Toxoplasma gondii: Bridging Morphology and Pathogenesis in a Protozoan Parasite

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These blood and tissue-dwelling protozoa can cause toxoplasmosis in both humans and animals. *Toxoplasma gondii* lives intracellularly within the cells of the reticuloendothelial system and parenchymal cells of both humans and mammalian animals, especially cats and birds.[1] A study by Hartono found that approximately 40% of 50 swine samples contained Toxoplasma cysts.[2] Toxoplasma cysts are commonly found in the muscle and internal organs of these animals. Based on their habitat, *T. gondii* has two forms: intracellular and extracellular. Intracellularly, the parasite has a round or oval shape, making it difficult to distinguish from *Leishmania* species. Extracellularly, the parasite is crescent-shaped and slender, with one pointed end and the other blunt. *Toxoplasma gondii* is approximately 2-5 µm in size and has a nucleus located at the blunt end of the parasite.[3] In the epithelial cells of the small intestine of cats, both asexual (schizogony) and sexual (gametogony, sporogony) cycles occur, producing oocysts that are excreted with feces.

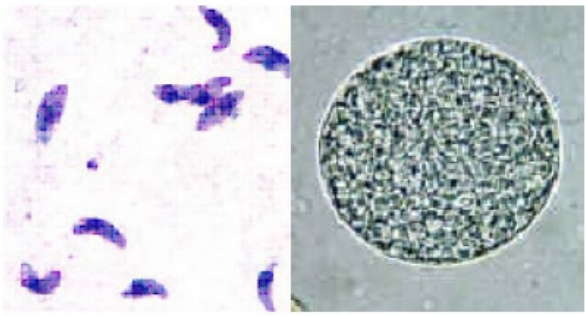

Figure 1. tachyzoites into bradyzoites of *Toxoplasma gondii*

Initial and acute infections begin with rapid tachyzoite replication. Approximately 10-14 days after infection, tachyzoites differentiate into bradyzoites, which divide slowly, resulting in the formation of tissue cysts. Tissue cysts can reside in the body without causing clinical manifestations. However, in immunocompromised individuals such as those with AIDS and malignancies, tissue cysts can rupture and bradyzoites can transform into tachyzoites, leading to acute reactivation. Three factors influence the differentiation of tachyzoites into bradyzoites or tissue cysts: the host's immune system, host genetic factors, and factors originating from the parasite itself. Firstly, the host's immune system, namely the cellular and humoral immune responses, plays a crucial role in the bradyzoite-tachyzoite differentiation stage by regulating parasite lysis or inducing the formation of tissue cysts. Secondly, the infecting Toxoplasma strain. There are strains that tend to change from the tachyzoite to the bradyzoite stage and form cysts, such as non-virulent strains, while virulent strains have tachyzoites that are slow to transform into bradyzoites. Thirdly, it is related to morphology and molecular biological changes, including the expression of specific antigens and changes in metabolism. The transformation of tachyzoites into bradyzoites is a complex process as it requires the expression of specific bradyzoite proteins and changes in the vacuole into a cyst through the process of depositing specific proteins for the cyst wall.[4]

Like other microorganisms in the apicomplexan family, *T. gondii* also has a complex apical structure involved in parasite penetration and its ability to survive intracellularly within host cells. The characteristic organelles of *T. gondii* are rhoptries, micronemes, and dense granules. *T. gondii* enters host cells through active invasion and does not involve any host cell activity. Parasite invasion into host cells takes approximately 5-10 minutes. The process of parasite entry into host cells is as follows:

a. Reorientation of the parasite so that contact can occur between the apical end of the parasite and the host cell plasma membrane. It is known that the host cell extracellular matrix involved in this attachment process is laminin.
b. Inside the infected host cell, the parasite forms a parasitophorous vacuole, which prevents the acidification of the lysosomal compartment and rapidly undergoes division. The parasitophorous vacuole is surrounded by a layer of host cell endoplasmic reticulum and mitochondria, which are used to meet the parasite's metabolic needs. Therefore, the phagocytic ability of the host cell is impaired, allowing the parasite to survive and multiply within the host cell.

The process of host cell infection involves the secretion of proteins from apical secretory organelles, namely micronemes and rhoptries. Microneme proteins are used for host cell recognition, attachment, and parasite movement. Rhoptry proteins are used for the formation of the parasitophorous vacuole, and proteins from dense granules are used to alter the shape of the vacuole into an active compartment for metabolic purposes.[5]

Toxoplasma gondii is widespread worldwide, with serological prevalence data indicating that 30-40% of the world's population is infected with *Toxoplasma gondii*. This infection is more common in low-lying tropical areas than in cold, high-altitude areas. France and countries whose populations enjoy eating raw or undercooked meat have high prevalence rates of toxoplasmosis.[3] Toxoplasmosis is widespread globally because it can infect any nucleated host cell. Approximately 85% of reproductive-age women in the United States experience acute infection with the parasite *Toxoplasma gondii*. The incidence of congenital toxoplasmosis depends on the proportion of pregnant women infected with Toxoplasma during pregnancy. Estimates of congenital infections in the United States range from 1 in 3,000 to 1 in 10,000 births. Based on regional study data, 400 to 4,000 cases of congenital toxoplasmosis occur in the United States each year.[6]

In Indonesia, the *T. gondii* parasite is widespread with varying antibody prevalence rates against *T. gondii*. In humans, it is found in 2-63%, cats 35-73%, dogs 75%, pigs 11-36%, goats 11-61%, and cattle/buffalo less than 10%. In human life, there are two populations that are likely at high risk of infection with this parasite, namely pregnant women and immunocompromised individuals.[5] *Toxoplasma gondii* has three stages:

a. Tachyzoites (proliferative form), Tachyzoites resemble crescents with one pointed end and the other slightly rounded. Tachyzoites are found in acute infections of various organs, such as muscles including the heart, liver, spleen, lymph nodes, and central nervous system.
b. Bradyzoite-containing cysts are formed within the host cell when dividing tachyzoites have formed a wall. Cysts can be found in the host's body for life, especially in the brain, heart muscle, and striated muscle.
c. Oocysts containing sporozoites, oocysts are oval, have a wall, and contain one sporoblast that divides into two; then both sporoblasts form a wall and become

sporocysts. During acute infection, oocysts excreted with cat feces are not yet infective. After several weeks, depending on environmental conditions, oocysts will sporulate and become infective. Humans and other intermediate hosts, such as goats and sheep, will become infected if they ingest these oocysts. Hot weather and moist soil can sustain oocysts for about a year. Oocysts cannot survive in dry soil and cold weather. After infection with *T. gondii*, parasitemia will occur, where the parasite attacks organs and tissues, multiplies, and destroys host cells.[6]

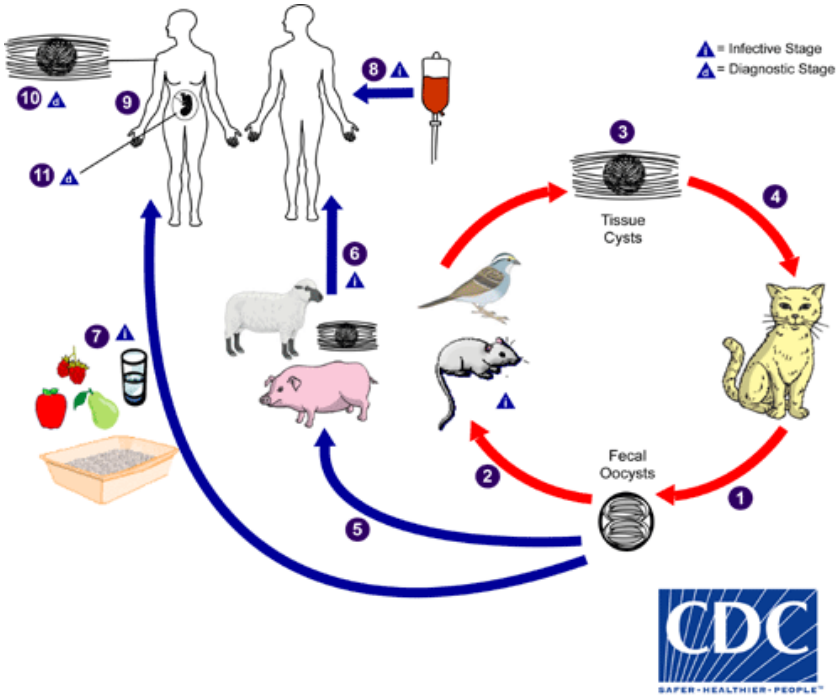

Figure 2. *Toxoplasma gondii* life cycle

In humans, tissue cysts are commonly found in muscle tissue, myocardium, brain, and eyes and will persist throughout the host's life. Diagnosis is typically made through serology and biopsy specimens. Diagnosis of congenital infection is done by detecting *T. gondii* DNA in amniotic fluid through molecular methods such as PCR.[7]

Pathological changes depend on the infectious stage entering the patient's body. The incubation period of toxoplasmosis ranges from 5-23 days. Through the bloodstream, the parasite will spread to various organs, such as the brain, spinal cord, bone marrow, lymph nodes, eyes, lungs, spleen, liver, and heart. In healthy, non-pregnant adults, because their immune system is able to fight the parasite infection, the clinical symptoms of toxoplasmosis are generally unclear and the patient has no complaints. Mild clinical symptoms are similar to the flu, including mild lymph node enlargement and muscle pain that only last for a few weeks. However, the parasite, which is in an inactive form in the patient's tissues and organs, will become active again if the patient's immunity decreases.

Toxoplasmosis is very evident in pregnant women, which can cause abortion, stillbirth, or babies born with signs of congenital toxoplasmosis. This is because the parasite causes damage to the organs and nervous system of the patient, namely babies and children. Pregnant women infected in the first trimester will experience spontaneous abortion or stillbirth. If it occurs in the late trimester, it causes babies born with congenital abnormalities such as encephalomyelitis,

cerebral calcification, chorioretinitis, hydrocephalus, or microcephaly. Patients with impaired immune systems such as AIDS/HIV will show severe clinical symptoms of toxoplasmosis, including fever, headache, altered consciousness, and impaired coordination. Patients will often experience recurrent relapses and re-infections.[4] People who can be infected with *Toxoplasma gondii* are:

a. Healthy individuals Healthy individuals infected with *Toxoplasma gondii* often have no symptoms because their immune system keeps the parasite in cyst form. This can become reactivated if the person becomes immunosuppressed.
b. Mother-to-child (congenital) Generally, if a woman has been infected before pregnancy, the unborn baby will be protected because the mother has developed immunity. If a pregnant woman is newly infected with Toxoplasma during or shortly before pregnancy, she can transmit the infection to her unborn baby. Eye disease (most often retinochoroiditis) in Toxoplasma infection can occur as a result of congenital infection or post-natal infection. Eye lesions due to congenital infection are often not identified at birth, but 20-80% of infected individuals will develop symptoms in adulthood. However, in the US, post-natal eye lesions are found in <2%.
c. Individuals with compromised immune systems Individuals with compromised immune systems can experience severe symptoms if they are infected with Toxoplasma when their immunity is low. For example, a person infected with HIV and experiencing reactivation can develop symptoms such as fever, headache, seizures, nausea, and poor coordination. People who acquire HIV and are newly infected with Toxoplasma are more likely to develop severe primary infection.

In conclusion, toxoplasmosis, caused by the parasite *Toxoplasma gondii*, is a widespread infection that can affect various organs and systems in humans. While most healthy individuals experience asymptomatic or mild infections, the disease can pose significant risks to pregnant women, newborns, and immunocompromised individuals. Congenital toxoplasmosis can lead to severe birth defects and lifelong complications. The parasite's ability to form tissue cysts and remain dormant in the body makes it challenging to eradicate. Understanding the lifecycle of *T. gondii* and the factors influencing infection and disease progression is crucial for developing effective prevention and treatment strategies. Public health measures aimed at reducing exposure to the parasite, especially through contaminated food and cat feces, are essential to minimize the burden of toxoplasmosis worldwide.

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