TOXOPLASMOSIS - AN OVERVIEW

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Abstract. Increasing concern over food safety has focussed attention on food-borne parasitic diseases, particularly toxoplasmosis. Infection by the protozoan parasite *Toxoplasma gondii* is widely prevalent in humans and in food animals. Cats are the main reservoirs of infection because they are only hosts that excrete environmentally resistant oocysts. *Toxoplasma gondii* infection is transmitted by ingesting undercooked infected meat, congenitally, and via feces of infected cats. The most severe clinical infections occur in congenitally infected children. Toxoplasmosis is a major cause of abortion and neonatal mortality in sheep, goats, and pigs. Strategies to control toxoplasmosis are outlined.

LIFE CYCLE AND SOURCES OF INFECTION

Infection due to the protozoan parasite, *Toxoplasma gondii*, is widely prevalent in man and many species of warm-blooded animals. *Toxoplasma gondii* is transmitted by three major modes: congenitally, through the consumption of uncooked infected meat, and via feces of cats. The life cycle is summarized in Fig 1.

Cats, including wild Felidae, are the only definitive hosts. Felidae excrete *T. gondii* oocysts in their feces. Excreted oocysts are nonsporulated and, therefore, are noninfectious. Sporulation (development of infectious sporozoites inside the oocyst) may take 1 to 5 days after defecation, and is dependent on environmental conditions. Oocysts can survive for several months to a year under severe environmental conditions, and are remarkably resistant to most disinfectants (Dubey and Beattie, 1988).

After ingestion of oocysts in food or water by a warm-blooded animal, the oocyst ruptures in the intestine, releasing 8 sporozoites. Sporozoites multiply intracellularly in the intestines and in associated lymph nodes, and tachyzoites (rapidly multiplying forms) are formed. Tachyzoites then spread to the rest of the body via blood and lymph and eventually encyst in the brain, skeletal and cardiac muscles, and liver. Encysted *T. gondii* are called bradyzoites or cystozoites (slowly multiplying forms). Tissue cysts are microscopic and survive in tissues as long as the host lives.

After ingestion of infected tissues, proteolytic enzymes dissolve the cyst wall, releasing bradyzoites, which infect the host. After entry into host cells, bradyzoites transform into tachyzoites. In the host cell, the tachyzoites may undergo repeated divisions, ultimately encysting in tissues. The cycle of *T. gondii* is completed when tissue cysts are ingested by the cat. In the intestine of the cat, bradyzoites initiate a series of genetically determined asexual generations (meronts) and the merozoites initiate the sexual cycle. After the male gamete fertilizes the female gamete, a wall forms around the fertilized female gamete to form the oocyst.

Transplacental infection can occur when a previously noninfected host becomes infected during pregnancy. *Toxoplasma gondii* multiplies

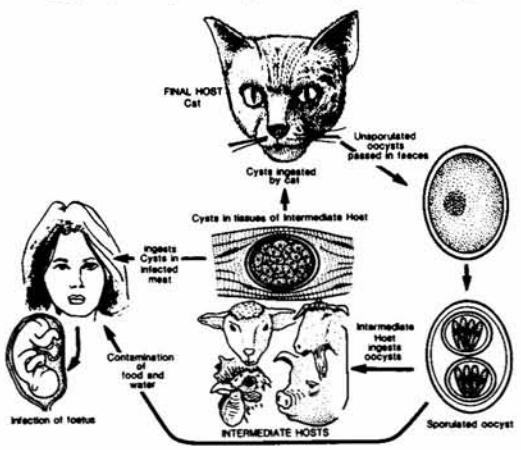

Fig 1–Life cycle of *Toxoplasma gondii*.

in the placenta and then spreads to fetal tissues. Although transplacental infection can occur at any stage of gestation, the fetus is affected more severely if the dam becomes infected during the first half of gestation.

Although *T. gondii* can be transmitted via transfusions of platelets and blood cells and via organ transplants, these modes of transmission are less common than transmission via meat and oocysts. However, disseminated and often fatal toxoplasmosis may result from organ transplantation because the patients are being given treatments that are immunosuppressive.

Transmission by cats

Cats are pivotal in the transmission of toxoplasmosis. Epidemiologic data indicate that most cats become infected in nature soon after they are weaned, either by eating raw pet food or by sharing food brought by the dam. Therefore, *T. gondii* infection is higher in feral cats than in domestic cats. Under laboratory conditions, most previously noninfected cats that are fed infected tissues shed oocysts, whereas <50% of these cats that are fed oocysts will shed oocysts. Moreover, the number of oocysts shed by a cat after ingestion of oocysts is far less than after ingestion of infected tissues. Although cats can repeat the shedding of *T. gondii* oocysts after reinfection (or even without reinfection), this shedding of oocysts probably is infrequent and the number of oocysts shed a second time is far less than that during a primary infection. Cats immune to *T. gondii* have been induced to shed large numbers of *T. gondii* oocysts a second time after superinfection with the feline coccidium *Isospora felis*. This second-time excretion of oocysts probably is not important epidemiologically because most cats become infected with *I. felis* early in life and probably maintain immunity through constant low-level reinfections. Although transplacental transmission can occur in cats, it is probably rare. However, congenitally infected kittens can excrete *T. gondii* oocysts.

Cats often defecate on soft ground and in hay, barns, food bins, gardens, and flower pots. Generally, feline feces are hard and may remain confined to the area of defecation for a long time. Unless cats are sick, little or no feces stick to their anal area. Because of their licking (grooming), fecal matter on cat fur rarely is found. Usually, cats are not diarrheic during the period that they are shedding oocysts. Therefore, the possibility of the transmission to human beings via touching or caring for a cat is minimal. The chance of becoming infected via soil contaminated by a feral cat probably is greater than the chance of becoming infected via soil contaminated by an indoor cat because feral cats usually hunt birds and small mammals in which a sylvatic cycle of *T. gondii* is maintained.

Cats can excrete millions of oocysts during a short period of oocyst shedding (usually 1 week). Although at any given time usually less than 2% of cats have been found shedding oocysts in nature, this observation does not diminish the importance of the cats in transmission of *T. gondii* because oocysts can survive in the environment for many months. Invertebrates (cockroaches, earthworms, flies) can act as transport hosts for oocysts. Wind, rain, and transport hosts can further disseminate oocysts in the environment.

Results of epidemiologic studies, based on shedding of oocysts by cats and the cultural habits and rates of *Toxoplasma* infection in the general human population in Costa Rica, indicate that the cat is important in the natural epidemiology of toxoplasmosis. Little or no information is available concerning the role of the cat in the transmission of toxoplasmosis in Asian countries, particularly Thailand, Indonesia, Philippines, Malaysia and the Indian Subcontinent. In most Asian countries cats are mostly feral. They are abundant in urban areas, particularly around temples, restaurants, and have intimate contact with the general human population.

Transmission by food animals

Toxoplasma gondii tissue cysts have been found in edible tissues of most food animals (Dubey and Beattie, 1988; Dubey, 1988). Experimental studies indicate that viable tissue cysts persist in animals probably for life. Tissue cysts are more prevalent in tissues of sheep, goats, pigs, and rabbits than in cattle, horses, and commercially raised fowl. Cattle and buffaloes have innate resistance to *T. gondii* and can eliminate tissue cysts from their tissues.

Venison and other wild animal meat also can be sources of toxoplasmosis. *Toxoplasma gondii* has been found in muscles of naturally infected

moose, deer, and pronghorn and *T. gondii* can encyst in elk and deer, and probably in other cervids. These wild cervids can serve as sources of infection for hunters and their families while eviscerating and handling the game and when meat from these animals is served undercooked or raw. More important, viscera and meat scraps left in the field could spread *T. gondii* to Felidae and other carnivores. Subsequent excretion of oocysts will further spread infection in the environment.

Toxoplasmosis has been reported in human beings after drinking raw goat's milk, and *T. gondii* has been found in milk of goats experimentally inoculated with *T. gondii*. Therefore, goat's milk should be pasteurized before human consumption. This is particularly important for its use in infants, which are more susceptible to toxoplasmosis than are adults. *Toxoplasma gondii* may survive longer in infants than in adults because the concentration of proteolytic enzymes in the intestine of an infant is less than that in the intestine of an adult. Although the risk of acquiring toxoplasmosis by drinking cow's milk is minimal, milk should be pasteurized or boiled to reduce exposure to other milk-transmitted pathogens.

CLINICAL TOXOPLASMOSIS AND UNSOLVED PROBLEMS

About 33-50% of the adult human population in America and Continental Europe have been estimated to have serum antibodies to *T. gondii* (Dubey and Beattie, 1988; Remington and Desmonts, 1990). Postnatally acquired *T. gondii* infections are generally asymptomatic or are manifest by mild flu-like signs and lymphadenopathy. Toxoplasmosis, however, can cause devastating illness in some adults and children. Retinochoroiditis and mental retardation are the two most important clinical symptoms in congenitally infected children. Although the child is infected before birth, such symptoms may not appear until adolescence. The diagnosis and clinical management of congenital toxoplasmosis in humans are major problems facing the medical profession because there are no simple inexpensive diagnostic tests and the currently available drugs are not effective in treating toxoplasmosis (Remington and Desmonts, 1990; Frenkel, 1990; McCabe and Oster, 1989; Daffos *et al*, 1988). Moreover, in most countries, there are no good estimates of rates of congenital toxoplasmosis (Wilson and Remington, 1980; Roberts and Frenkel, 1990; Jeannel *et al*, 1990). The compulsory practice of screening of all women during pregnancy required by law in France and Austria is expensive and may not be economically feasible in most Asian countries.

The clinical and often fatal toxoplasmosis in patients with acquired immunodeficiency syndrome (AIDS) is also a major medical challenge. Encephalitis is the main clinical manifestation of toxoplasmosis in AIDS patients, resulting from reactivation of a latent infection. Diagnosis of toxoplasmosis in AIDS patients using serological tests is difficult because of their depressed humoral responses.

Toxoplasmosis is widespread and an important cause of abortion and neonatal deaths in sheep, goats, and pigs (Dubey, 1986 1987; Dubey and Beattie, 1988).

NEWER DIAGNOSTIC TESTS AND SUBUNIT VACCINES

Recent studies indicate that the persistence of live organisms in the host is not necessary for the maintenance of protective immunity (Waldeland and Frenkel, 1983). Fortunately, all strains of *T. gondii* so far investigated share important antigens (Cesbron-Delauw *et al*, 1989; Burg *et al*, 1988; Kasper, 1989; Couvreur *et al*, 1988; Johnson *et al*, 1989). Thus there appears to be no potential strain-dependent vaccination or diagnostic problems. Although a subunit vaccine for toxoplasmosis will take many years to develop, excellent progress has been made in characterizing protective proteins, cloning genes encoding these proteins, and making fusion proteins in vectors (Hermentin and Aspöck, 1988; Johnson, 1989). Genes for at least 3 proteins (P30, P22 and P14) have been cloned and expressed in vectors (Burg *et al*, 1988; Kasper, 1989; Prince *et al*, 1990; Johnson, 1989). Some of these cloned and amplified genes are being explored for diagnosis (Decoster *et al*, 1988; Johnson and Illana, 1991; Tenter and Johnson, 1991). With refinement leading to mass production, the cost might be lowered so that DNA probes can be used for diagnosis (Burg *et al*, 1989; Grover *et al*, 1990).

CONTROL STRATEGIES

Strategies to control toxoplasmosis should include prevention of infection in livestock, identification of infected animals in the food chain, removal or treatment of infected carcasses to render the meat safe for human consumption, and prevention and treatment in populations at risk (AIDS patients, transplant recipients, pregnant women and animals).

Toxoplasma gondii tissue cysts can be rendered noninfective by heating meat to 67° C (Dubey *et al*, 1990), by freezing at –12° C (Kotula *et al*, unpublished) and by irradiation (Dubey *et al*, 1986) at 50 kilorads of cesium 137 without affecting the quality of meat.

Prevention and control

To prevent infection of human beings by *T. gondii*, hands should be washed thoroughly with soap and water after handling meat. All cutting boards, sink tops, knives, and other materials coming in contact with uncooked meat should be washed with soap and water because the stages of *T. gondii* in meat are killed by water. Meat of any animal should be cooked to 70° C before human or animal consumption, and tasting meat while cooking or seasoning homemade sausages should be avoided. Pregnant women, especially, should take precautions when handling cats, soil, and raw meat. Pet cats should be fed only dry, canned, or cooked food. The cat litter should be emptied every day, preferably not by a pregnant woman. Gloves should be worn while gardening. Vegetables should be washed thoroughly before eating because they may have been contaminated with cat feces. Expectant mothers should be aware of the dangers of toxoplasmosis. Euthanasia of the pet cat will not solve the problem.

Cats should be neutered to control the feline population on the farm. Pigs and other dead animals should be removed promptly to prevent cannibalism by pigs and scavenging by cats. Sheep that have aborted due to toxoplasmosis usually do not have recurrent toxoplasmic abortions, and thus can be saved for future breeding. Fetal membranes and dead fetuses should not be handled with bare hands and should be buried or incinerated to prevent infection of felids and other animals on the farm. Cats should not be allowed near pregnant sheep and goats. Grain should be kept covered to prevent oocyst contamination.

To prevent infection of zoo animals with *T. gondii*, cats, including all wild Felidae, should be housed in a building separate from other animals, particularly marsupials and New World monkeys. Cats as a rule should not be fed uncooked meat. However, if a choice has to be made, frozen meat is less infective than fresh meat, and beef is less likely to contain *T. gondii* than is horse meat, pork, or mutton. Dissemination of *T. gondii* oocysts in the zoo should be prevented because of potential exposure of children. Brooms, shovels, and other equipment used to clean cat cages, and cat enclosures should be autoclaved or heated to 70° C for at least 10 minutes. While cleaning cages, animal caretakers should wear masks and protective clothing. Feline feces should be removed daily to prevent sporulation of oocysts.

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