Toxoplasmosis

Toxoplasma gondii is an obligate intracellular protozoan. It derives its name from a North African rodent the gondi, from which it was first isolated in 1908. First case of a congenitally infected human baby was reported in 1923. Until 1969, life cycle of parasite was fully elucidate with the discovery of its definitive host, cats and other felines. Its life cycle includes two phases called the intestinal (or enteroepithelial) and extraintestinal phases.

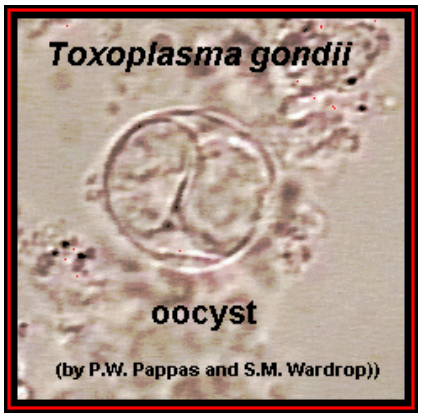
Toxoplasma gondii:

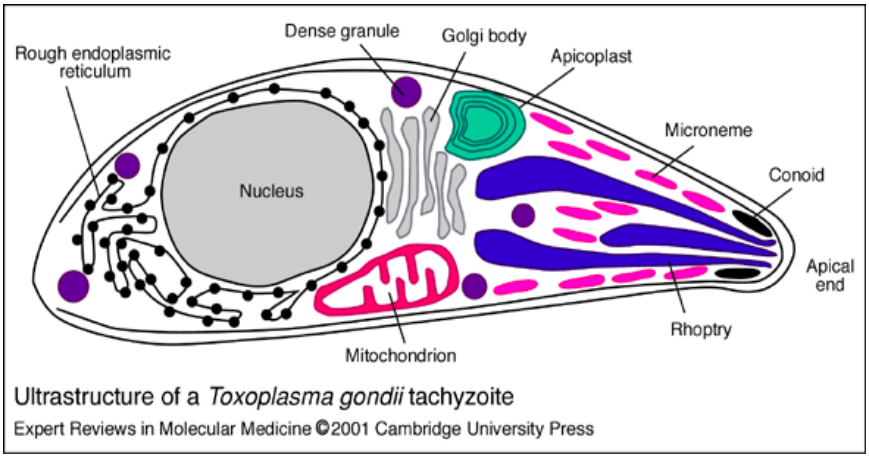
Toxoplasmosis is the result of infection by Toxoplasma gondii, an obligate intracellular protozoan parasite in the phylum Apicomplexa.

The major forms of the parasite are:

Oocyst:

Oocyst are formed as a results of fertilization between male and female gametocytes and are found in the epithelial cells of the intestines of definitive host. They are oval and 10-12 μm in diameter. Oocysts are excreted in the faeces of the cat, contamination with which results in human infection. Oocysts are highly resistant to environmental conditions and can remain infectious for as long 18 months in water or warm, moist soils. They do not survive well in arid, cool climates.



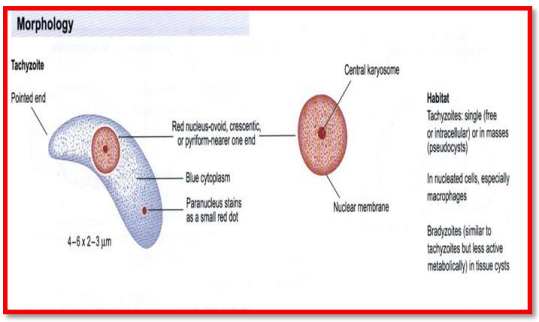


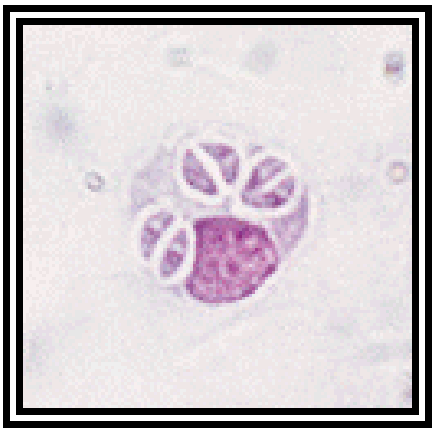
Ultrastructure of a *Toxoplasma gondii* tachyzoite

Expert Reviews in Molecular Medicine ©2001 Cambridge University Press

Trophozoites:

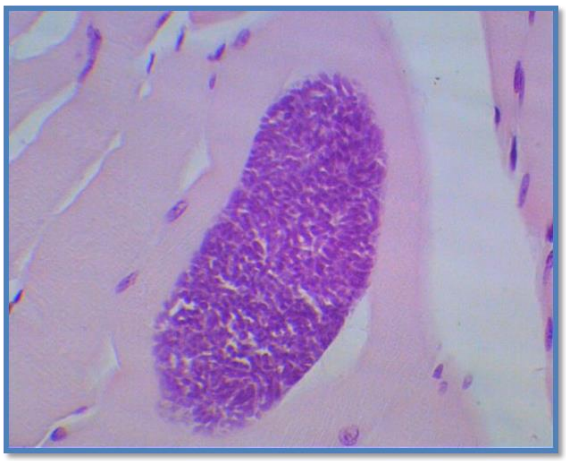
Trophozoites crescent shaped with one pointed end and the other rounded end, and measure approximately 3-7µm, released from the ingested oocysts, invade epithelial cells of the intestinal tract of the host, disseminate via blood and lymph to most of the organs. multiply in a host cell by a process known as internal budding. The rapidly proliferating trophozoites, as known as tachyzoites. The trophozoites are either eliminated by the immune system of the host or by a drug or they are transformed into cysts. Tissue cysts can remain infectious for weeks in body fluids at room temperature, and in meat for as long as the meat is edible and uncooked. Tachyzoites are more fragile and can survive in body fluids for up to a day and in whole blood for as long as 50 days at 4°C.



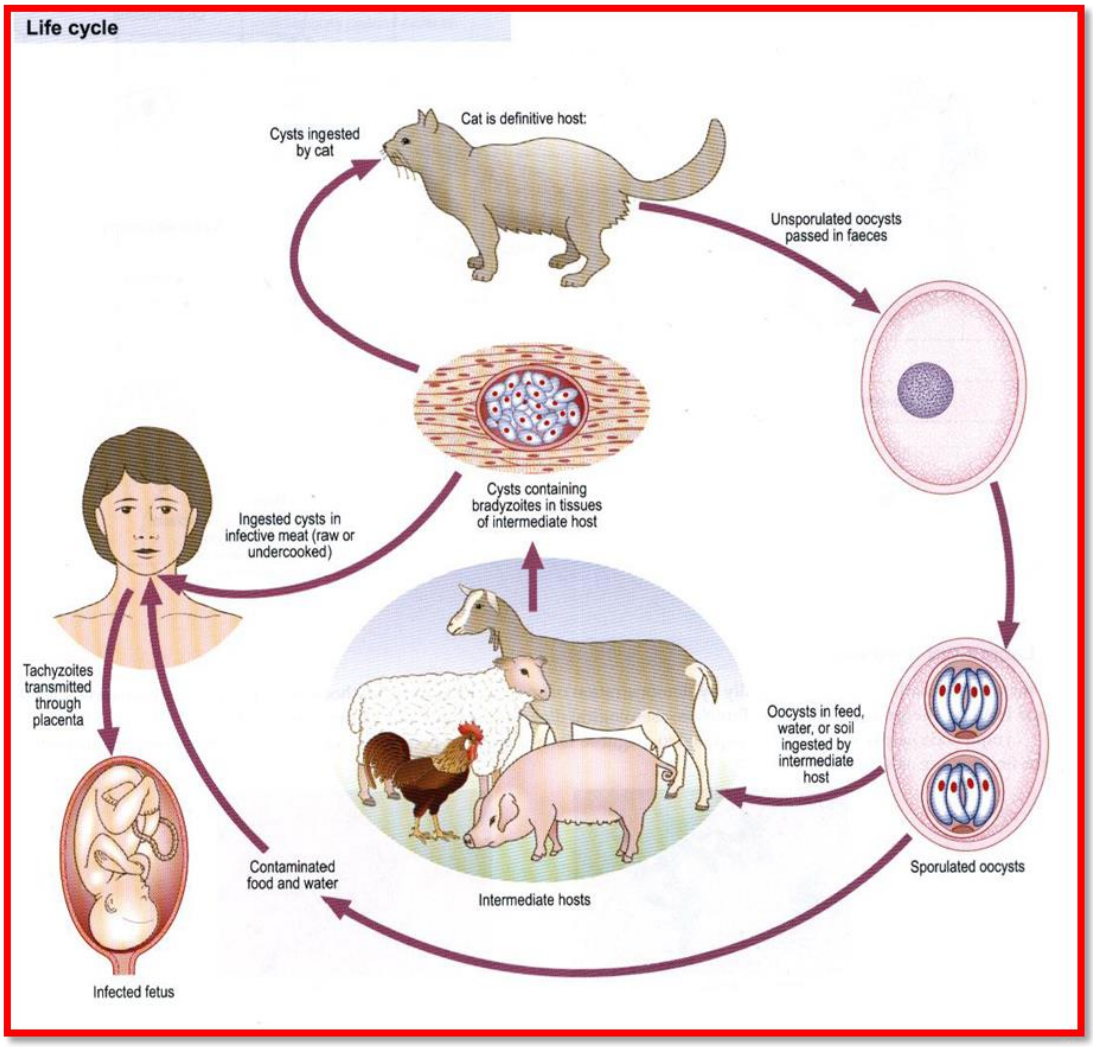


Tissue cysts:

Tissue cysts are 10-100 µ in diameter and contain thousands of slowly multiplying forms of the parasite known as bradyzoites. Formed within the host cells are early as 7 days after the entry of trophozoites. Predominantly found in heart and skeletal muscles and central nervous system. Known to persist within the tissue for the entire life span of the host and are responsible for the recrudescence of the infection, especially in immuno-compromised hosts.



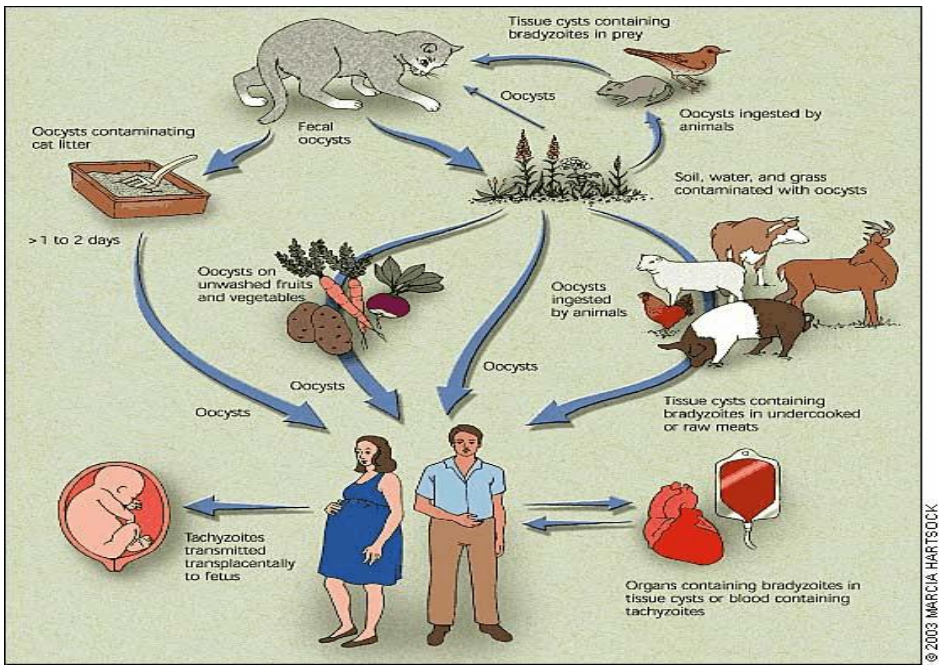
T. gondii is a causative agent of toxoplasmosis has two of hosts: a definitive host - like cats and other felines, an intermediate host - man and other . It multiplies by sexual reproduction in the definitive hosts, and by asexual multiplication in definitive as well as intermediate hosts.



In both kinds of hosts, the Toxoplasma parasite invades cells and forms a space called a vacuole. Inside this specialized vacuole, called a parasitophorous vacuole, the parasite forms bradyzoites, which are the slowly replicating versions of the parasite T. gondii replicates itself (by endodyogeny) until the infected cell fills with parasites and bursts, releasing tachyzoites, the motile, asexually reproducing form of the parasite. . The vacuoles containing the reproductive bradyzoites form cysts mainly in the tissues of the muscles and brain. Since the parasites are inside cells, they are safe from the host's immune system, which does not respond to the cysts.

Geographic Distribution:

Toxoplasmosis is found worldwide. Infections are particularly common in warm, humid climates. Over 500 million humans around the world are infected with T. gondii. App. 90% of the population in France, 40 % in the in the USA and 30% in the UK, 27% in Iraq are infected.



Incubation Period:

- 10 to 23 days after ingesting contaminated meat,
- 5 to 20 days after exposure to infected cats.

Clinical Signs:

Usually asymptomatic. App 10-20% develop lymphadenitis or a mild, flulike syndrome characterized by fever, malaise, myalgia, headache, sore throat, lymphadenopathy and rash. In some cases, may mimic infectious mononucleosis. symptoms usually resolve without treatment within weeks to months, although some cases may take up to a year. Severe symptoms, including myositis, myocarditis, pneumonitis and neurologic signs including facial paralysis, severe reflex alterations, hemiplegia and coma, are possible but rare. Ocular toxoplasmosis with uveitis, often

unilateral, can be seen in adolescents and young adults; this syndrome is often the result of an asymptomatic congenital infection or the delayed result of a postnatal infection.

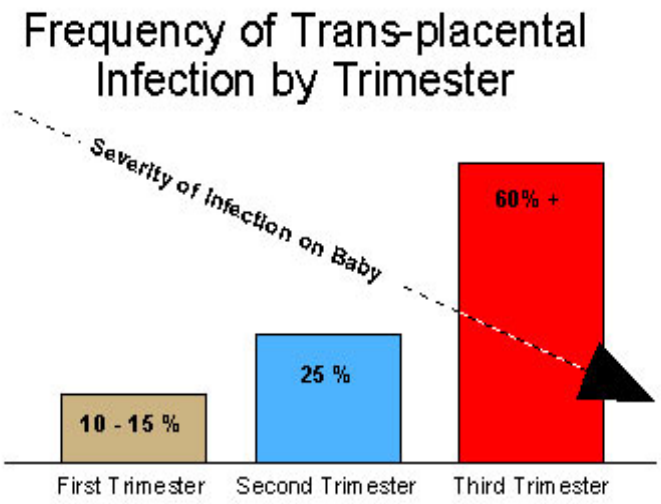
In immunosuppressed patients:

- Toxoplasmosis is often severe.
- Neurologic disease is the most common sign, particularly in reactivated infections.
- Symptoms are:
    - Encephalitis,
    - Necrosis from multiplication of the parasite can cause multiple abscesses in nervous tissue, with the symptoms of a mass lesion.
    - Chorioretinitis, myocarditis and pneumonitis.
    - Both humoral and cell mediated immune responses are stimulated in normal individuals. CMI is protective and humoral response is of diagnostic value.
    - Since the parasites are inside cells, they are safe from the host's immune system, which does not respond to the cysts.
    - Unlike the bradyzoites, the free tachyzoites are usually efficiently cleared by the host's immune system, although some of them manage to infect cells and form bradyzoites, thus maintaining the infection.

Toxoplasmosis during pregnancy:

- not a cause of habitual abortion.
- Only pregnent women with primary active infection leads to Toxoplasmosis.
- It is a congenital toxopasmosis.
- Development of active immunity once, protects subsequent pregnancies.

Rate of Transmission:

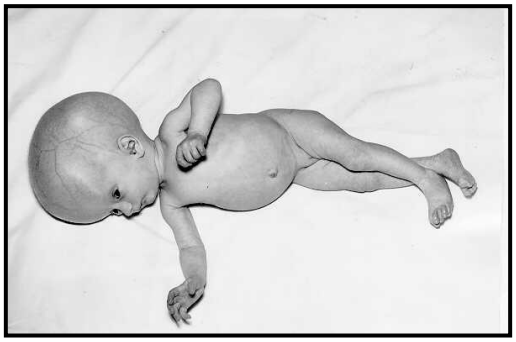


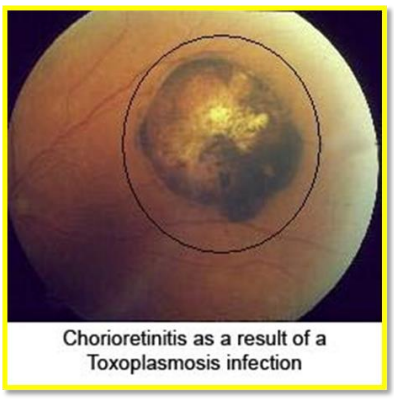
Congenital toxoplasmosis :

The consequences of the infection of fetus can be very different between subclinical to very serious.

- Abortion or still birth.
- Overt disease - Symptoms with classical triad.
  - Hydrocephalus
  - Intracranial calcification
  - Chorioretinitis
- Sub clinical infection - Usually asymptomatic at birth

Later on develops hearing defects, visual defects, mental retardation and learning disabilities, even severe, life-threatening infections later in life, if left untreated.




Chorioretinitis as a result of a Toxoplasmosis infection

mild cases with only slightly diminished vision. Ocular disease is usually bilateral. The most common symptom is chorioretinitis but strabismus, nystagmus and microphthalmia may also be seen. Infants infected late in gestation may have a fever, rash, hepatomegaly, splenomegaly, pneumonia or a generalized infection.

Both humoral and cell mediated immune responses are stimulated in normal individuals. CMI is protective and humoral response is of diagnostic value.

Since the parasites are inside cells, they are safe from the host's immune system, which does not respond to the cysts.

Unlike the bradyzoites, the free tachyzoites are usually efficiently cleared by the host's immune system, although some of them manage to infect cells and form bradyzoites, thus maintaining the infection.

Diagnosis of toxoplasmosis:

May be established by

- Serological tests,
- Polymerase chain reaction (PCR),
- Histological demonstration of the parasite.
- Or isolation of the organism

Serological Tests:

- **IgM test**
  - Determine recent infection.
  - Significant potential of misinterpretation of +ve result, should be confirmed by other tests.
  - Kits often have low specificity
  - IgM antibodies can persist for months to more than one year.
  - Persistence of these IgM antibodies does not appear to have any clinical relevance

- **IgA Antibodies:**
    - IgA antibodies may be detected in sera of acutely infected adults and congenitally infected infants using ELISA .
    - May persist for many months to more than one year.
    - Of little additional assistance for diagnosis of the acute infection in the adult.
    - Has increased sensitivity of IgA assays over IgM assays hence useful for diagnosis of congenital toxoplasmosis.
- **IgE Antibodies:**
    - Detectable by ELISA in sera of acutely infected adults, congenitally infected infants, and children with congenital toxoplasmic chorioretinitis.
    - The duration of IgE seropositivity is less than with IgM or IgA antibodies and hence appears useful as an adjunctive method for identifying recently acquired infections.
    - Recently, several tests for avidity of toxoplasma IgG antibodies have been introduced to help discriminate between recently acquired and distant infection.

IgG Antibodies

- Recently, several tests for avidity of toxoplasma IgG antibodies have been introduced to help discriminate between recently acquired and distant infection.
- Avidity is the binding force of the antibody (serum specimen) with the corresponding antigen.
- Low avid IgG antibodies in the early stage of infection can be differentiated from high avid antibodies associated with a past infection.
- The determination of IgG antibody avidity is an additional analysis to the classic serology in regard to the status of a Toxoplasma gondii infection.

confirmatory test, the Toxoplasma Serological Profile (TSP):

TSP, differentiate between recently acquired and chronic infection, is superior to any single serological test.

- TSP consist of -
    - Sabin-Feldman Dye Test (DT)

- ELISA.

Sabin-Feldman Dye Test (DT).:

DT is a sensitive and specific neutralization test in which live organisms are lysed in the presence of complement and the patient's IgG T. gondii-specific antibody. The test is based on the presence of certain antibodies that prevent methylene blue dye from entering the cytoplasm of Toxoplasma organisms. normal toxoplasma cells become rounded, and the nucleus and cytoplasm deeply stained, when treated with methylene blue; conversely, when dye is mixed with organisms and antibody, the cells retain their crescent shape and only the shrunken nuclear endosome is stained.

ELISA :

- Detect IgG, IgM. antibodies

Polymerase Chain Reaction (PCR):

- Used to detect T. gondii DNA in body fluids and tissues.
- Used to diagnose congenital, ocular, cerebral and disseminated toxoplasmosis.
- PCR performed on amniotic fluid has revolutionized the diagnosis of fetal T. gondii infection .
- PCR has allowed detection of T. gondii DNA in brain tissue, cerebrospinal fluid (CSF), vitreous and aqueous fluid, bronch-oalveolar lavage (BAL) fluid, urine, amniotic fluid and peripheral blood.

Avoiding toxoplasmosis:

1. only eat meat which has been thoroughly cooked (i.e. with no trace of blood or pinkness) .
2. wash hands after preparing raw meat.
3. wash all fruit and vegetables thoroughly to remove all traces of soil .
4. don’t drink unpasteurised goats’ milk or eat dairy products made from it.
5. wear gloves when gardening and wash hands.
6. if you eat while gardening wash your hands first, and try to avoid gardening in areas which may have been soiled with cat faeces .

Treatment:

- Spiramycin is drug of choice.
- If fetus is infected there can be replaced by or addition of Sulfadiazine + pyrimethamine . Oral administration of pyrimethamine, usually accompanied by sulfadiazine, is the treatment of choice at this time. Since pyrimethamine is an antifol and thus can cause folic acid deficiency in the host, supplemental folic acid may also be added to the regimen as a precautionary measure.
- Clindamycin or Dapson : If patient has sulfa drug allergy.

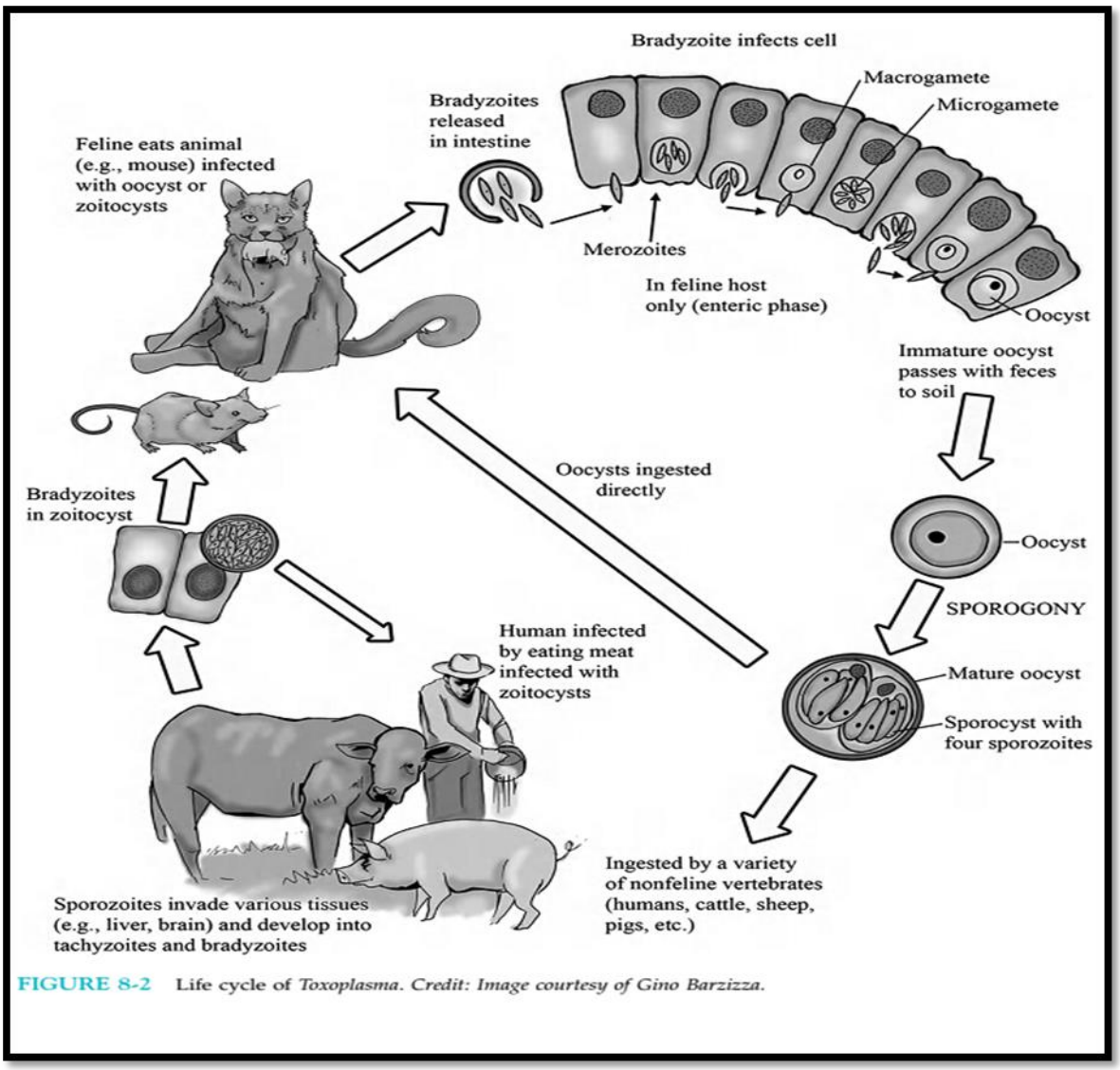


FIGURE 8-2 Life cycle of *Toxoplasma*. *Credit: Image courtesy of Gino Barzizza.*