Review Article

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The Zoonotic Aspect of *Toxoplasma Gondii* in Human and Animals : A Review

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Abstract

Toxoplasmosis is caused by the apicomplexan parasite *Toxoplasma gondii,* which may infect any nucleated cell in mammals. This parasite infects over two billion individuals worldwide, and while only a tiny fraction of infected persons may develop significant disease, the parasite's ubiquity makes it one of the highly dangerous zoonotic infections in the world. This disease can cause serious encephalitis in immunocompromised persons, miscarriage or congenital malformations in the new-borns if infected during pregnancy, and significant ocular illness even in immunocompetent people. The illness has a complicated aetiology, as it is caused by the ingestion of oocysts shed in the faeces of definitive feline hosts that pollute water. In this review we demonstrated the current insight into zoonotic aspect of toxoplasmosis in humans, and animals providing a complete discussion of the environmental mechanisms via which *T. gondii* oocysts, and tissue cysts might infect animals and humans, such as contaminated foods, water, animals' meat or soil. This review also included mode of transmission and preventative strategies outlining fundamental control measures for lowering the threat of oocyst direct contact, as well as chances for future collaboration and new studies possibilities targeting reducing oocysts load and tissue cyst-borne of toxoplasmosis in people, farm and wild animals. Conclusively, the infection occurs in both humans and animals, causes abortion in women and serious economic losses in animals. Transmitted to humans horzontally by injestion of food and water contaminated by oocysts, also meat of infected farm animals or vertically through placenta. Cats get infected through ingestion of intermediate host containing tissue cysts. Heating, salting, freezing and radiation are the main ways enforced to reduce tissue cysts burden in animals meat used for human consumption

Keywards: ***Toxoplasma gondii*, bradyzoite, control, oocyst, tissue cyst,**

الجانب المرضي المشترك لداء المقوسات في الانسان والحيوان: مقالة

الخلاصة

المسبب الرئيسي لداء المقوسات هو طفيلي (*Toxoplasma gondii*)، حيث يتكاثر الطفيلي في الخلايا ذات الانويه في الثدييات. ويصيب أكثر من ملياري شخص في حول العالم، وعلى الرغم من أن نسبة ضئيلة فقط من المصابين قد يظهرون علامات سريريه، فإن انتشار الطفيليات يجعل منها واحدة من أخطر الأمراض الحيوانية في العالم. إن داء المقوسات مرض ذو مظاهر متنوعة: فهو يمكن أن يسبب التهاباً دماغياً قاتلاً في الأشخاص ذوي المناعة الضئيلة، والإجهاض أو التشوهات الخلقية في المواليد الجدد إذا أصيبوا أثناء الحمل، ويصيب العين حتى في الأشخاص ذوي الكفاءة المناعية. وهذا المرض معقّد من حيث التوسّع، حيث ينتقل عن طريق ابتلاع أكياس البيض الموجودة في براز المضائف النهائية التي تلوّث المياه والاعشاب المحيطة. استعرض في هذا المقال الجانب المشترك لهذا المرض بين الانسان والحيوان، مع مناقشة كاملة للآليات البيئية التي يمكن من خلالها أن يصيب هذا الطفيلي، وكيسات الأنسجة الحيوانات والبشر، مثل الأطعمة أو المياه الملوثة أو لحوم الحيوانات أو التربة. وشمل هذا الاستعراض أيضاً طرق الانتقال والتدابير الوقائية الاستراتيجية للحد من خطر التعرض للمرض، فضلاً عن سبل البحث الجديدة التي تهدف إلى الحد من انتشار أكياس البيض والاكياس النسيجية التي تحمل في الخلايا في البشر والحيوانات المنزلية والحيوانية البرية. . قطعيا تصيب المقوسة الغوندية البشر والحيوانات على حد سواء، وتسبب الإجهاض لدى النساء وتسبب خسائر اقتصادية جسيمة في الحيوانات. وينتقل إلى الإنسان أفقياً عن طريق تناول الطعام والماء الملوثين باكياس البيض، وكذلك لحوم حيوانات المزرعة المصابة أو عمودياً عن طريق المشيمة. تصاب القطط بالعدوى عن طريق تناول مضيف وسيط يحتوي على كيسات نسيجية. يعد التسخين والتمليح والتجميد والإشعاع من الطرق الرئيسية المستخدمة لتقليل عبء الأكياس النسيجية في لحوم الحيوانات المستخدمة للاستهلاك البشري

Introduction

Toxoplasma gondii is a protozoan parasite that may be found in almost every part of the planet. It may infect a broad range of hosts including humans. Human toxoplasmosis was discovered in the second half of 1930s. In 1939, Sabin announced that Toxoplasma from man and animals were identical. Later on, in 1948, the finding of methylene blue by the scientist Sabin and Feldman confirmed the worldwide spread of T. gondii, through seroepidemiological studies in humans and other animal (1). As a result, one out of three of the world's human population is thought to have been exposed to the parasite throughout their life (2). Nevertheless, seroprevalence rates in humans and animals vary greatly depending on the geographical areas and groupings of individuals living in the same locations. Therefore, 5 to 100% adult human populations in different countries were test positive to T. gondii, during the last three decades (3). T.gondii is capable of inducing multiple transmission pathways inside and between various host species. The three infectious stages; that are infectious to man and animals are; tachyzoite and bradyzoite which are inside tissue cysts, and the sporozoite which is inside sporulated oocysts (4,5). The parasite can be passed on from or among various definitive and intermediate hosts. T.gondii infection, is not limited to a specific host species, its could be transmitted through tissue cysts between intermediate hosts, or oocysts between definitive hosts (6).

1. Life cycle

The life cycle of T. gondii includes sexual development that occurs in cats, the definitive host, and asexual development in the intermediate hosts that involves large scale of vertebrates (7,8). Cats consume the parasite through feeding on intermediate hosts infected with encysted bradyzoites. Under the effect of gut enzymes and acid digestion, bradyzoites are liberated from cysts and penetrate small intestine epithelial cells. Bradyzoites undergo several morphological stages (schizonts) in the gut in few days before reaching the merozoite stage (9). Merozoites will then differentiate into microgametes (male) and macrogametes gametes (females) after a numerous cycle of asexual division. Gametes will then unite into diploid oocysts encased in a thick impenetrable walled oocyst (10). Ten myriads of oocysts will be shed with faeces to the outside. Following, sporulated oocysts get sporulated with cellular division to form infectious sporozoites (11,12). The oocysts wall makes it impermeable and resistant to harsh environmental conditions for extended periods of time, allowing them to spread in both wet and dry environments (13).

Intermediary hosts acquire sporulated oocysts with food and water. Sporozoites penetrate cells of the host, where they immediately evolve to tachyzoites. Tachyzoites proliferate and invade rapidly and spread throughout the body cause cute symptoms of toxoplasmosis. Tachyzoites can move via blood streams or the lymph to a variety of organs. The weakening of animal's immune cells allows parasites to spread throughout the body (14), and they may even breach the blood-brain barrier in the brain (10,13). Immunocompetent patients can eventually manage this early phase of infection, but as the immunity of the host develops, fast-dividing-moving tachyzoites going to develop into slow-growing encysted forms known as bradyzoites, which get concealed from the immune system (11). These tissue cysts form typically lie in the CNS and muscle, where they can survive for an extended period of time (10,12). This mechanism guarantees the transmission of toxoplasmosis to the definitive host, when cats prey the intermediate host. Although intermediary hosts are not usual cats' food, parasites can nevertheless be transferred to different intermediary hosts via flesh-eating,

allowing a parasite transmission cycle to continue without the necessity for sexual reproduction (13) (Figure 1.).

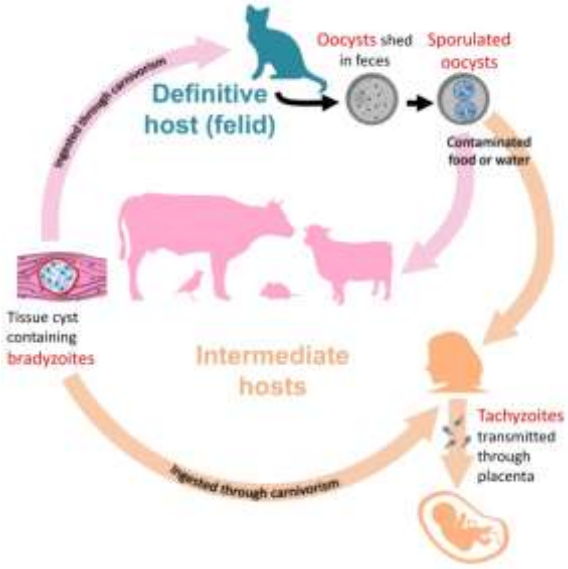

Figure 1. Life cycle of Toxoplasma gondii. Image taken from (14)

2. Transmission of Toxoplasmosis

Human can get infected through the ingestion of sporulated cysts, shed by cats into the environment, with food and water, also, via tissue cysts in undercooked or raw meat of intermediate host. In intermediate hosts, infection produced by oocyst ingestion is more severe than this caused by tissue cyst ingestion (4). Hence, the most important factor that interprets T. gondii's global spreading on all continents is the protozoa's ability and to develop different transmission ways. Carnivorism and anthropophagy contribute to and exacerbate the protozoan's persistence in the environment, even in the lack of the sexual development in cats (12).

Some literatures reported that new born babies or animals can get infected from colostrum infected with tachyzoites, through breast-feeding. Congenital transfer of tachyzoites from diseased dam mother to the growing foetus via the placenta, is another way of infection (2). Moreover, blood or organ donation from infected donors to intact recipient are another potential source of infection, therefore, prenatal infection rates in new-borns range from 1 to 120 per 10,000 and seroprevalence rates in pregnant women range from 4 to 85%, (4,5). However, not all probable routes of infection are relevant epidemiologically, and sources of infection might differ substantially between ethnic groups and geographical areas (15,16).

3.1. Tachyzoites in the intermediate host

Tachyzoites are crucial for vertical transmission of T.gondii. They, on the other hand, are highly sensitive the environment and are typically destroyed quickly when they shed out of the host. As a result, it is often assumed that transmissions through tachyzoites have little epidemiological significance (4). They may, however, occur occasionally. T. gondii infections have been reported to affect liver, heart, kidney, and bone marrow transplantation in recent years (3). Tachyzoites may have also been transmitted via blood transfusion, particularly those containing the white cell component, and through unintentional laboratory injection (15). However, parasitaemia normally lasts for a short time after initial infection. As a result, it has been proposed that there is only a low risk of contracting T. gondii by routine blood transfusion (1).

Although tachyzoites are discovered in the intermediate hosts milk, acute toxoplasmosis in humans is only linked to the intake of unpasteurized goat's milk. Tachyzoites are proteolytic enzyme sensitive and are normally eliminated by stomach digestion (17). However, recent research found that tachyzoites can persist for up to 2 hours in pepsin acid, and the excessive dosages of tachyzoites can cause severe infection in mice and cats (18). The tachyzoites can enter the mucosal tissue of the host through entrance the

blood or lymph circulations previously to stomach entry (16). This explains the occurrence of toxoplasmosis in a breast-fed newborn mother that had a previous T. gondii infection. Goat milk is an important source of toxoplasmosis to children, as a result, it is recommended that dairy products being pasturized, before consumed (1).

This is especially significant for newborns, that have low levels of proteolytic enzymes in their digestive tracts and are more susceptible to Toxoplasma infection than adults. Previously, it has been widely assumed that the danger of contracting T. gondii infection from drinking cow's milk was limited, but the raw milk is a possible source of infection (2,17). Tachyzoites have been found in saliva, sputum, urine, tears, and sperm besides body fluids and blood (1). T. gondii tachyzoites were found from chicken eggs that experimentally made infection in an early investigation (16). Furthermore, because tachyzoites are particularly sensitive to heat and salt concentration during cooking through destroy tachyzoites in eggs. The majority of horizontal transmissions to humans are initiated by ingestion of. tissue cysts in infected meat or offals (viscera) or oocysts contaminated food and water (17). Types of transmissions illustrated in Figure 2.

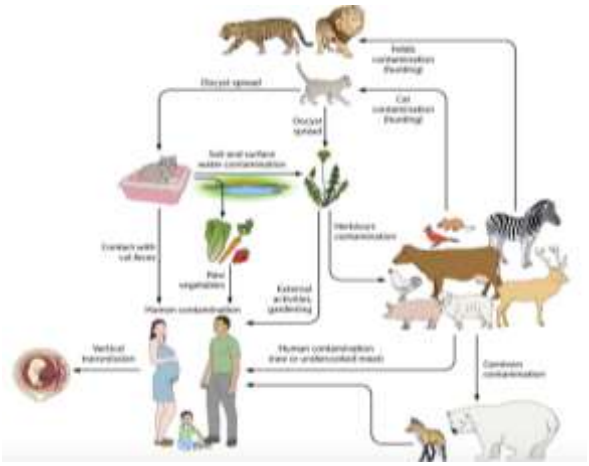

Figure 2. Transmission of T. gondii. Image taken from (18).

3.1. Tissue cysts in animals' meat

T. gondii tissue cysts seen in cattle meat are a main cause of infection for humans. They can form during 6-7 days after oocysts or other tissue cysts infect intermediate hosts. They are likely to live for the whole of the host's life (1). T. gondii tissue cysts are commonly detected in the tissues of infected intermediate hosts (pigs, sheep, and goats, and less frequently in poultry, rabbits, dogs, and horses) (13). These cysts are uncommon in the meat of beef or buffalo, while antibodies are about 90% of cattle and 20% of buffaloes proof a previous infection (19, 20).

Undercooked meat containing tissue cyst is the major source of infection to humans worldwide. Seroprevalence studies showed that sheep and goats had the highest infection rate compare to other farm animals (21). Genetics, housing conditions, feeding manner have potential effect on the infection rate in livestock (22). Due to the lack of control measures, meat-induced toxoplasmosis has been remarkably increased. However, further screening of the parasites in addition to preventative measures like freezing, heating, salting and radiation might reduce the infection and protect public health (23, 24).

3.2. Cats are the only source of oocysts

Toxoplasma gondii infections are often asymptomatic in feline, and vertical transmissions may occur. Latent T. gondii infections, on the other hand, are widespread in local and wild cats in the worldwide (5). About 17 species of wild cats, (European and African), are reported shedding T. gondii oocysts. T. gondii antibodies can be found in 74% of cat populations in domestic cats, dependent on the diet type and if cats are raised indoor or outdoor (15). Serological prevalence's are often greater in stray than domestic cats. However, between 9 and 46% of companion cats in Europe, South America, and the United States have serological

evidence of prior parasite exposure, whereas seroprevalences of T. gondii infections in Asia are estimated to be 6 to 9% (24).

Local cats can get infection with T. gondii by eating sporulated oocysts or tissue cysts of intermediate hosts. Cats are infected by hunting of T. gondii-infected rodents or birds (1,5). T. gondii may infect up to 73% of small rodents and 71% of wild birds, according to species of the host, geographic location, and time of the year (25). Cats often shed significant quantities of oocysts following an initial T. gondii disease. It was thought that shedding of oocysts followed reinfection with lack of T. gondii reinfection was uncommon. However, new research has revealed that this immunity does not last the cat's entire life (26). In cats challenged with T. gondii in early life, a second excretion of oocysts might happen 6 years later post primary infection (15). Furthermore, short time of reshedding of oocysts is reported in rare situations in cats are not reinfection which still unknown until today in natural situations. Superinfection with other coccidia has been shown in experiments to induce oocyst shedding. Cats are wandering on farmhouses might pollute the surroundings with oocysts, that can infect cattle killed for human consumption (1,25). Cat oocysts, on the other hand, are unsporulated and consequently not immediately infectious. As a result, direct contact with cats is frequently resulting in toxoplasmosis (27).

4. Prenatal toxoplasmosis in new-borns

Toxoplasma gondii infection generally leads to lifelong immunity against toxoplasmosis in immunocompetent hosts. As a result, if an initial infection occurs 120-180 days before gestation or earlier, protecting immunity typically prevents congenital toxoplasmosis exposure in future (8). The rare happens occurs in low immunity mothers with AIDS that earlier infected recorded positive serological tests to T. gondii vertical transmission to the fetus. If mothers got infected during first term of gestation, they may pass T. gondii to the fetus in immunocompetent mothers. The mechanism of vertical transmission is yet unknown (28, 29,30). Temporary parasitaemia in a pregnant woman who is predominantly infected may result in tachyzoites invading the placenta and multiplying inside placental cells. Possibly, eventual transcend the placentation and reach the embryonic flow and tissues (31). Vertical toxoplasmosis can result in abortion, neonatal mortality, or foetal anomalies, all of which are harmful to the fetus. It may also have a negative impact on the wellness of survival children with a perinatal transmission (32).

During last 30 years, the incidence of prenatal transmissions of T. gondii the total number of cases are ranged between 1-100 per10000 infants in various states. The risk of intrauterine infection of the foetus, the risk of congenital toxoplasmosis manifestation, and the severity of the disease are determined by maternity infection during gestation, the immune status of mother during infection, the amount and types of the Tachyzoites transferred to the foetus, and the foetal stage at the spread time (1,33,34). The risk of infection occurrence within the uterus raised during pregnancy from 14% in the first 3 months of pregnancy if not treated. to 59% in the last 3 months of pregnancy (8). Based on serological research, the incidence of maternity contamination during gestation in Europe, Asia, Australia, and the Americas ranged from roughly 1 to 310 per 10,000 pregnancies. These rates be governed by occurrence of transmission are slightly higher if pregnant mothers are integrated. (35).

The consequences showed less pathogenic on the embryo if diffusion happens later in pregnancy, with most newborns contaminated during last trimester of gestation with no clinical signs at delivery. About 67-80% of

congenitally infected newborns have a subclinical illness that may identify via immunological tests. These newborns seem to be in good health at delivery time, but they can eventually improve medical signs (1). These defects mostly infect the eyes (blindness), the central nervous system (psychomotor, seizures, cerebral retardation), or the ear (deafness). The anticipated of one-quarter of infants infested during pregnancy would acquire vision impairment later in life (23,33,36).

5. Diagnostic methods

Toxoplasmosis can be diagnosed directly by detecting the parasite in stained tissues, blood, and even in the tissues (37). Due to challenges in processing and staining tissues and specimens, serological testing is the most common and reliable alternatives of diagnosing toxoplasmosis (6). Toxoplasma gondii generates intense humoral immune response with easily detectable antibody titers in infected people. In a study in AL-Najaf /Iraq, the prevalence was 33.7% by ELISA (7). The IgM antibodies can be seen first one week after infection and a confirmed diagnostic test in acute infection; nevertheless, it can be persistent for months or even a year (3). IgG antibodies can be identified 1-2 weeks after infection and reaches the peak during the 1-2 months then, declining (8). However, various serological tests have been developed as alternative methods for various studies on Toxoplasma infection in human and animals. The test's sensitivity, specificity, and findings may differ. Thus, tests done in the same laboratory do not always provide the same results as shown in several studies (3,6,9). In Mosul city, the total infection rate in cats like 6% (38). In Al-Anbar, blood samples from humans, pet and stray cats were implemented to Latex Agglutination (TLAT) and PCR tests. The results were 24% and 30% in humans and 7.6% and 60% in pet and stray cats using TLAT and PCR, respectively (39).

6. Control and preventative measures of toxoplasmosis

Toxoplasmosis in cats can be reduced by reducing exposure to sporulated oocysts excreted in the surroundings. Felines would eat professionally prepared, cooked meals and should not be fed raw tissues or intermediate hosts like rodents (21). Therefore, cats ought to be prevented contact to food science animal facilities and nutrients storage places. Since cats excret oocysts for a short period, the risk of exposure is quite low (5). Having a cat pet not usually guarantee that you may have infection with T. gondii. Because T. gondii oocysts in cat feces take at least 24 hours for sporulation, regular elimination of stool from the litter box, putting gloves and wash hands afterwards reduces risk of disease. T. gondii infection is unlikely in indoor cats that pursue raw prey (19). However, cats' owners inside houses are not always get T. gondii infection as cat feces are removed from the household on a regular basis (1,15).

Tissue cysts are sensitive to freezing, heating, salts, chemicals and radiations. It seems that they can resist freezing 1-8°C for 7-10 days, but some strains can survive over freezing (21, 22). Heating to over 50-67°C for 1-10 minutes is also critical and kill tissue cysts in meat, however, uneven cooking methods such as microwave or barbeque may result in persistent viable cysts (23). Processed meat in salt or sugar or low temperature smokes also considered tissue cyst free and suitable for human consumption. T. gondii cysts in sausages can be burst at 6% NaCl and destroyed by gamma irradiation of 1.0 kGy at room temperature, though, radiation is prohibited in developed and some developing countries (22,23).

There is also the chance of infection after

gardening in soil infected with cat feces, which may be reduced by using gloves during gardening (40). Pregnant women and immunocompromised people are more vulnerable to health issues following toxoplasmosis. Humans are more concerned about in utero infection (35,36). Billions of infants delivered to moms infected with T. gondii during gestation. Infants of infected women with no symptoms may be at risk of developing infection-related signs in late life, such as mental disability, hearing impairment and eventually and death (40,41). In people are exposed to immunosuppressive treatment or they are immunosuppressive patients like acquired immunodeficiency syndrome (AIDS) may show have high mortality rate (42). Thus, immunocompromised patients and pregnant women were recommended to avoid cats (43).

Conclusion

It has been known that the fundamental sources of T. gondii transmission are altered in people of different society and dietary behaviors. There are various reasons that have crucial impact on etiology of toxoplasmosis, like controlling of livestock development, sanitary principles of slaughterhouses, technology of diet handling, the numbers felines populations in the surroundings area, and climatic surroundings that effect the sporulation of oocysts.

Recently researches have elevated knowledge of the waterborne dissemination of oocysts is necessary as environmental contamination to people's importance than has been believed previously. The threat of getting illness by T. gondii through contamination of oocysts from cats shedding of their holders might be considerably reduced by traditional vaccination of pet animals, good hygiene sanitation and valuable regulation of infectious environment. For sensible future prevalence educations on T. gondii ought to reflect the possible causes of contamination for individuals and animals.

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