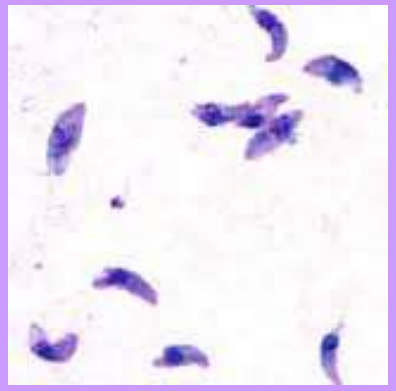


Toxoplasma gondii (toxoplasmosis)

Toxoplasmosis is an infectious parasitic zoonosis with world-wide distribution, caused by *Toxoplasma gondii,* a protozoa that can infect man and warm-blooded animals.

Toxoplasma gondii

T.gondii was first discovered in 1908 in desert rodent ,the gondii, in a colony maintained at the Pasteur institute in Tunis.

T.gondii

- T.gondii is a intracellular parasite in many tissues, such as intestinal epithelum and muscle.
- The organisms can be found also free in the blood and peritoneal exudate.
- In the fetal life, the parasite infection can lead to death (Human & sheep)

- *Toxoplasma gondii* is an intestinal coccidium that parasitizes members of the cat family as definitive hosts and has a wide range of intermediate hosts.

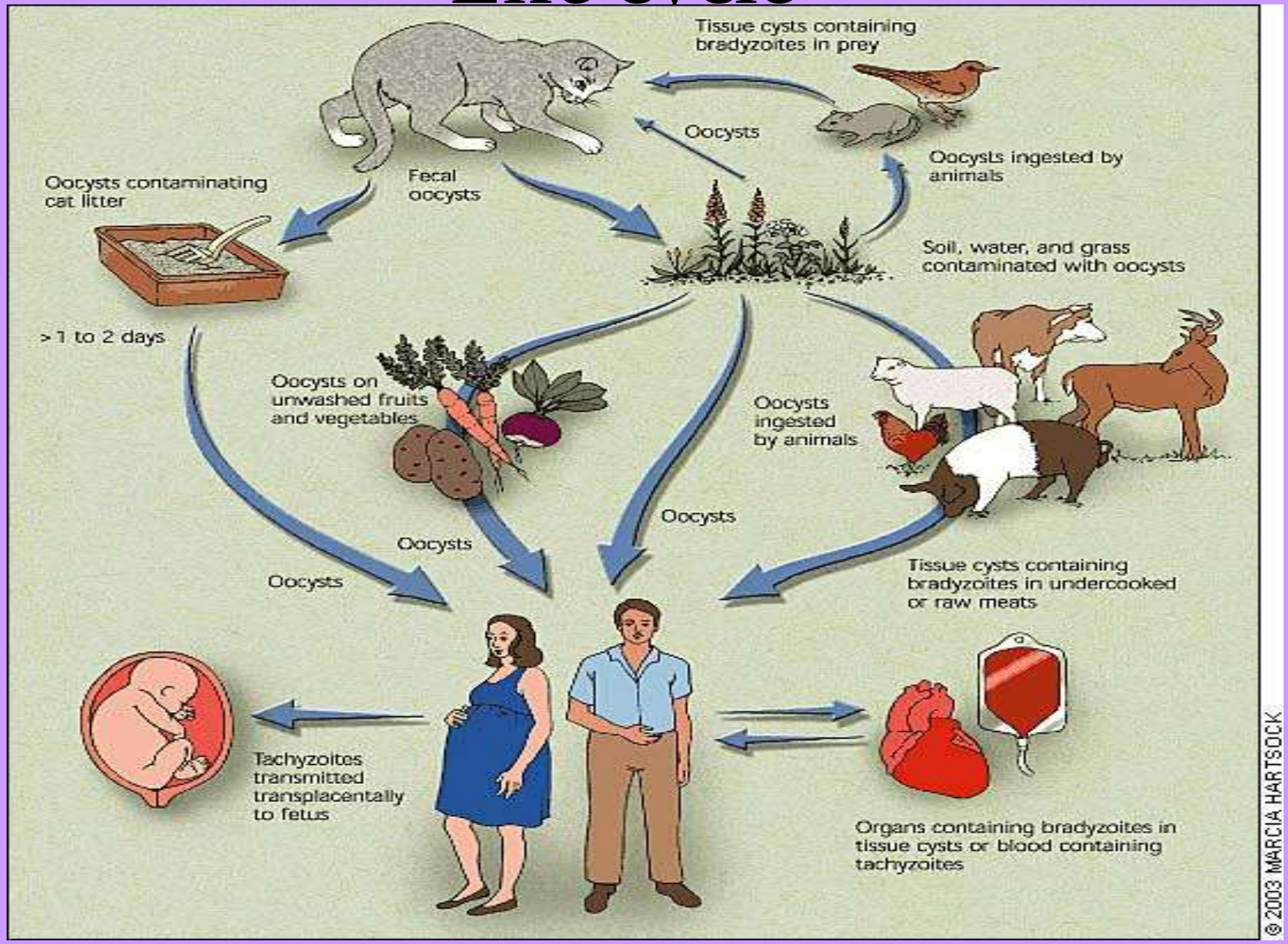
Definitive host

- Mainly domestic and wild cats.
- Cats can become infected by ingesting sporulated oocyst or infected rodent or a bird.

Intermediate host

- Human, cattle, birds, rodents, pigs, and sheep.
- Humans get the disease through* ingestion of a cyst, *infected raw meat, vegetables contaminated with oocysts, *transplacentally,
- * organ transplantation or blood transfusion.

Life cycle


Tissue cysts containing bradyzoites in prey
Oocysts
Oocysts ingested by animals
Oocysts contaminating cat litter
Fecal oocysts
Soil, water, and grass contaminated with oocysts
> 1 to 2 days
Oocysts on unwashed fruits and vegetables
Oocysts ingested by animals
Oocysts
Oocysts
Oocysts
Tissue cysts containing bradyzoites in undercooked or raw meats
Tachyzoites transmitted transplacentally to fetus
Organs containing bradyzoites in tissue cysts or blood containing tachyzoites
© 2003 MARCIA HARTSOCK

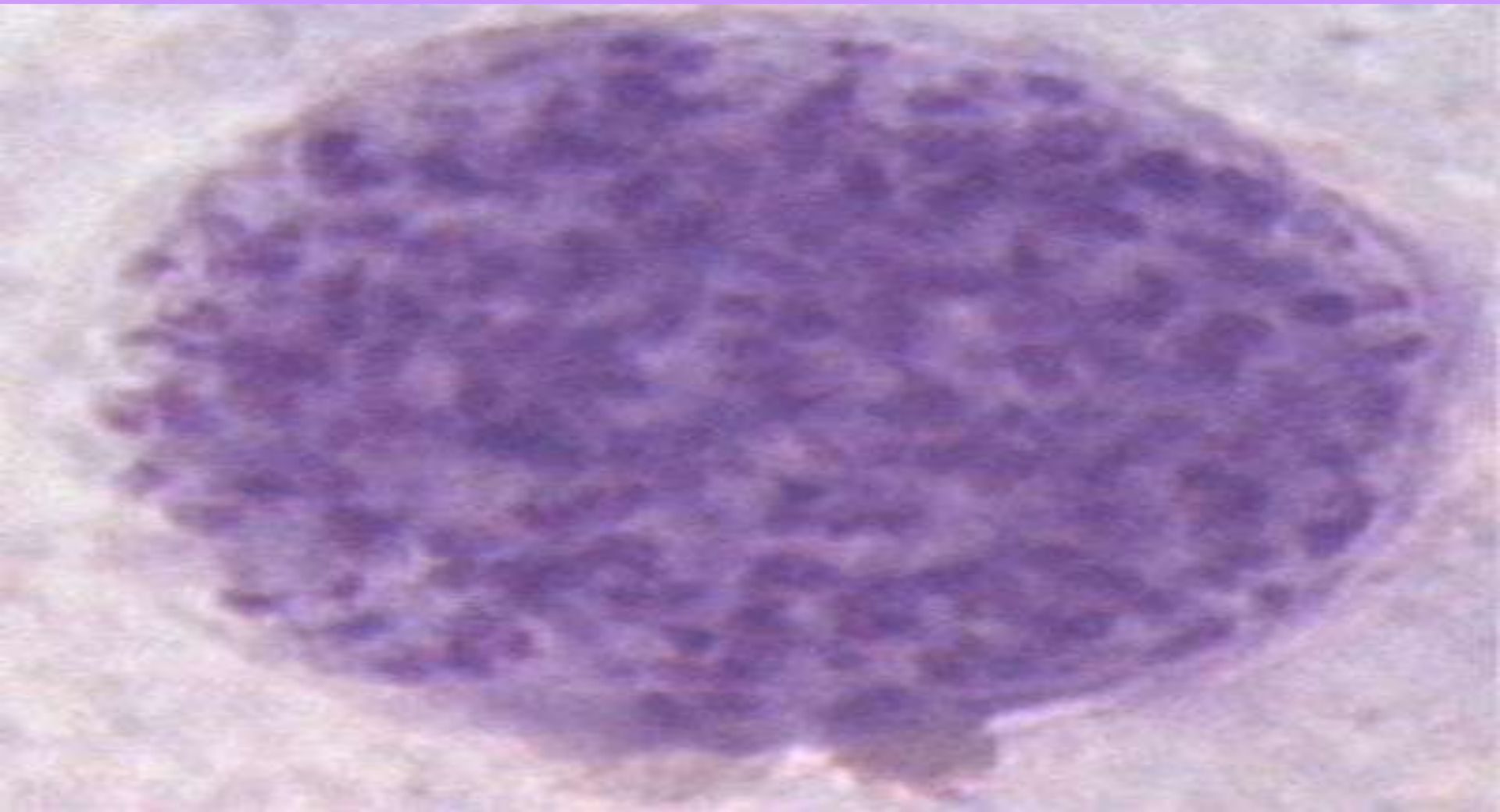
The lifecycle of *T. gondii* can be broadly summarized into two components:

1) a sexual component that occurs only within cats (felids, wild or domestic),

2) an asexual component that can occur within virtually all warm-blooded animals, including humans, cats, and birds.

Because *T. gondii* can sexually reproduce only within cats, they are defined as the definitive host of *T. gondii*. All other hosts – hosts in which only asexual reproduction can occur – are defined as intermediate hosts.

The wall of mature pseudocysts is believed to represent a combination of host and parasitic components.



Tissue cysts of *T gondii.*

A.

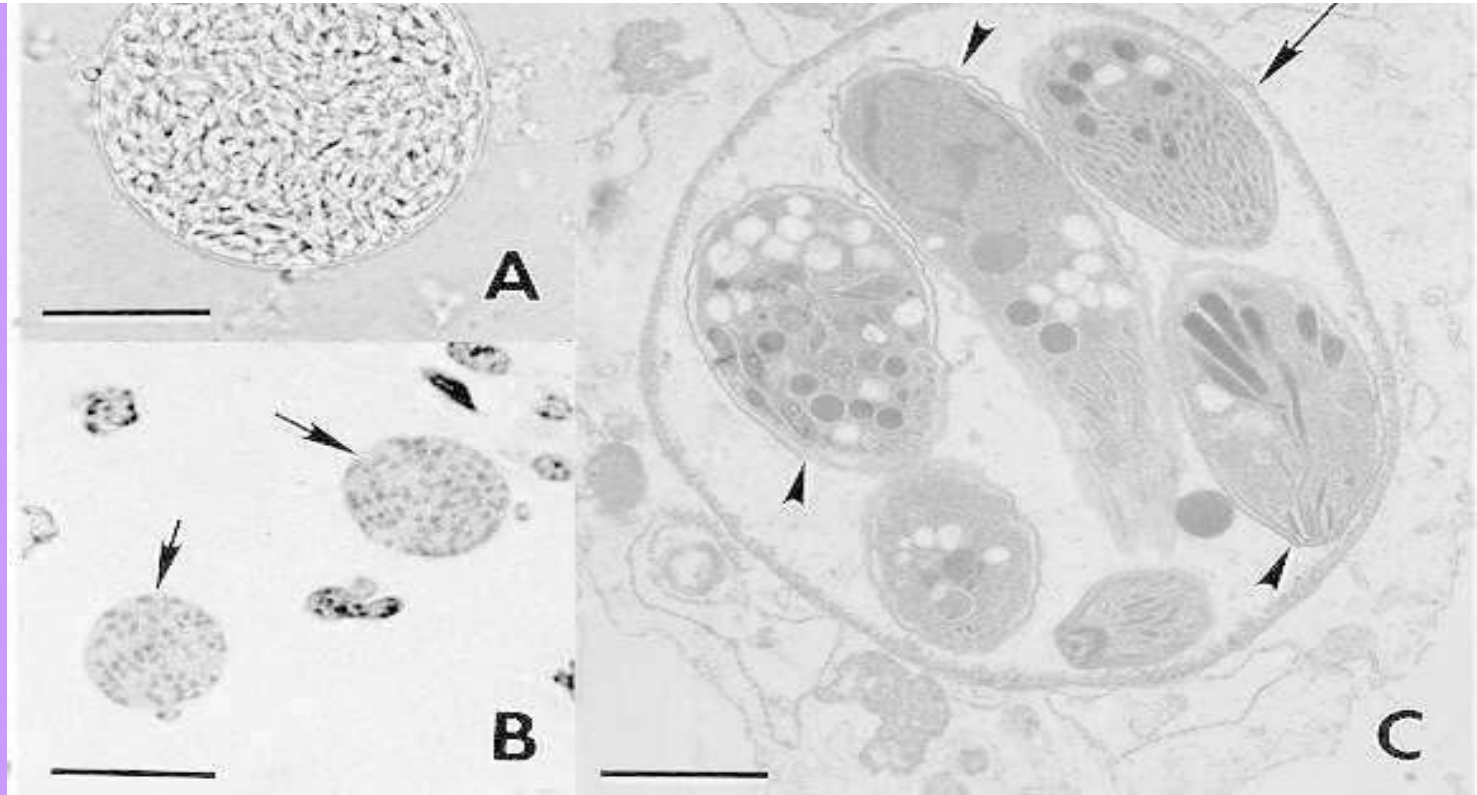
Tissue cyst freed from mouse brain. Note a thin (arrow) cyst wall enclosing hundreds of bradyzoites. Unstrained. Bar = ٢٠ µm.

B.

Two tissue cysts (arrows) in section of brain. Hematoxylin and eosin stain. Bar = ٢٠ µm.

C.

Transmission electron micrograph of a small tissue cyst in cell culture. Note thin cyst wall (arrow) enclosing ٦ bradyzoites (arrowheads .(



Tachyzoites of T gondii

A.

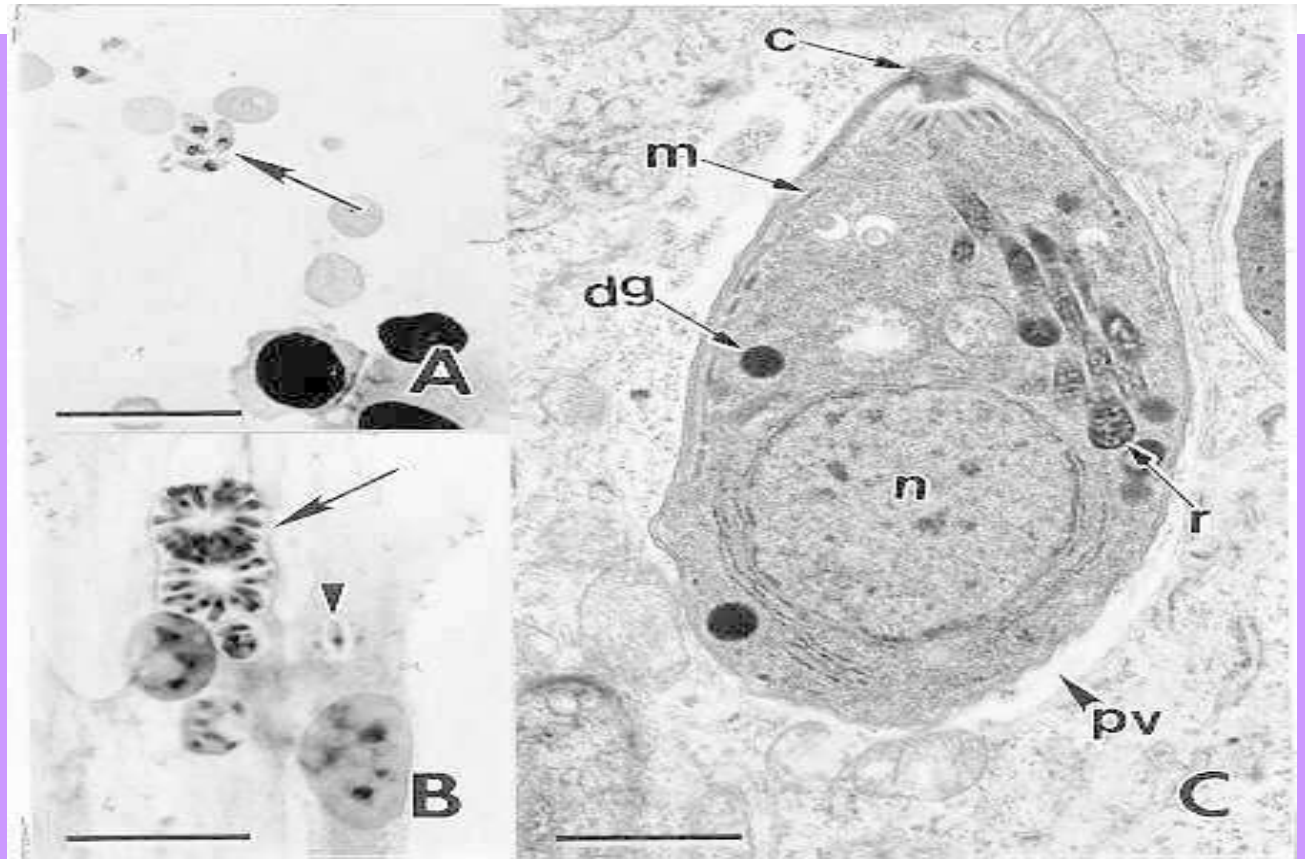
Extracellular (arrow) released from host cells. Compare their size with red blood cells and a lymphocyte. Impression smear, Giemsa stain. Bar = ٢٠ μm.

B.

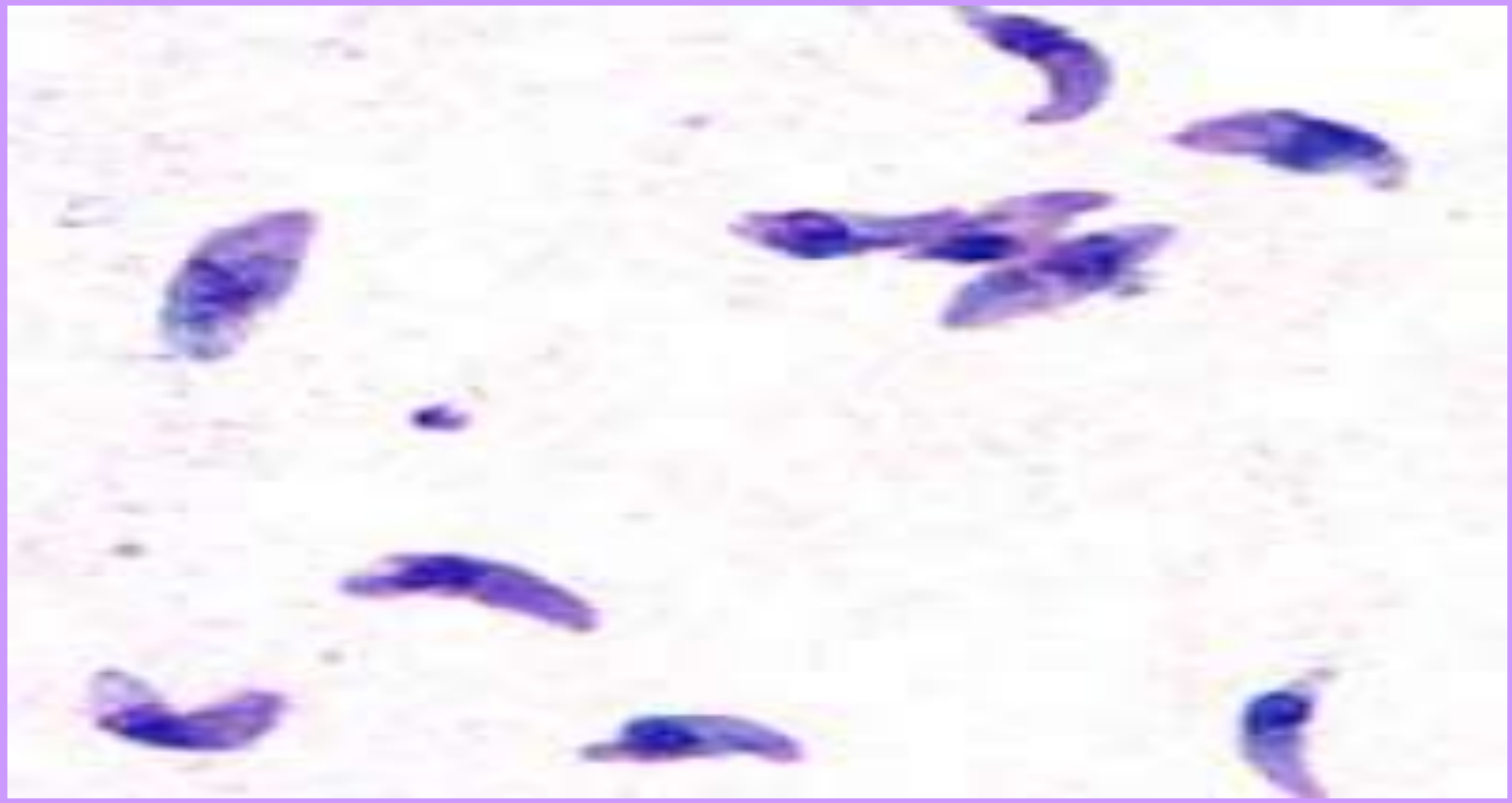
Intracellular in cell culture. Note a group arranged in a rosette (arrow) and vacuole (arrowhead) around a tachyzoite. Immunohistochemical stain with a tachyzoite-specific monoclonal antibody. Bar = ٢٠ μm.

C.

Transmission electron micrograph of an intracellular tachyzoite. Note a parasitophorous vacuole (PV) around the tachyzoite .



Tachyzoite stage



Tachyzoites are typically crescent shaped with a prominent, centrally placed nucleus."

- There are 3 major genotypes (type I, type II, and type III) of *T gondii*. These genotypes differ in their pathogenicity and prevalence in people. In Europe and the United States, type II genotype is responsible for most cases of congenital toxoplasmosis.

Economic impact

- Toxoplasma gondii has a devastating economic impact on the countries who export livestock.
- Toxoplasmosis is leading cause of abortion stillbirths, in sheep and goats.

Mode of infection

Toxoplasma can infect animals and man by the three forms of its life cycle:

(1) orally, by the ingestion of oocysts in cat faeces,

(2) by ingestion of cysts lodged in tissues of intermediate hosts, and

(3) via the uterus, by transplacental transmission of tachyzoites.

(4) *T. gondii* can also be transmitted in products of blood origin, or by ingestion of tachyzoites in non-pasteurized goat milk

Pathogenesis

Host cells are destroyed by active multiplication of *T gondii*. Necrotic foci may result.

Congenital infection often involves the retina and brain; focal chorioretinitis may result in impaired vision. Brain involvement in immunosuppressed patients may lead to large necrotic abscesses. Disease reactivation in immunosuppressed patients may result from the rupture of a tissue cyst.

Clinical Findings

The tachyzoite is the stage responsible for tissue damage. therefore, clinical signs depend on:

- the number of tachyzoites released,
- the ability of the host immune system to limit tachyzoite spread,
- and the organs damaged by the tachyzoites.

Because adult immunocompetent animals control tachyzoite spread efficiently, toxoplasmosis is usually a subclinical illness.

- in young animals, particularly puppies, kittens, and piglets, tachyzoites spread systemically and cause interstitial pneumonia, myocarditis, hepatic necrosis, meningoencephalomyelitis, chorioretinitis, lymphadenopathy, and myositis.

- The corresponding clinical signs include fever, diarrhea, cough, dyspnea, icterus, seizures, and death.
- *T gondii* is also an important cause of abortion and stillbirth in sheep and goats and sometimes in pigs.
- **After infection of a pregnant ewe, tachyzoites spread via the bloodstream to placental cotyledons, causing necrosis.**

Finally, immunocompromised adult animals (eg, cats infected with feline immunodeficiency virus) are extremely susceptible to developing acute generalized toxoplasmosis.

- *Toxoplasma gondii* usually parasitizes both definitive and intermediate hosts without producing clinical signs.
- In humans, severe disease is usually observed only in congenitally infected children and in immunosuppressed individuals, including patients with acquired immune deficiency syndrome (AIDS).

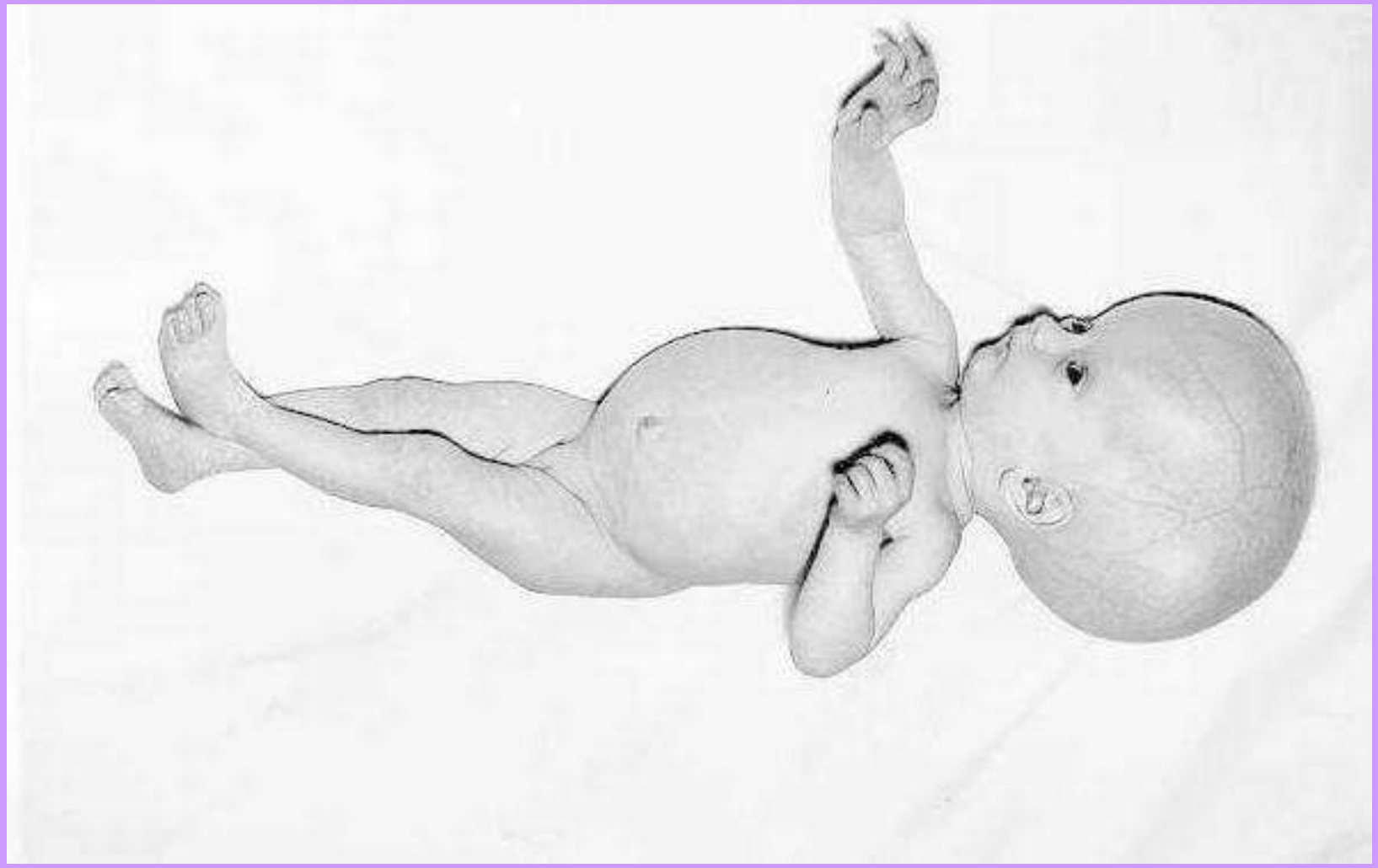
- Lymphadenitis is the most common manifestation in humans. Any node can be infected, but the deep cervical nodes are the most commonly involved. Infected nodes are tender and discrete but not painful; the infection resolves spontaneously in weeks or months.
- Lymphadenopathy may be accompanied by fever, malaise, fatigue, muscle pains, sore throat, and headache.

- Encephalitis is an important and severe manifestation of toxoplasmosis in immunosuppressed patients including patients with AIDS.
- Symptoms may include headache, disorientation, drowsiness, hemiparesis, reflex changes, and convulsions. Coma and death may ensue.

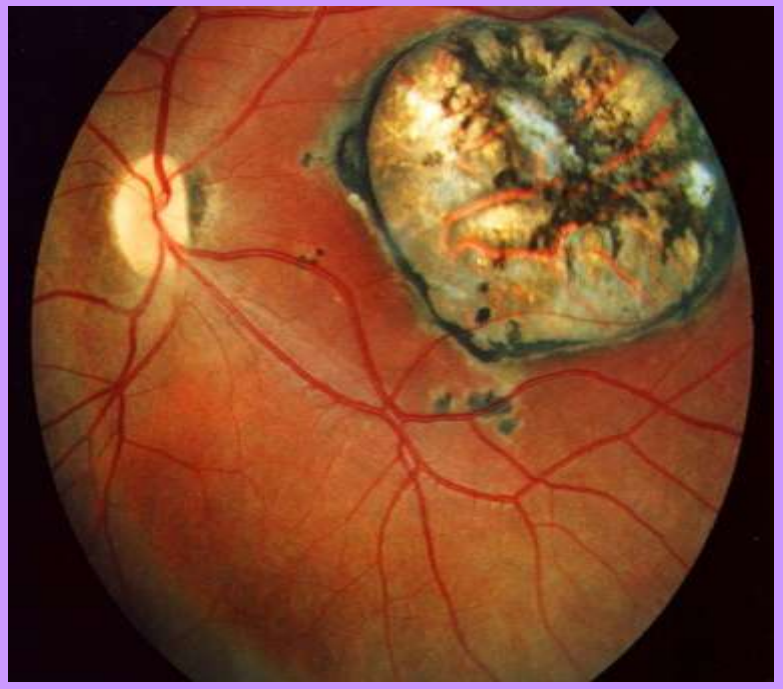
Prenatally acquired *T gondii*

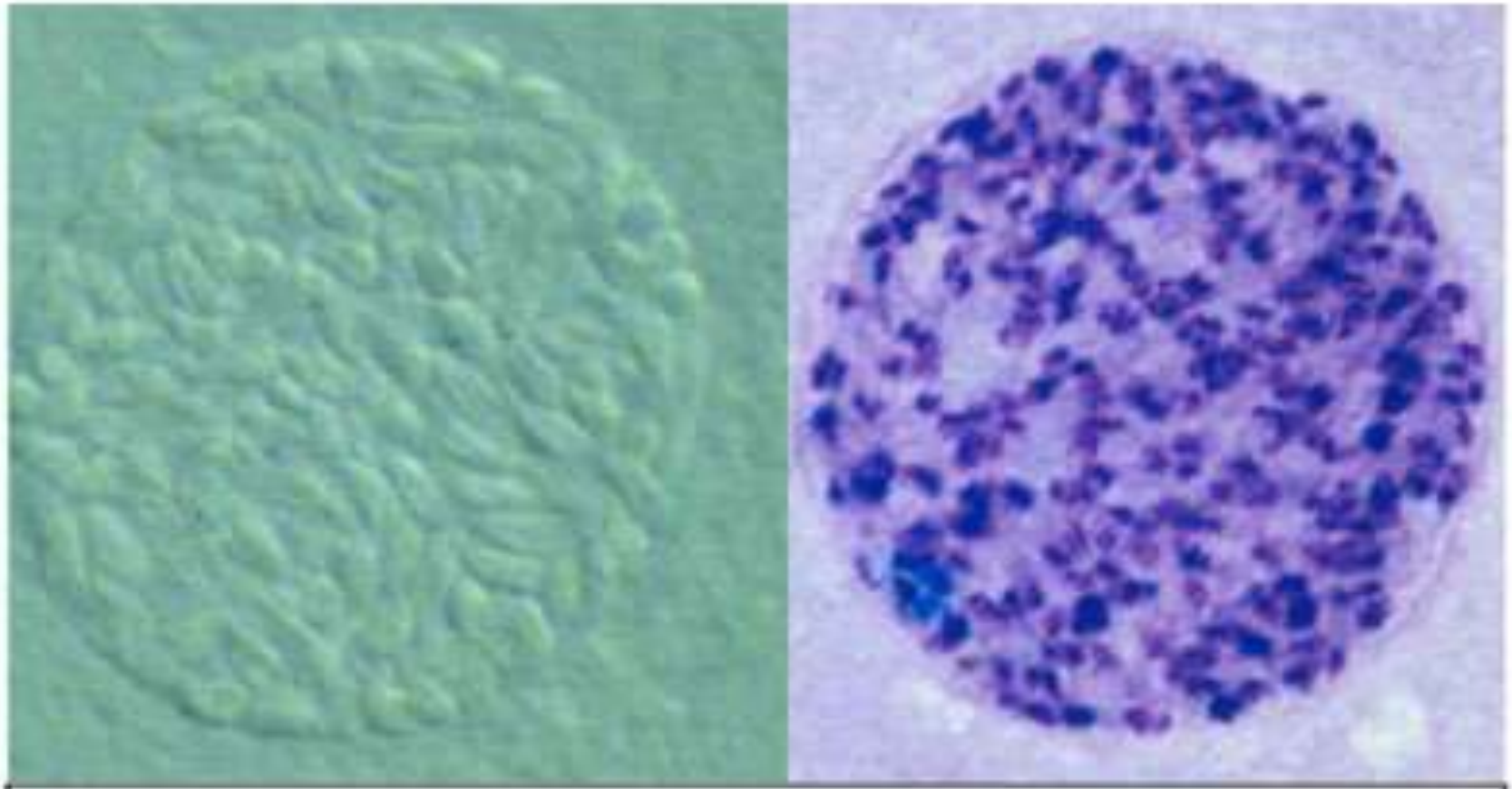
- infects the brain and retina and can cause a wide spectrum of clinical disease.
- Mild disease may consist of slightly diminished vision,
- whereas severely diseased children may exhibit a classic tetrad of signs: retinochoroiditis, hydrocephalus, convulsions, and intracerebral calcifications. Hydrocephalus is the least common but most dramatic lesion of congenital toxoplasmosis.

Girl with hydrocephalus due to congenital toxoplasmosis



Chorioretinitis is an inflammation of one of the layers of the eye,





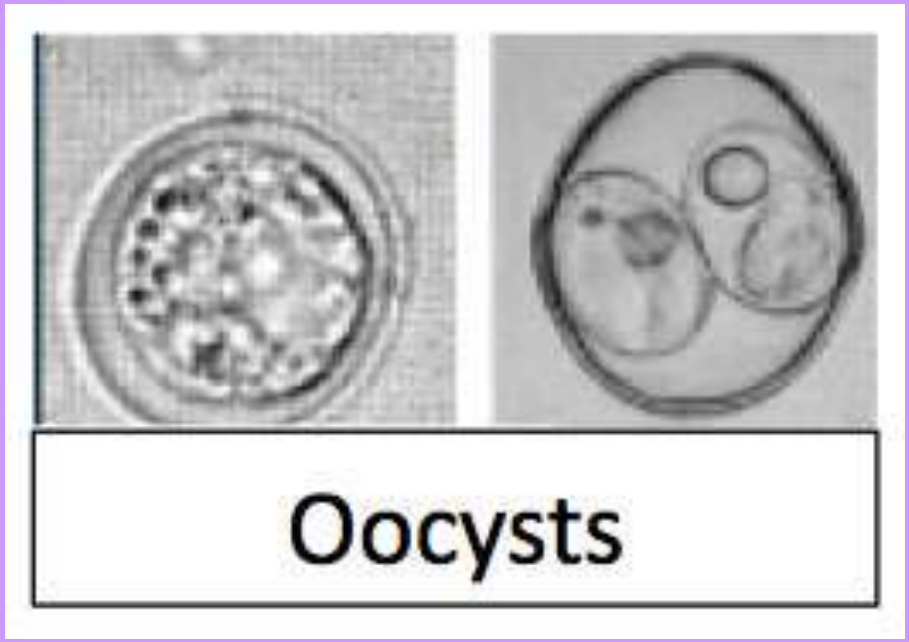
Bradyzoites

- Immunity – no additional abortions or clinical signs if re-exposed

Diagnosis

Diagnosis is made by **biologic, serologic, or histological** methods, or by combination of the above.

1. Fecal examination (e.g., flotation) can identify active shedding of unsporulated oocysts (10 µm by 12 µm) are shed in feline feces. , which only occurs over a short period (i.e., 1 to 3 weeks) so it is of limited value

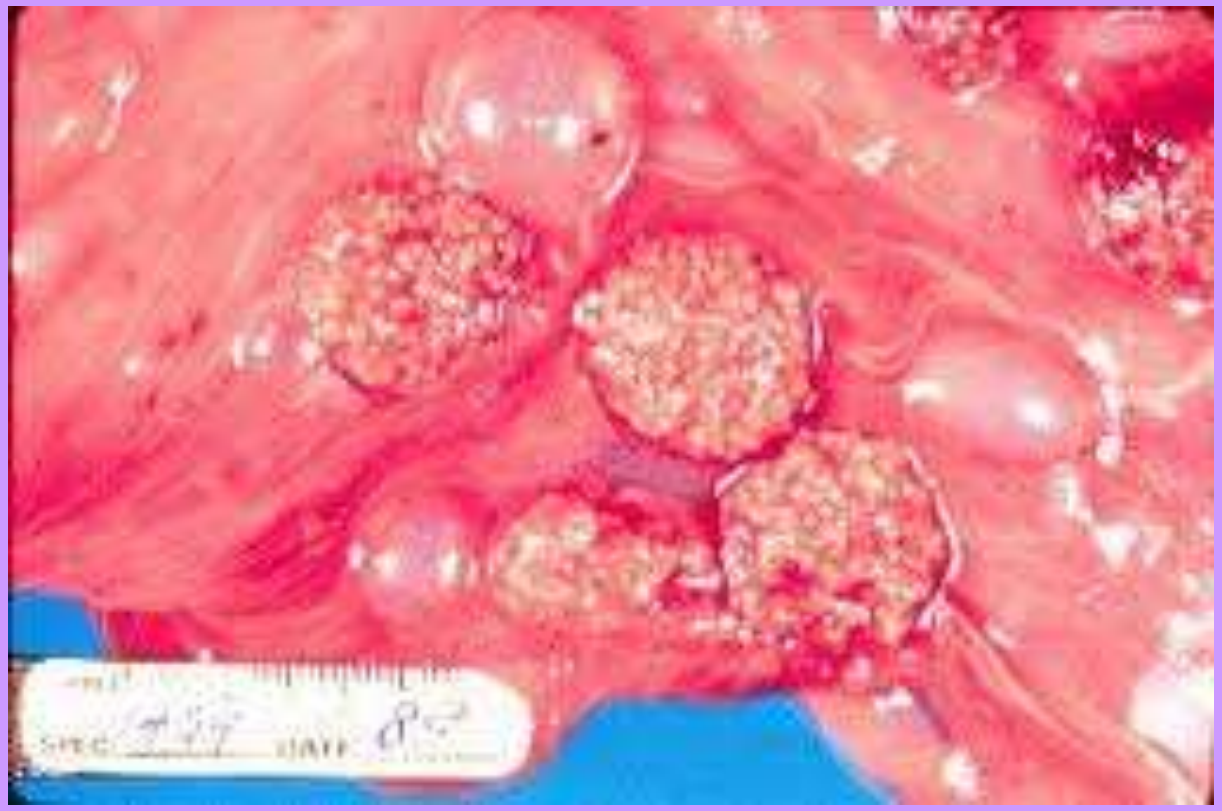


2. A rapid, direct and simple method is the detection of T. gondii in air-dried, Geimsa-stained slides of centrifuged sediment of fetus stomach contents, vaginal discharge(immediately after abortion) CSF or of brain aspirate or in impression smears of biopsy tissue as cotyledons or faetal tissues. Tachyzoites may appear inside macrophages or free with **red** nucleus and **blue** cytoplasm. tachyzoites may also be in circulating WBC, marrow, lung, spleen.

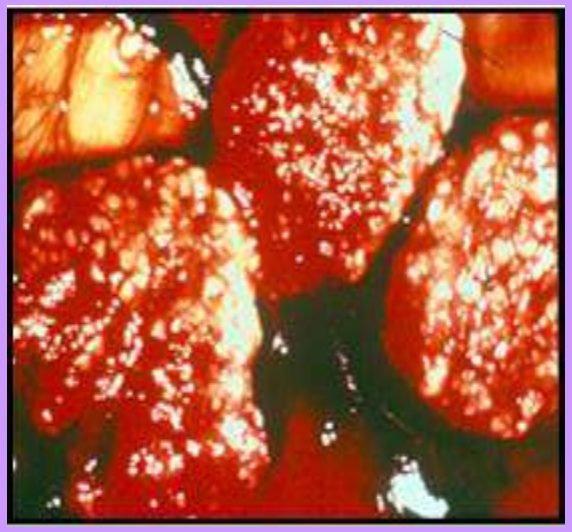
Geimsa stained slide

- Intracellular tachyzoites of *Toxoplasma gondii*.

- **Toxoplasmosis lesions on the cotyledons of a placenta.**

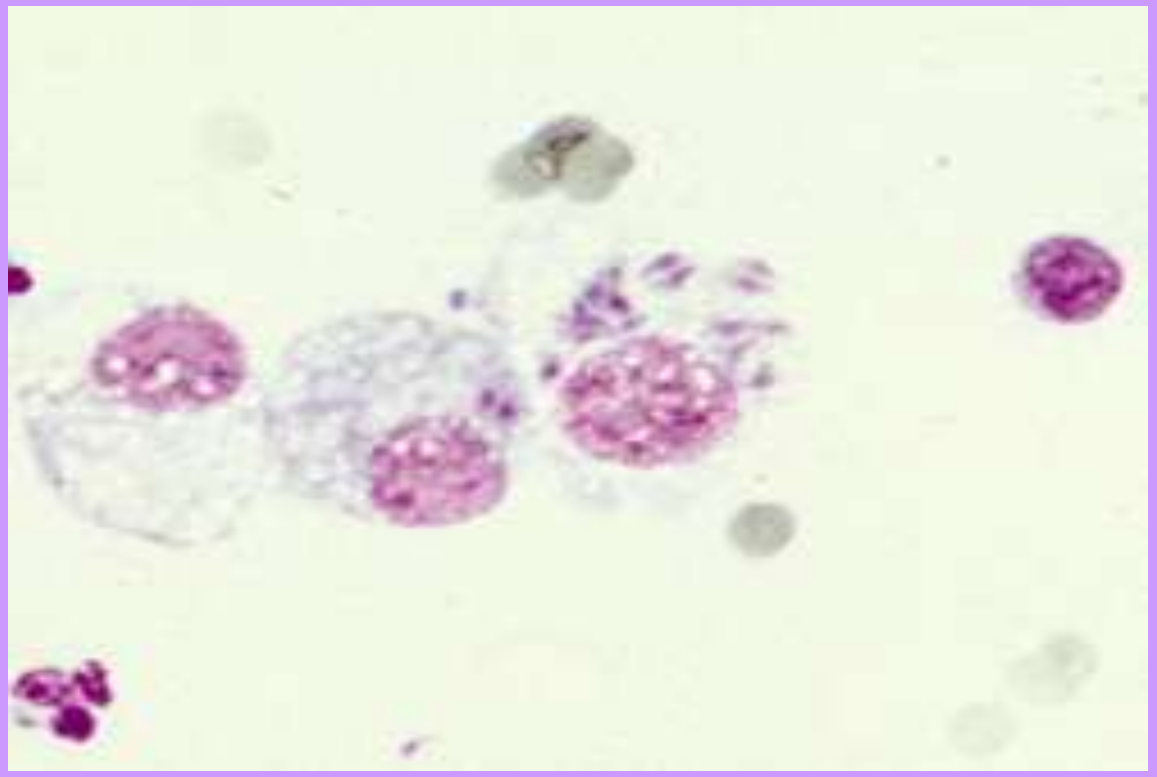


- **Ovine protozoal placentitis, toxoplasmosis, abortion, placenta, sheep**
- oedema of intercotyledonary area, white multifocal necrosis and inflammation of cotyledons
  Toxoplasma gondii-induced abortion in sheep and goats.



- Sheep, placenta. This cotyledon has been immersed in water to demonstrate numerous pale foci of villous mineralization and necrosis.

- Cat, transtracheal aspirate. This transtracheal aspirate fluid contains macrophages with intracytoplasmic *Toxoplasma gondii.*



Diagnosis

- 3. Serological tests: Different serological tests often measure different antibodies that possess unique patterns of rise and fall with time after infection. A combination of serological tests is frequently required to establish whether an individual has been more likely infected in the distant past or has been recently infected.

- **IgM antibodies appear sooner after infection than IgG antibodies but generally do not persist past 3 mo after infection. Increased IgM titers (>1:256) are consistent with recent infection.**
- In contrast, IgG antibodies appear by the fourth week after infection and may remain increased for years during subclinical infection. To be useful, IgG titers must be measured in paired sera from the acute and convalescent stages (3–4 wk apart) and must show at least a **4-fold increase in titer.**

- Serological diagnosis may be accomplished by indirect haemagglutination assay, indirect fluorescent antibody assay, latex agglutination test, dye test or ELISA.

The Sabin- Feldman-dye test uses live, virulent Toxoplasma tachyzoites, a complement-like 'accessory-factor' and test serum.

Sabin–Feldman dye test is a serologic test used to diagnose toxoplasmosis**.** The test is based on the detection of antibodies in patient serum.

- **Serial dilutions of serum are made in test tubes.**
- **then equal amount of live toxoplasma are added to all dilutions. complements are added as as activator.**
- **Add methylene blue stain after a period of incubation.**
- **Made slide and observe the percentage of stained toxoplasma.**

- Antibodies **prevent** **methylene blue** dye from entering the **cytoplasm** **of** ***Toxoplasma*** organisms. If anti-Toxoplasma antibodies are present in the serum.
- because these antibodies are activated by complements and lyses the parasite membrane, and Toxoplasma trophozoites are not stained **(positive result);**
- if there are no antibodies, trophozoites with intact membrane are stained and appear blue under microscope **(negative result)**

4. PCR amplification is used to detect T. gondii DNA in body fluids and tissues. It has been successfully used to diagnose congenital, ocular, cerebral and disseminated toxoplasmosis. PCR performed on amniotic fluid has revolutionized the diagnosis of fetal T. gondii infection by enabling an early diagnosis to be made, thereby avoiding the use of more invasive procedures on the fetus

4. Histological Diagnosis

- **Demonstration of tachyzoites in tissue sections or smears of body fluid (e.g., CSF, amniotic fluid) establishes the diagnosis of the acute infection.**

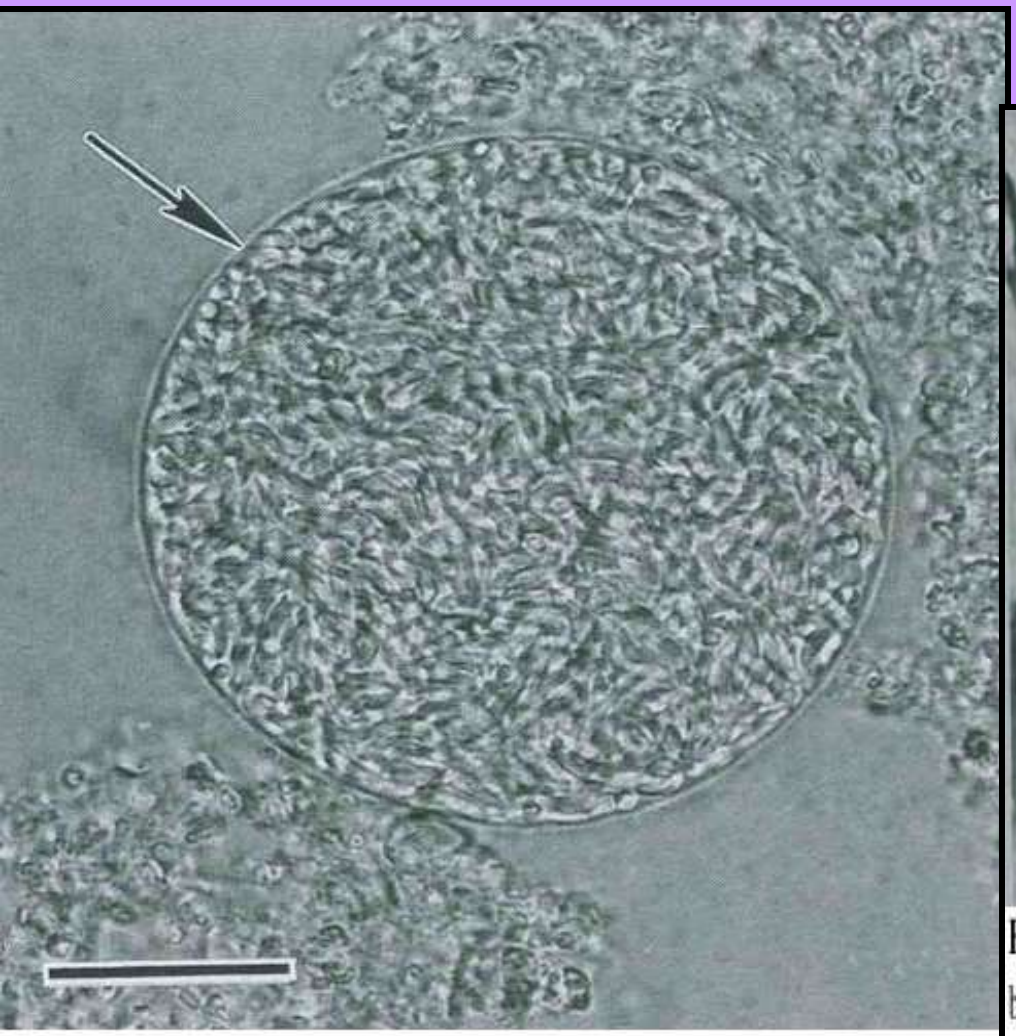


Figure 21.3 Tissue cysts of T. gondii in brain. Impression smear, unstained. This tissue cyst was freed by grinding a piece of brain in a mortar with a pestle. Note thin, elastic cyst wall (arrow) enclosing hundreds of bradyzoites. Bar =20μm.

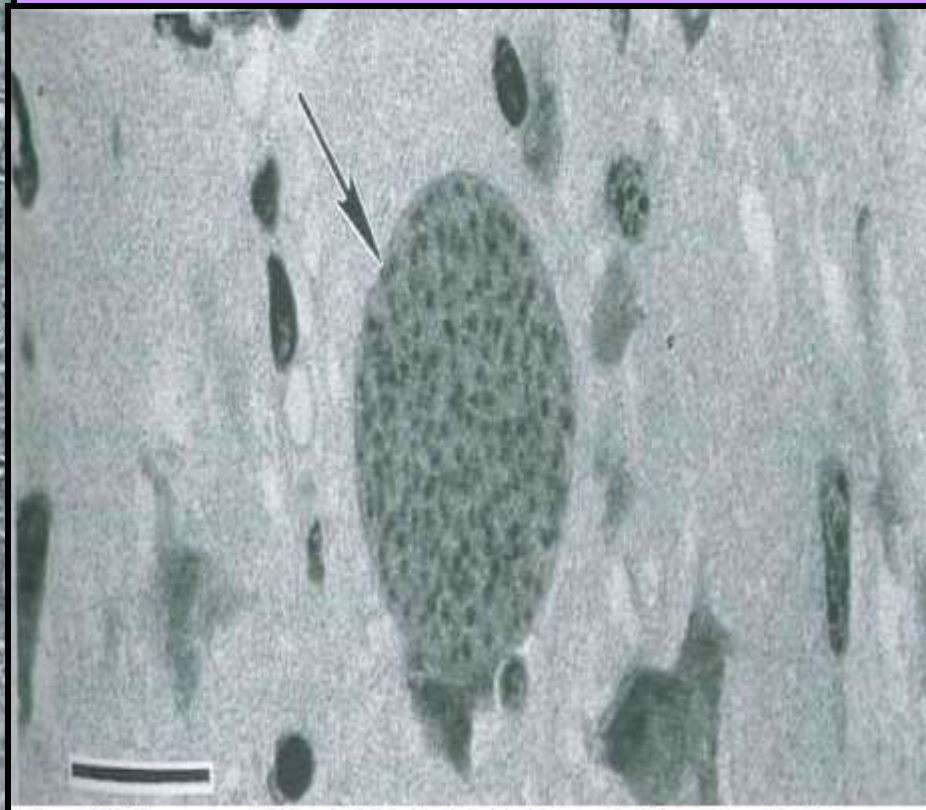
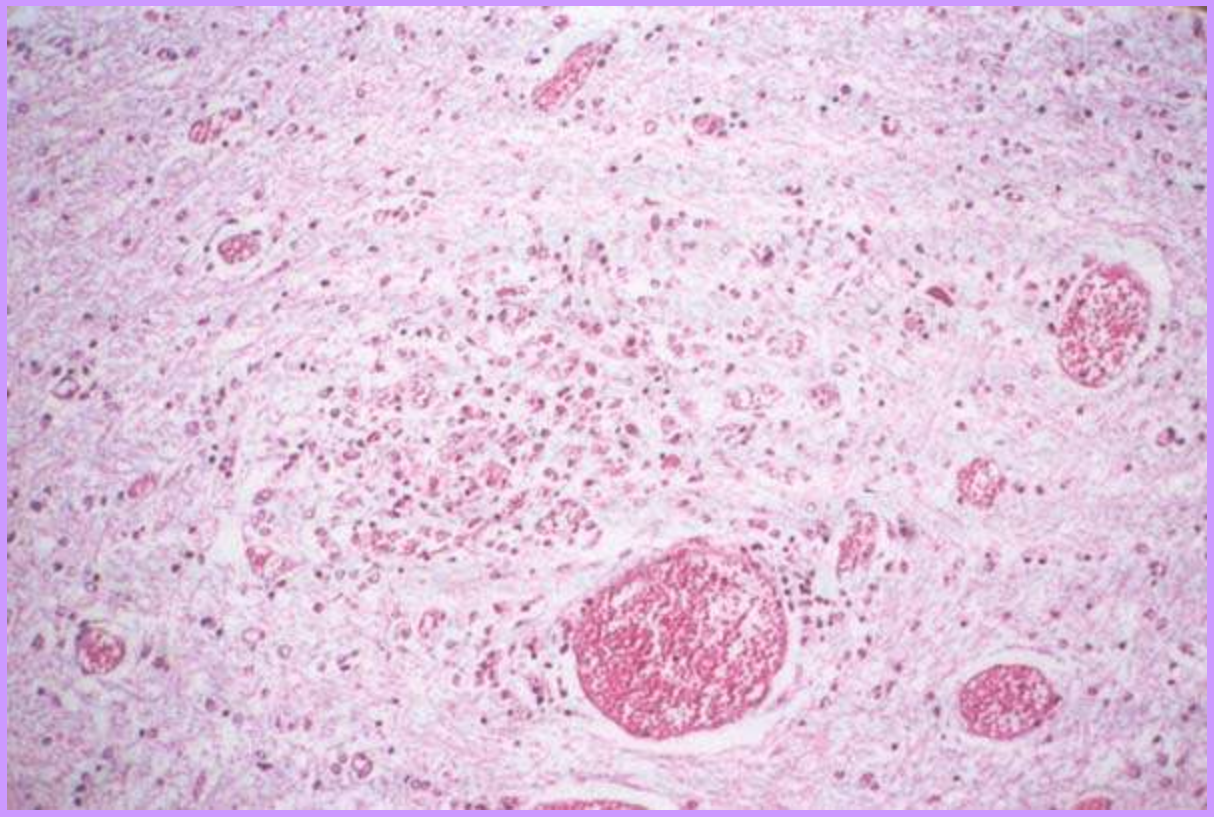
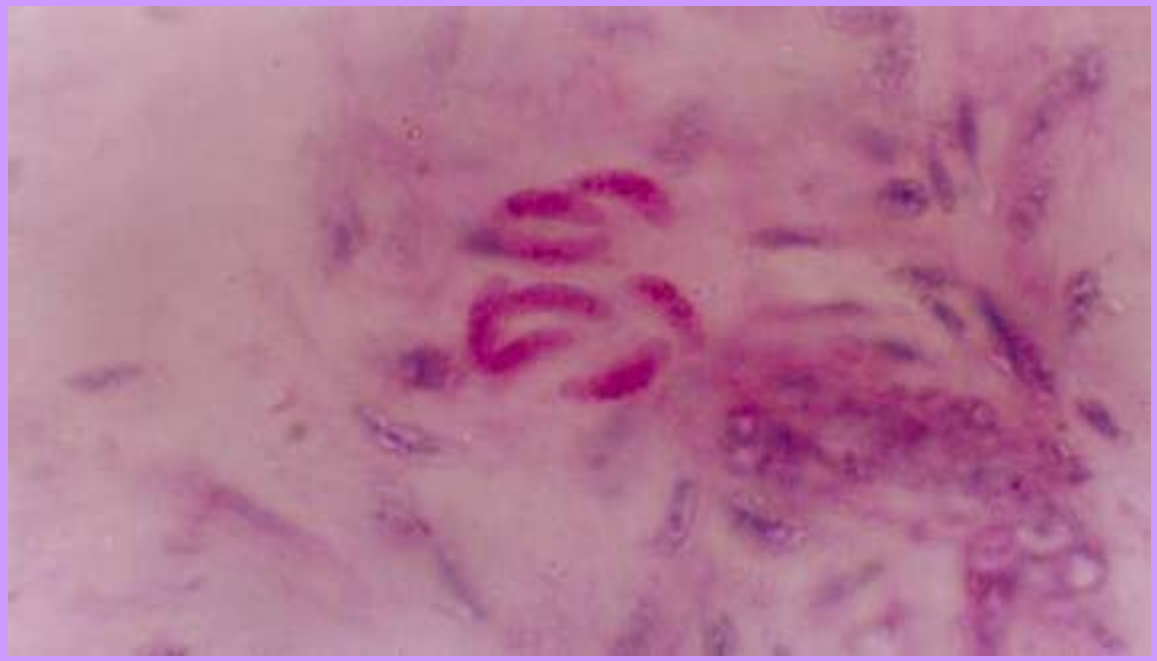


Figure 21.3 Tissue cysts of T. gondii in brain. Histological section. Note only nucleii of bradyzoites are visible. H&E. Bar = 20μm.

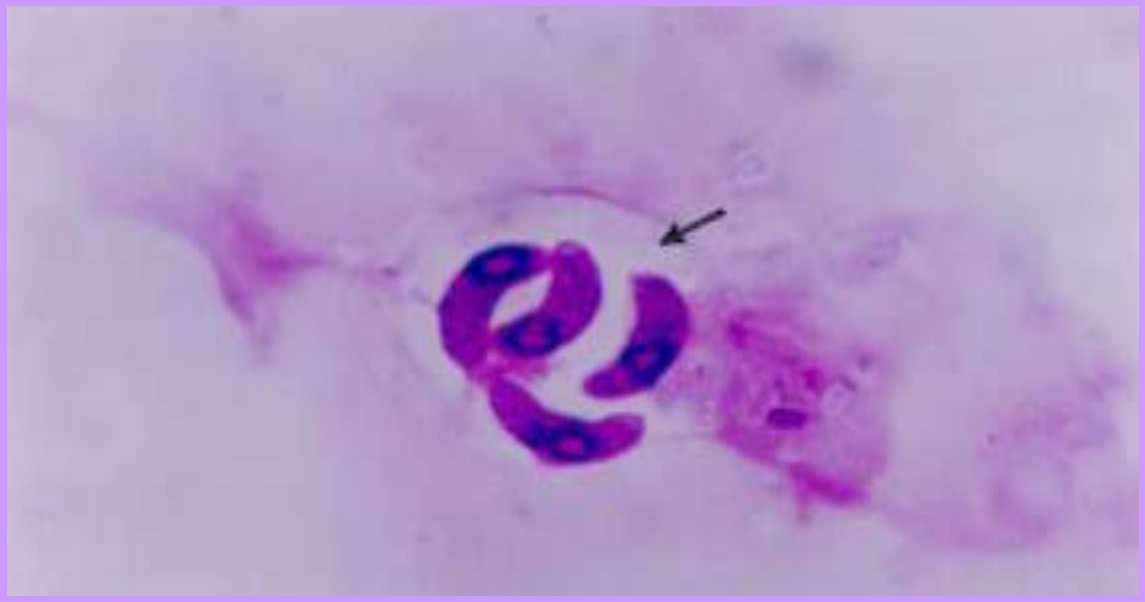
Toxoplasmosis. Inflammation of the brain (encephalitis). Tachyzoites are distributed throughout the brain where they encysts and produce bradyzoites.



- Heart of aborted caprine fetus showing presence of dark purple tachyzoites in between the muscle fibers. [PAS
- stain, X400]



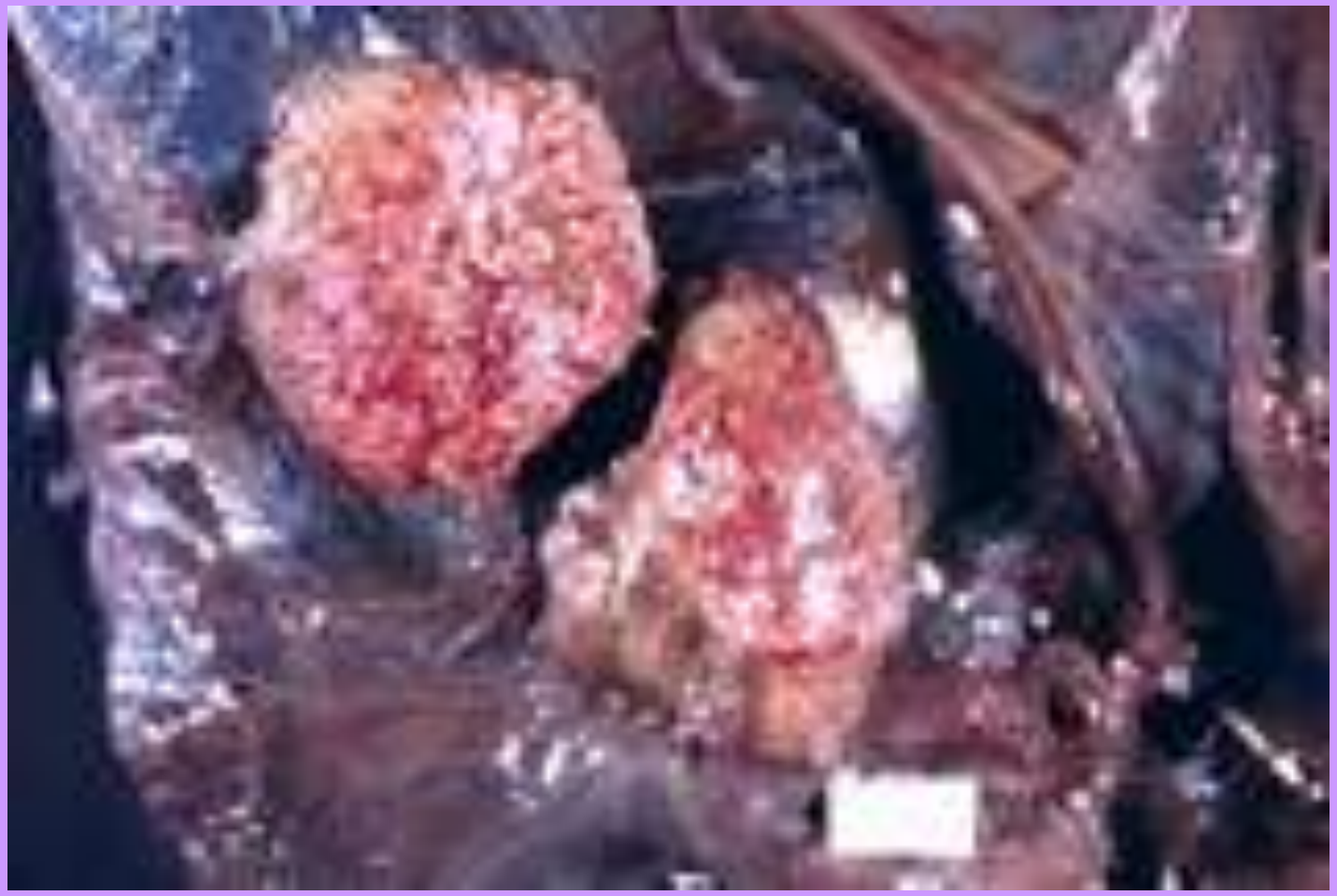
- Heart of aborted caprine fetus showing clusters of dark purple banana-shaped tachyzoites (arrow) with apical nucleus and granulated cytoplasm. [PAS stain, X1000].



5. Culture or animal inoculation

(rare) Isolation of parasites from blood or other body fluids, by intraperitoneal inoculation into mice or tissue culture. The mice should be tested for the presence of Toxoplasma organisms in the peritoneal fluid 6 to 10 days post inoculation; if no organisms are found, serology can be performed on the animals 4 to 6 weeks post inoculation.

6.Detection of parasite genetic material by PCR, especially in detecting congenital infections in utero.



To avoid Toxoplasma infection (and other problems):

- Cleanliness is important, especially around feeding areas.
- It is especially important to try to prevent cats from defecating in hay, bedding, grain, or water that will be fed to pregnant animals. Any fetal membranes and dead fetuses should be disposed of properly (burned or buried).

- To prevent transmission of infection to more animals, and aborted females should always be separated from the flock.
- A successful prevention/treatment of toxoplasmosis can be achieved by adding cocciodiostats such as decoquinate (Decox) or lasalocid (Bovatec- is an antibacterial agent and a coccidiostat, It is the drug in the feed additive called **Bovatec** to the diets of sheep and goats.

Treatment

- For animals other than humans, treatment is seldom warranted.
- Sulfadiazine (15–25 mg/kg) and
- Pyrimethamine(antiprotozoal) (0.44 mg/kg) act synergistically and are widely used for treatment of toxoplasmosis.
- While these drugs are beneficial if given in the acute stage of the disease when there is active multiplication of the parasite, they will not usually eradicate infection. These drugs are believed to have little effect on the bradyzoite stage.

- Certain other drugs, including Diaminodiphenylsulfone (**Dapsone** antibacterial), Atovaquone (antiparasitic and therapeutic effects), and Spiramycin are also used to treat toxoplasmosis in difficult cases. Clindamycin is the treatment of choice for dogs and cats, at 10–40 mg/kg and 25–50 mg/kg respectively, for 14–21 days.