

Toxoplasmatidae

Toxoplasma, Neospora

Toxoplasmatidae

■ Genus

- *Toxoplasma*
- *Besnoitia*
- *Hammondia*
- *Neospora*

■ The developments are similar to the species belonging to *Eimeria* and *Isospora* genus.

■ The main difference is that asexual and sexual phases occur in intermediate and definitive hosts, respectively.

■ The structures of the oocysts are similar to the oocysts of *Isospora* spp.

■ Development is obligatory or facultative heteroxene.

- **The definitive hosts are mammals or raptors.**

- The intermediate hosts are ruminants, pig, horse and human.

■ The cysts formed in the intermediate host contain a large number of bradizoides.

■ These parasites are Isosporoid coccidia that generate cysts in the host.

Genus: *Toxoplasma*

Species: *Toxoplasma gondii*

- The intermediate hosts are all mammals (including human) and birds.
- They are obligatory intracellular parasites.
- The definitive hosts are domestic cats and other felids.
- Toxoplasmosis (*Toxoplasma gondii*)

Toxoplasma

- The definitive hosts are felids.
- The intermediate hosts have over 200 animal species (mammals, birds and reptiles)
- Cats can be both definitive host and intermediate host.
- They are obligatory intracellular parasites.
- There are two period in their developments
 - *Intestinal form*
 - This form is only seen in cats.
 - They undergo merogony and gametogony stages in the epithelial cells of small intestine.
 - Sporogony occurs in the nature (Oocyst; 2 sporocysts X 4 sporozoites)
 - *Extra-intestinal form*
 - This form is seen in both cat and the intermediate hosts and is characterized with the cyst formation. The reproduction is endodyogenic.
 - Tachyzoite stage: The pseudocysts are formed in all nucleated cells. Very rapid proliferation is seen in this stage (acute toxoplasmosis).
 - Bradyzoite stage: The pseudocysts are formed in the striated muscles, brain and eyes. Slow proliferation is seen in this stage.

- The asexual forms cause infection in human and various animals.
- There are two different asexual form.
 - The initial asexual form called as trophozoite can firstly infect neurons, microglia, endothelial cells, liver parenchyma cells, lung and gland epithelial cells, heart and skeletal muscle cells, placenta, leucocytes and other various cells. They multiply rapidly and cause death of cells.
 - This form causes acute infection.
 - The second asexual form called bradyzoite multiplies slowly and forms cysts. The cysts are formed in mostly brain, muscles, lung and other tissues.
 - Bradyzoite stage causes latent infection slowly inside cyst in a long period.

- On the one hand, the protozoa multiply by means of schizogony and gametogony in the epithelial cells of small intestine (called as entero-epithelial cycles),
- On the other hand, they develop and multiply simultaneously in the mentioned organs and tissues of the intermediate host (cats and other felids).
 - Due to this characteristic, cats and other felids are both intermediate and definitive host for *T. gondii*.

Bradyzoite stage- pseudocyst formation

Stagnant period, slow reproduction

They found as pseudocyst in brain and muscles of intermediate host.

Chronic and latent infection

Those found in the brain are spherical and 70 μm .

Muscle cysts are elongated and 100 μm .

The thickness of cyst wall is less than 1 μm and the inside of the cysts is not divided into compartments.

Endodyogeny

Tachyzoite stage

They enter to RES cells of the intermediate host and multiply in there (Endodyogeny).

Then, they diffuse all over the body.

Acute toxoplasmosis.

Merogony and Gametogony

These stages occur in the small intestine epithelial cells of felids.

The unsporulated oocysts are thrown out with feces.

The sporulation occurs in environments (in soil).

Isosporoid type oocyst (2x4)

The unsporulated oocysts are thrown out with feces are spherical and $10 \times 12 \mu\text{m}$. The oocyst wall is two-layered and colorless. After having spent the sporogony stage outside, it gets a slightly oval structure. The sporulated oocysts are average $13 \times 11 \mu\text{m}$.

The sporulation takes place in 2-3 days at 24°C .

*The trophozoites found in intermediate hosts are called as tachyzoite and endozoite. They are half moon or crescent shape and $2-6 (2-4 \times 4-8) \mu\text{m}$. The front end is pointed, while the rear end is curved.

*The tissue cysts founded in various tissue and organs of the intermediate host include bradyzoites. The sizes of the bradyzoites are $1.5 \times 7 \mu\text{m}$. They multiply by endodyogeny.

Transmission

- The main infection source is sporulated oocysts that are initially thrown out by feces of felids as unsporulated.
 - Foods contaminated felids' feces.
- Or infection can be occurred by **trophozoites** or **tachyzoite** that are formed with endodyogeny in various tissue and organs of the intermediate host and also with the **bradyzoites** or **cystozoites** that are founded inside pseudocysts in tissues of the intermediate host.
 - Raw or undercooked meat (sheep, goat)
 - Milk?
 - These three transmission routes (by oral taking of sporulated oocysts, tachyzoites and bradyzoites) are called as **acquired toxoplasmosis**.
- Intrauterin transmission
 - Human, Sheep, Goat
 - It is a type of the infection that occurs with maternal trophozoites caught infections during pregnancy by passing through the placenta. This is called as **congenital toxoplasmosis**.

Infection with foodstuffs such as beef and eggs is regarded as negligible.

- The entero-epithelial cycles completes on 3-10. days following infection with tissue cysts, 18. day following infection with oocysts and 13. day following infection with trophozoites.
 - Oocyst production begins at the end of these periods.
 - No clinical infection occurs in cats as a result of this intense proliferation seen in the intestines of the cat.
 - *T. gondii* oocysts are less infective and less pathogenic for the cats.

Pathogenesis

- Acquired toxoplasmosis
 - 1-2 weeks incubation
 - There is a period of acute parasitemia that lasts for weeks until the formation of the cysts.
 - Generally asymptomatic (%80)
 - Lymphadenopathy, sometimes fever and myalgia.
 - If the immune system is suppressed, it may go through acute stage again.
- Toxoplasmic encephalitis
 - Usually in immunosuppressive patients (HIV)
 - Lethargy, convulsions
 - The prognosis is not good
- Congenital toxoplasmosis
 - There must be an acute infection during pregnancy.
 - Abort, stillbirth (%5-10)
 - Anomalous birth (%18-23)
 - Hydranencephali, microcephalus
 - Retinochorditis,
 - Normal birth (%58-72)
 - Retinochorditis after puberty
 - Behavioral disorders

TOXOPLASMOSIS in HUMANS

- The infection can be congenital or acquired types.
- Primary infections are generally either asymptomatic or it can not be diagnosed.
- General finding that can be described are painless cervical lymphadenopathy and mild fever.
- **Other symptoms are fever, headache, malaise, lymphadenopathy, hepato-splenomegaly, myalgia and atypical lymphocytosis.**
- The cysts open in the tissue of immunosuppressive patients who are infected with *T. gondii*. Recurrent infections can occur. Generally, eye disorders and lethal encephalitis develop.

- *Toxoplasma* can infect placenta within the period of acute infection.
- The influence of fetus is more severe in the first period of the pregnancy.
- The risk of congenital infection is very low in individuals who have been infected during the previous mounts from pregnancy.
- Transplacental transmission rate and severity of the disease vary according to the period of pregnancy.
- The majority of the offspring born with toxoplasmosis are asymptomatic (75%).
 - Findings related to chorioretinitis arise in a large part of the congenital infected infants after months or years.

Congenital toxoplasmosis

- The most important disorders are chorioretinitis, cerebral calcifications, hydrocephalus, microcephaly and psychomotor disorders.
- In the first trimester and at the beginning of the second trimester, abort, stillbirth or severe neonatal infection can be seen. The most affected organ is the brain.

TOXOPLASMOSIS in CATS

- Clinical toxoplasmosis is very rare in cats.
- Main symptoms;
 - enteritis
 - growth in lymph nodes
 - pneumonia
 - degeneration in CNS
 - encephalitis
 - chronic interstitial nephritis

TOXOPLASMOSIS in DOGS

- Acute toxoplasmosis cases and occasional deaths have been reported.
- Fever, anorexia, pneumonia, and diarrhea are seen in infected dogs.
- Pneumonia and neurological manifestations can be seen.

TOXOPLASMOSIS in CATTLE

- Occasionally, clinical infections have been reported in cattle.
- Main manifestations;
 - dyspnea
 - cough
 - wheezing respiration
 - nasal discharge
 - tremor
 - occasionally increase in body temperate.

TOXOPLASMOSIS in SHEEP and GOATS

- Body temperature increases in acute toxoplasmosis.
- With the emergence of a protective immunological response, the infection stops and the agents transform to bradyzoite form in the tissue cysts.
- Infections in the early stages of the pregnancy (up to 45-55 days) can result in fetal death.
- In the later period (until the 90th day), abortion occur.
 - Lesions formed in the cotyledons on the placenta can be seen by the naked eye.
 - The most obvious change in the lambs and the yeanelings is mummified fetus.
- In the last period of the pregnancy (until the 120th day), the fetal immunity is relatively developed, so there is no clinical effect, the offspring is normal but infected and immunized.
- In acute infections in the goats, the agents can be found in the milk. The consumption of these milk without pasteurization may be the source of infection for humans.

TOXOPLASMOSIS in PIGS

- Clinical manifestations;
 - fever
 - tremor
 - weakening
 - cough
 - relaxation in abdominal muscles
 - diarrhea
- Encephalitis, pneumonia and aborts can be seen.

TOXOPLASMOSIS in HORSES

- Clinical infections have been reported to be very rare.

TOXOPLASMOSIS in BIRDS

- Sudden deaths due to acute infection have been reported, and symptoms such as anorexia, weakness, diarrhea and blindness have been identified in the survivors.

TOXOPLASMOSIS in OTHER ANIMALS

- Sporadic or common toxoplasmosis outbreaks can be seen in rabbits, mink and various domestic and wild animals.

Diagnosis

- In definitive host (cat)
 - Observation of unsporulated oocyst in stool ??
 - However, it is difficult to distinguish from *Hammondia* and *Besnoitia* oocysts.
- In intermediate host
 - Fever, myalgia, chorioretinitis, abort.
 - Mouse inoculation with biopsy material.
 - Observation of pseudocysts in the muscles and brain during necropsy.
 - Serologic methods (**Sabin-Feldman Dye Test**; 1:64)
 - IgM>IgG
 - ELISA
 - PCR

Treatment

- Antifolats (pyrimethamine+ sulphadiazine)
- Spiramycin
- Anticoccidials can be tried in cats.

Prevention

- Meat, milk
 - $>60^{\circ}\text{C}$ heat
 - Glove use
 - Hand hygiene
- Cat
 - Cat litter should change within 24 hours.
 - Without sporulation
 - Hunting behavior of cats should be prevented.
 - Cats should be kept away from sheep and goat herds.
 - Wastes must be burned.

Genus: Neospora

- *Neospora* infection was reported for the first time in 1984 in Norway with cases of encephalitis in puppies,
- and than, similar cases has been reported from America
- The agent was accepted into the Toxoplasmatidae family and was called as *Neospora caninum*.

Genus: Neospora

- *N. caninum* is similar to *T. gondii* as for structure, genetic and immunological properties. However, they form biologically different infection.
- While *T. gondii* causes an important infection in humans, sheep and goats, *N. caninum* causes similar infection in cattle.

Genus: Neospora

- It is a heteroxene protozoon.
- The definitive host is dog
- Intermediate host is cattle. In addition; sheep, goat, horse and deer can be intermediate host.
- It is the fastest parasite in cattle and it has been found that up to 90% of cattle are infected in some herds.
- Dogs also serve as intermediate host during prenatal infections.
- In many countries, it is one of the important reasons for aborts in cattle.

Morphology and Development

- The developmental cycle includes three distinct infectious stages: trophozoites, tissue cysts, and oocysts.
 - Trophozoites and tissue cysts are found intracellular in intermediate host.
 - Domestic dogs are the only known definitive host. However, foxes and coyotes have also been reported to be the definitive host.
 - The size of the oocysts was determined to be 11.3x11.7 micron.

- **Morphologically similar oocysts**

- *Toxoplasma gondi*
 - *Hammondia hammondi*
 - *H. heydorni*

Morphology and Development

- **Intermediate host:** 1. the size of trophozoites are 2x6 micron. 2. Tissue cysts are round or oval in shape and can be up to 107 micron. They are found especially in the central nervous system. The thickness of the cysts wall can be up to 4 micron and it contains bradyzoites. Tissue cysts can also occur in muscle tissues.
- **Definitive host:** The oocysts become infective by passing the sporogony stage outside the host.

Transmission and Contamination

- Carnivores are likely to get infected by eating tissues included bradyzoites, and herbivores taking food and water contaminated with *N. caninum* oocysts.
- Transplacental infections are shaped by the passage of tachyzoites through the infected mother during pregnancy.
- There is little information on the transmission of *N. caninum* and its distribution in tissues in naturally infected animals.

NEOSPOROSIS in CATTLE

- *N. caninum* causes abort and neonatal death in cattle.
- They can be transmitted as transplacental and cause abort in congenital infection.
- Abort is the only clinical symptom in cows, therefore it causes economical losses.

NEOSPOROSIS in CATTLE

- Abort can occur in cows of all ages that are in the first trimester of pregnancy. The disease may be overlooked because the dead fetus will be resorbed.
- Abortions are more common in 5-6. months of the pregnancies. The fetus can die in the uterus, can be resorbed, can be mummified or autolysed and stillbirth may be seen. Live but with clinically symptomatic calves and normal appearance but with chronic infected calves can be born.
- The abortions may be found throughout the year.

Clinical Infection

- The abortion is the only clinical symptom in cows. Encephalitis is the most important lesion in aborted fetus.
- Weakness and slowing growth along with neurological symptoms are seen in live calves.
- The hind, front or all legs may be stretched or excessively elongated.
- In neurological examination, ataxia, decrease in patella reflex, stretching in feet and legs, lack of balance and loss of consciousness are seen.

Diagnosis

- Histological examination of the fetus is necessary.
- The brain, heart, liver, body fluids and blood serum are the best samples for diagnosis.
- The necrosis and focal encephalitis characterized by nonsuppurative inflammation are the most characteristic lesions in neosporiosis.

NEOSPOROSIS in DOGS

- The disease affects both adult dogs and puppies.
- Severe symptoms can occur in the puppies, although their mothers are asymptomatic.
- The paresis that develops in the hind legs of young dogs turns into progressive paralysis.
- Extreme deformation develops in the hind legs.
- Other dysfunctions include swallowing difficulty, laryngeal paralysis, muscle loosening, muscle atrophy, and heart failure.

Toxoplasmatidae

Besnoitia, Hammondia

Genus: *Besnoitia*

- Besnoitiosis caused by the species belonging to *Besnoitia* genus was originally called as skin globidiosis or elephant skin disease.

Genus: *Besnoitia*

- *Besnoitia* species complete their developments in two separate hosts.
- **The intermediate hosts is cattle.**
- **The definitive hosts are domestic and wild cats.**
 - The pathogens locate in the skin, subcutaneous connective tissue, eye and other organs, especially fibroblasts cells. They form cysts containing bradyzoites (banana shaped) and are found in parasitophorous vacuoles.
 - **Schizogony and gametogony** stages occur in the definitive host, while sporogony occurs in the environment.
 - Oocysts infect only the intermediate hosts.

Genus: *Besnoitia*

- Besnoitiosis is a disease characterized by infertility, painful swelling and thickening in the skin, alopecia, and death in severe cases.
- These defects occurring in the skin are often permanent and lead to economic losses in the leather industry.

BESNOITIOSIS in CATTLE

- *Besnoitia besnoiti*
 - The definitive hosts are domestic and wild cats.
 - Oocysts are oval shaped and 12x14 μ m.
 - The intermediate host is cattle
 - Bradyzoite-containing cysts are found in the skin, subcutaneous connective tissue, fascia, serosa, nasal mucosa, pharynx, larynx, trachea and testes.

BESNOITIOSIS in CATTLE

■ Clinical manifestations

- 1. Fever stage 41.7°C

■ Skin lesions

Excessive thickening is observed in the skin and skin elasticity is lost. Alopecia is seen in the swollen parts of the skin.

- 2. Alopecia stage

- 3. Dry seborrhea stage

BESNOITIOSIS in GOATS

- *Besnoitia besnoiti*
- Lesions are seen in the skin and genital system.
- Skin lesions occur on the ventral face of the abdomen and on the legs.
- The worst lesions are found around the heel.

BESNOITIOSIS in EQUIDAE

- *Besnoitia bennetti*

- The intermediate hosts are horses and donkeys.
 - Stiffness and peeling in the skin, subcutaneous edema in head, neck, scrotum and extremities, muscular atrophy and difficulty in walking are seen.
- The definitive hosts and oocysts are not yet known.

BESNOITIOSIS in OTHER HOSTS

- *Besnoitia tarandi*
 - Intermediate hosts are deer and caribou.
 - Definitive hosts are not yet known.
- *Besnoitia darlingi*
 - Intermediate hosts are opossums and reptiles (Panama lizards).
 - Definitive host is cat.
- *Besnoitia jellisoni*
 - Intermediate hosts are mouse and rat.
 - Definitive hosts are not yet known.
- *Besnoitia wallacei*
 - Intermediate host is Norway rat.
 - Definitive host is cat.

Genus: *Hammondia*

■ *Hammondia hammondi*

- Definitive host is cat.
- Natural intermediate host is mouse.
 - The pathogens go to the skeletal and heart muscles, and brain and form cysts in there.

■ *Hammondia heydorni*

- Definitive hosts are dogs, foxes, and coyotes.
- Intermediate hosts are cattle, sheep, goats, water buffalo, deer and Guinea pigs.
 - Cysts are found in skeletal, heart and esophagus muscles.