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TOXOPLASMA GONDII: LIFE CYCLE, PATHOGENESIS, IMMUNE RESPONSE: A REVIEW

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ABSTRACT

Toxoplasma gondii is an obligate intracellular parasite and the causative agent of Toxoplasmosis. Cats and members of Felidae are definitive hosts while humans and other mammals are intermediate hosts for the parasite. The parasite spreads all over the world and humans acquire the infection by ingesting tissue cysts in undercooked or raw meat or by consuming oocyst via unwashed vegetables and coming into contact with the feces of infected cats. The parasite infects all vital organs in the body, especially in the acute stage of the disease, as it may be present in the blood, cerebrospinal fluid, semen, and may cause miscarriage when it is transferred from the mother to the fetus through the placenta. Cell-mediated immunity plays a very important role in determining infection prevalence as well as cytokines in addition to the production of immunoglobulins.

Keywords: *Toxoplasma gondii*; Life cycle, Pathogenicity, Immune response

Introduction

Toxoplasma gondii is an obligate intracellular parasite, which is the cause of toxoplasmosis. It was first discovered in 1908 in a rodent living in the desert. Janku was classified in 1923 as cause of reticulitis. Since that time the parasite was discovered in carnivores and insectivores, herbivores and other mammals as well as in birds. The parasite is spread all over the world, especially "in hot and humid areas, and the rate of infection is estimated at around 30% of the world's population. The infection rate in children increases in areas where cats are abundant, as well as in adults as a result of eating meat that is not cooked well or raw (Geraled, and Larry 2005). The importance of the parasite to humans has stimulated a tremendous amount of research and since the mid-1980s it has been classified within a group of parasites that infect immuno-suppressed patients. In cases of acute infection, the parasite may also be present in the blood and peritoneal exudate, and it may be present in the nucleus of the host cell, but most likely it lives in the cytoplasm (Wieffer *et al.*, 2005).

Life cycle

Cats and all species of Felidae are definitive hosts for the parasite, while reptiles, birds, and other mammals, including humans, are intermediate hosts.

The life cycle of *T. gondii* includes three infective stages, which are tachyzoites with a crescent shape to oval, found in acute infection, and is transmitted through the placenta from mother to fetus, blood transfusions, and organ transplantation.

Tissue cyst contains thousands of bradyzoites and is transmitted to humans through the consumption of raw or undercooked meat, often combined with chronic infection, and reactivated, especially in people with weakened immunity (Levinson and Jawetz, 1994).

Oocyst is excreted with the feces of infected cats and transmitted to human through ingestion and direct contact with cat feces and this stage is the most tolerant form of environmental conditions, is highly resistant to disinfectants, and plays a major role in the transmission of infection to humans (Dubey, 2002a).

T. gondii enters its host via the gastrointestinal tract, and when it invades the intestinal epithelial, it encounters a physical barrier that includes a layer of epithelial cells known as enterocytes that are tightly bound together by a tight junction.

When a person eats a cyst in undercooked meat or comes into contact with the feces of an infected cat, the cyst in the small intestine is broken down by proteolytic enzymes and the stages that hit the intestinal wall are liberated and engulfed by macrophages and are characterized very quickly into tachyzoites that kill cells to infect other cells (Lee *et al.*, 2006)

Cellular immunity plays a very important role in determining the spread of infection, and the parasite enters the host's cells either in the brain, muscles and other tissues and develops into a cyst that includes within it slowly proliferating stages called bradyzoites. These tissue cysts are very important in diagnosing the infection and are considered a source of the parasite when the cyst ruptures in an immunocompromised patient (Menncht *et al.*, 2004).

In cats, the life cycle begins when tissue cysts are ingested in raw meat such as mice. The bradyzoites are released from the cyst in the small intestine of the final host and infect the epithelial cells and are distinguished into male and female gametocytes that combine and form an oocyst

and excreted with the feces of the infected cat and are unsporulated and become infectious when suitable environmental conditions present such as heat, humidity and the cyst remains active and infectious for 12 months when appropriate conditions are available (Dubey, 2007).

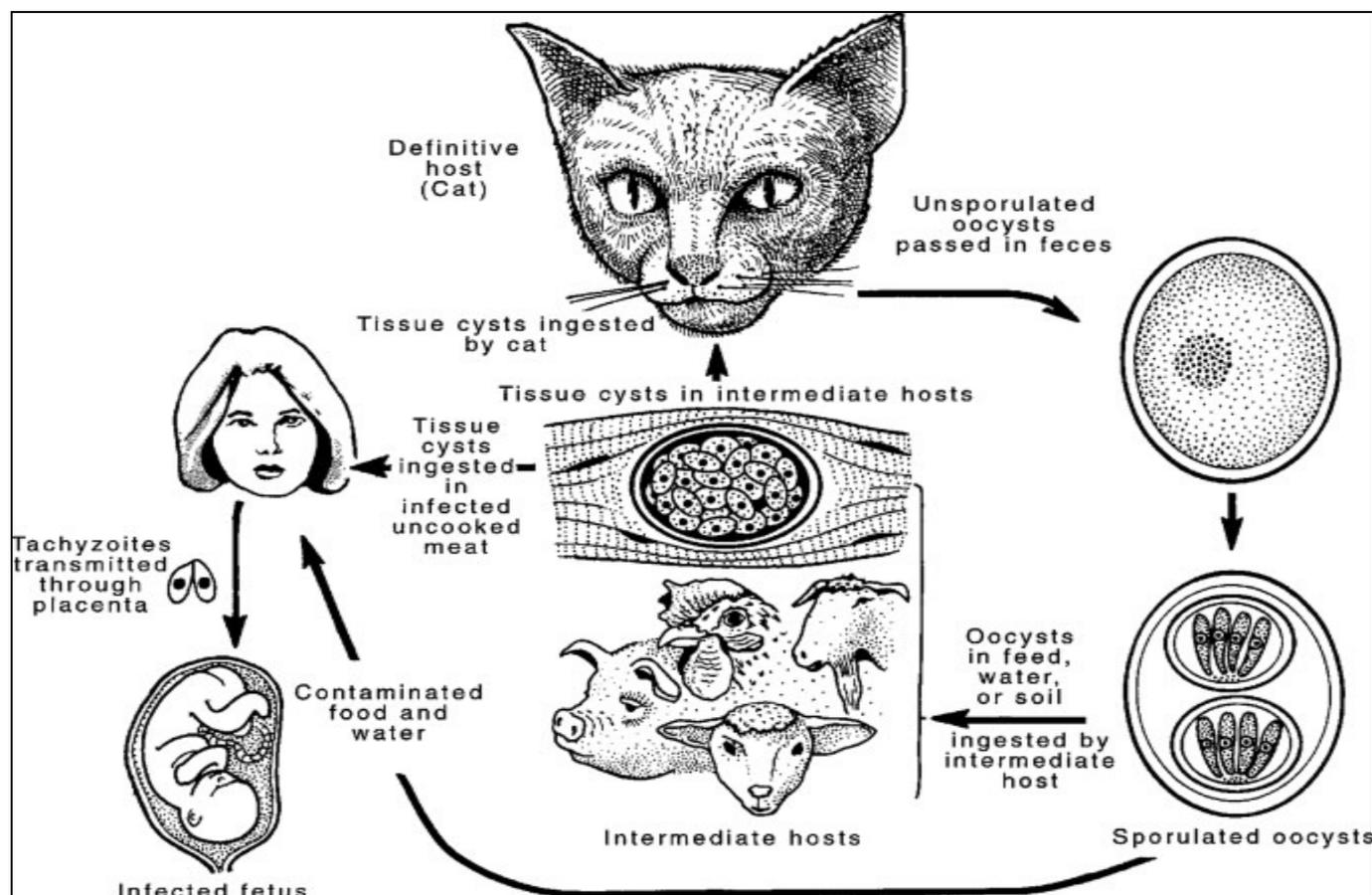


Fig. 1 : Life cycle of *Toxoplasma gondii* (Ikpeze and Olofintoye,2008)

Pathogenesis

Studies have proven the presence of anti-*T. gondii* antibodies in people around most of the world and that most of the infections are asymptomatic or mild, and there are several factors that control this, which are the virulence of the parasite strain, its sensitivity to its hosts, the age of the host and the acquired immunity (Cook *et al.*, 2000)

Infection with *T. gondii* occurs through digestion, and most of the primary infections are asymptomatic because the parasite remains in the tissues, whether it is the maggot, lung, liver, and eyes. Inflammation does not occur and the individual is normal until an immunodeficiency occurs that allows the parasite to be activated. The parasite is also transmitted by placental transmission from the infected mother to the fetus during the first trimester and is more severe than second trimester and third trimester as it causes severe fetal damage, hydrocephalus, intercerebral calcification, retinochoroiditis, mental disorders, blindness, and pneumonia (Hassan *et al.*, 2019).

Because of the dependence of infection on age, infection in the elderly is without symptoms, but suddenly it may turn into an acute, semi-acute or chronic infection if you take immunosuppressive drugs such as corticosteroids (Lyons *et al.*, 2002).

In acute infection, the patient feels pain and swelling of the lymph nodes in the neck, along with fever,

headache, and muscle pain similar to flu symptoms that do not cause death (Geraled and Larry, 2005).

In chronic infections it is possible for the cyst to remain without symptoms for a long time if the host's defenses are strong (Harma *et al.*, 2004).



Fig. 2 : Girl with hydrocephalus due to congenital toxoplasmosis (Ikpeze and Olofintoye,2008)

Immune response against *T. gondii*

First the parasite enters into the mucous layer in lamina propria and Peyer's patches, dendritic cells and macrophages represent guards and are able to receive invading microbes.

When the parasite penetrates into enterocytes and infects dendritic cells and macrophages, the goal of the immune response is to remove the parasite and these cells can be directly act as microbicidal and also represent a source of cytokines such as Interleukin 12 (IL12) and Tumor Necrosis Factor α (TNF α) that contribute to differentiate T-cell into T-helper type1 (Th1) cells, the hallmark of which is the production of Interferon- γ which enhance clearing up the parasite by dendritic cells and macrophages (Wert, 2008).

B-cells also produce antibodies that cross the epithelial barrier by active transport to reach the parasite, as studies have shown that infection with *T.gondii* stimulates many immune changes within the body and leads to the production of immunoglobulins (IgM), (IgG), (IgA), and this is consistent with (Prusa *et al.*, 2010).

In general, the immune response in the non-immunosuppressed host "is the one that possesses and protects the fetus while the parasite is present as bradyzoites inside the cysts. In immunodeficiency as it is in AIDS patients, the bradyzoites are released from the cyst and transformed into tachyzoites, which damages the brain."

Therefore, cellular immunity is the main key in host immune reactions and includes macrophages, dendritic cells, T-lymphocytes, and Natural Killer cells (NK), and the other part are cytokines, whose function is to protect and regulate the immune response and this sometimes appears in an exaggerated manner, especially in some immune diseases and in People who are immunosuppressed depending on the genetic nature of the host, its immunity and the parasite strain that causes the disease (Belloni, 2000).

In mice, scientists also found that TNF α -mediated activation of macrophages and Interferon-are necessary to direct the toxicity activity against *T. gondii*.

There are several mechanisms to inhibit and destroy a parasite's ability to replicate and destroy it, including oxidative mechanisms.

Second, a non-oxidative mechanism involving the production of Nitric oxide (NO) by macrophages and the activator with INF- γ , and it also has a major role in preventing the spread of the parasite during the chronic phase. (Spits *et al.*, 2016)

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