et al.* show that seropositivity in women of reproductive age is higher in countries with, wet climate [52].

Environmental changes may also lead to transformations in the life ecology of the parasite intermediate hosts and transmitters. During warm and humid winters, a greater number of insects – possible mediators of the infection transmission – are observed. Flies may carry the oocysts on their exoskeleton, contributing to infection in birds and mammals [29]. Rodents may also be hosts for *T. gondii* and play a significant role in infecting animals, particularly pigs [33, 34].

For all the above reasons, the risk of transmitting the infection to cats or other animals (accidental hosts) increases, and consequently may lead to a greater prevalence of the pathogens in the environment and to a greater number of infection cases in humans.

It is interesting that acute toxoplasmosis infection in pregnant women have been found more frequently in winter than in summer. Cases of acute toxoplasmosis in the winter-spring season were significantly more frequent than in the summer-autumn one. This phenomenon should be taken into consideration when designing preventive measures, especially for pregnant women [26].

**ENVIRONMENTAL FACTORS CONducIvE TO *T. GONDII* INFECTION IN PREGNANT WOMEN***

The most important recognized factors influencing the risk of *T. gondii* infection are: having a dog or a cat, doing household work, lower education level, hygienic habits, eating raw vegetables, and work in contact with soil [38].

Infection of humans with the parasite is possible after ingesting the tissue cysts in meat, or the oocysts shed by cats (definitive hosts) contaminating the environment [33]. It is known that lesser environmental exposure to the infection risk factors leads to a decrease in toxoplasmosis cases during pregnancy and reduces the risk of congenital toxoplasmosis.

In scientific reports there are many discrepancies concerning the mentioned factors. At first, contact with cats and bad hygienic habits related to nutrition were considered the greatest hazards.

In a study conducted in six European cities, published in 2000, analysing the risk factors of *T. gondii* infection, no statistically significant relation was found between acquiring infection during pregnancy and contact with cats (adult or young), their diet and hunting habits, or cleaning litter trays [9]. According to the study, work with farm animals or with their meat caused a greater risk of infection. Travelling outside Europe and drinking unoiled or untreated water also increased the risk of infection, but the very fact of living on a farm did not affect it [9].

It was found that the risk of infection rises in women who taste meat when preparing meals or eat raw or undercooked beef, lamb or other meats, but not pork. A significant increase in the risk was detected in people eating undercooked veal, beef, salami, dried poultry or raw sausage. Drinking non-pasteurised milk and consuming milk products also concurs with more frequent infections [9, 17, 18]. Cook *et al.* did not find differences in risk factors according to the country or region (Scandinavian countries, central
Europe and Italy). However, eating lamb or other meat was a more important risk factor in northern and central Europe than in Italy. In this country, 6–7% of infections were related to contact with soil, while in other countries it was 16–17% [9].

Changes in diet and nutritional habits can be observed: there is a shift from beef consumption to eating more pork, lamb and poultry, and an increase in consumption of giblets and processed meat products [22]. These tendencies may cause greater exposure to T. gondii in pork and lamb, leading to a greater infection risk in comparison to beef and poultry. Free-range animals are exposed to a greater environmental risk of T. gondii infection than farm animals [2].

Acute T. gondii infection is associated with different kinds of meat. In Norwegian studies, uncooked lamb and pork, but not beef, are considered as infection risk factors [32], while in France risk factors were beef and lamb, but not pork [6]. In both studies, however, eating smoked pork was a significant risk factor [6, 7].

Lamb, goat, venison, pork are generally more recognized as a source of infection than beef and poultry that rarely happen to be contaminated with the viable cysts [15, 49]. The risk of infection for humans also depends on the age of an animal, time an animal staying outside the farm [15], cleanliness on the farm [15, 49] and preparation for consumption of specific tissues such as heart or tongue that are more at risk of containing the cysts than skeletal muscles [14, 19]. Most pork is produced in a closed farming system and many products are frozen. As freezing kills the cysts, the risk of infection from ingesting raw or undercooked pork is lower. However, pork used in manufacturing salami contains many organs other than skeletal muscles and may be supplemented with meat from older animals kept outside the farm [9].

The connection between the infection and tasting meat dishes during cooking, as well as consuming non-pasteurised milk and its products, was demonstrated. T. gondii tachyzoites were isolated from cow milk and udders [19]. The infection may be caused by contamination due to dirty equipment used in milk production. T. gondii was also isolated from hen eggs, but they were not considered as an important source of infection via the oral route [47].

Contact with soil, vegetables or fruit contaminated with the oocysts is a confirmed risk factor of infection in pregnancy [9, 17, 18, 33, 34]. A significant role of the oocysts in the epidemiology of toxoplasmosis in humans is corroborated by the data on the high seroprevalence in vegetarians, who are not exposed to the tissue cysts, but their exposure to the oocysts on inadequately washed vegetables and fruit is greater than in the remaining population [30].

Cats shed the oocysts (ca. 10 million a day) for 2 weeks after the infection [47]. The oocysts become infectious after 1–5 days from shedding, contaminate water, and may survive for over a year. In this context, contact with contaminated soil or water is a more important infection risk factor than contact with cats [32]. The oocysts may be transmitted by insects dwelling on faeces (flies, cockroaches) and subsequently contaminating food and water, or by birds and rodents that infect cats [4, 51]. Drinking contaminated water may also cause the infection [50].

In areas with a high prevalence of T. gondii and large numbers of dogs and cats, immunocompromised and pregnant persons should be warned against the possibility of acquiring the infection also from dogs. Dogs may become mechanical vectors as they roll in noxious substances and eat faeces [21].

Studies conducted in Australia in women with seroconversion did not corroborate the influence of any of the known risk factors [54]. The results of Australian studies, as well as research by other authors on the differences in T. gondii infection risk factors, confirm the need of further investigation.

**PRIMARY PROPHYLACTICS OF T. GONDII INFECTION IN PREGNANT WOMEN**

In the extensive study of 2000, women in European cities indicated contact with cats, eating raw meat and eating raw and unwashed vegetables and fruit as sources of the infection [9].

Research conducted in Poland showed low awareness of the risk of infection with toxoplasmosis. It was also observed that the awareness of a possible risk does not necessarily lead to behaviour according to the guidelines [36].

It is known that effective prevention of congenital toxoplasmosis depends on avoiding infection in pregnancy. There are many health centres and obstetric departments, both in Poland and in the world, that do not adopt any policy of preventing or informing patients on the risk of toxoplasmosis infection. Therefore, the confirmed information on the possibility of the disease prevention should be systematized and used in a wide-ranging education in this area, especially in women at reproductive age. A health promotion strategy in this field should be based on making women at the reproductive age aware of the infection risk factors this should lead to a change in health behaviour.

Prevention should focus on three main infection sources:

1) **Meat:** Well-cooked meat, or meat frozen prior to preparation, should be eaten; raw food should not be prepared at the same place and with the same utensils as those used to handle raw meat. Finger-mouth contact should be avoided during raw meat handling. It is believed that avoidance of the infected meat reduces the risk of infection in pregnancy from 30–60%.

2) **Environment:** Vegetables and fruit should be well washed prior to consumption, including vegetables and fruit from the consumer’s own garden or orchard. Pregnant women should avoid contact with soil, work with farm animals, and drinking non-pasteurised milk.

3) **Domestic animals:** Domestic cats should be fed with canned food rather than with raw meat. Contact with any utensils that may have been contaminated with cat’s faeces
and cat’s litter should be strictly avoided. Hands should be washed after contact with soil, dogs, cats, and before meals.

Women should be informed about the correct way of handling a potentially infectious product or material (e.g., freeze meat, use protective gloves, improve the cleanliness in households). At preparing meat meals, cleaning cat’s litter trays, working in a field or garden, women should wear protective gloves. Cat’s litters should be disinfected daily with boiling water.

All the primary preventive measures concern mainly agricultural areas, veterinary practices, zoological shops and gastronomy. Secondary prevention by serological monitoring of seronegative pregnant women should be closely connected with detailed primary prevention.

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