Extraintestinal Coccidia

Large group of organisms important to humans and animals
Most oocysts look alike - difficult to differentiate among species.
Cysts in extraintestinal tissues often used for identification.

How do extraintestinal coccidia get transmitted?
Toxoplasma gondii has very low host specificity, and it will probably infect almost any mammal.

Reported from birds, and has been found in virtually every country of the world.

Apicomplexan: Toxoplasma is an obligate intracellular parasite. Its life cycle includes two phases called the intestinal and extraintestinal phases. The intestinal phase occurs in cats only (wild as well as domesticated cats) and produces "oocysts."

The extraintestinal phase occurs in all infected animals (including cats) and produces "tachyzoites" and, eventually, "bradyzoites". The disease toxoplasmosis can be transmitted by ingestion of oocysts (in cat feces) or bradyzoites (in raw or undercooked meat).
**Toxoplasma gondii**

- cosmopolitan distribution
- seropositive prevalence rates vary
  - generally 20-75%
- generally causes very benign disease in immunocompetent adults
- tissue cyst forming coccidia
  - predator-prey life cycle
  - felines are **definitive host**
  - infects wide range of birds and mammals (**intermediate hosts**)

**Definitive Host**
- adult forms
- sexual reproduction

**Intermediate Host**
- immature forms
- asexual reproduction
**THE LIFE CYCLE OF *TOXOPLASMA GONDII* (TOXOPLASMOsis)**

**THIS PHASE OF THE LIFE CYCLE OCCURS IN ALL ANIMALS, INCLUDING "CATS."**

The resulting tachyzoites reproduce asexually rapidly, liberating more tachyzoites and causing cell death. Tachyzoites are distributed throughout the host's body.

Bradyzoites or sporozoites infect cells (macrophages) in the mucosa of the small intestine.

After several weeks the parasites divide slower, producing zotocysts filled with bradyzoites.

The host is infected by ingesting oocysts or eating bradyzoites in the tissues of a reservoir.

Bradyzoites or sporozoites from the oocyst penetrate the cells of the small intestine.

Oocysts become infective (sporulate) in about 24 hours.

The parasite undergoes asexual and sexual reproduction and oocysts are produced.

Asexual reproduction in the intestinal epithelium is self-limiting, so oocysts are passed by cats for only a few weeks.

Oocysts are passed in the "cat's" feces.

**THIS PHASE OF THE LIFE CYCLE OCCURS ONLY IN "CATS."**

(Parasites and Parasitological Resources)
The life cycle of *Toxoplasma gondii* consists of two phases, an intestinal phase and an extraintestinal phase. The intestinal phase occurs only in cats (wild and domesticated cats), and results in the production of oocysts.

The extraintestinal phase occurs in all infected animals (simultaneously with the intestinal phase in cats), and results in the production of tachyzoites and, eventually, bradyzoites. The disease toxoplasmosis can be transmitted by ingestion of either oocysts (in the feces of cats) or bradyzoites (in raw or undercooked meat).
Tachyzoites of *Toxoplasma gondii*. Note the characteristic crescent shape.
A sporulated oocyst of *Toxoplasma gondii*. The oocyst contains two sporocysts, each of which contain four sporozoites. Thus, they resemble the oocysts of *Isospora* sp. Only cats will produce and pass *Toxoplasma* oocysts; approximate diameter = 10 \( \mu \text{m} \).

A zoitocyst of *Toxoplasma gondii* filled with bradyzoites; this zoitocyst is in cardiac muscle.
When a cat is infected with *Toxoplasma*, the parasites enter the cells lining the cat's small intestine and undergo rapid asexual reproduction; this part of the life cycle remains localized to the cells of the cat's small intestine. **The intestinal phase in cats is self-limiting.** The extraintestinal phase of the life cycle occurs in all infected animals. In cats it occurs simultaneously with the intestinal phase. The extraintestinal phase can last as long as the animal is alive.

After a few days the asexual forms produce sexual forms (gametes) that fuse, and this results in an oocyst. The oocyst is passed in the cat's feces, and after two to three days outside of the cat the oocyst becomes infective.

The asexual stages disappear from the cat's small intestine after about two weeks, so the cat also stops producing oocysts. During the two to three week period during which a cat produces oocysts, literally millions (perhaps billions) of oocysts can be produced. Since cats will also harbor extraintestinal stages of the parasite, it is common to find cats that are infected with *Toxoplasma* but are no longer passing oocysts.
Transmission of toxoplasmosis can occur via oocysts or bradyzoites. Since cat feces are the only source of oocysts, exposure to oocysts can be minimized, but not prevented completely.

The oocysts are very resistant to adverse environmental conditions, and oocysts in garden soil, sand boxes, etc., can remain infective for months. Infections via bradyzoites occur when raw or undercooked meat is eaten. House cats can be infected this way when they eat rodents and birds. Humans can be infected when they eat raw or undercooked meat products, and considering the very low host specificity of *Toxoplasma*, no meat product should be considered absolutely "safe." Heating meat to approximately 160 F or cooling it to 0 F (a hard freeze) should kill most of the zoitocysts.
Human Transmission

- ingestion of sporulated oocysts (cat feces + incubation)
- ingestion of zoites (undercooked meat)
- congenital infection (only during acute stage)
- organ transplants
  - chronic infection in donor
  - immunosuppression
- blood transfusions (only during acute stage)
A. Extracellular (arrow) released from host cells.
B. Intracellular in cell culture.
C. Transmission electron micrograph of an intracellular tachyzoite. Note a parasitophorous vacuole (PV) around the tachyzoite. Parasite organelles visible in this picture include a conoid (c), micronemes (m), dense granules (dg) nucleus (n) and rhoptries (r).
A. Tissue cyst freed from mouse brain. Note a thin (arrow) cyst wall enclosing hundreds of bradyzoites.

B. Two tissue cysts (arrows) in section of brain.

C. Transmission electron micrograph of a small tissue cyst in cell culture. Note thin cyst wall (arrow) enclosing 6 bradyzoites (arrowheads).
In most humans infected with *Toxoplasma*, the disease is asymptomatic.

However, under some conditions, toxoplasmosis can cause serious pathology, including hepatitis, pneumonia, blindness, and severe neurological disorders. This is especially true in individuals whose immune systems are compromised (e.g., AIDS patients).
Toxoplasmic Encephalitis

- common complication associated with AIDS during the 1980's
- recrudescence of latent infection
- multifocal disease associated with immunosuppression
- lesions detectable with CT or MRI
- little spread to other organs
- symptoms include: lethargy, apathy, incoordination, dementia
- progressive disease → convulsions
Toxoplasmosis can be transmitted transplacentally. This accounts for a very small percentage of all infections, but they result in some of the most severe infections. In humans, toxoplasmosis can be transmitted transplacentally if a women is infected with toxoplasmosis while she is pregnant. If a women is infected before she is pregnant, transplacental transmission will not occur.

The tachyzoites cross the placenta and infect the tissues of the fetus. Depending on the age of the fetus when it is infected and the virulence of the *Toxoplasma*, this can result in a spontaneous abortion, a still born child, or a child that is born with some degree of mental or physical retardation.

Thus, women are often told to minimize contact with cats while they are pregnant, and to avoid emptying their cat's litter box. However, pregnant women must also remember that oocysts are not the only source infection, and take additional precautions to prevent infections via raw or undercooked meat.

In an immunocompromised host, toxoplasmosis can be a very serious disease, and this can occur if a person is infected with toxoplasmosis before or after his/her immune system is compromised. In particular, toxoplasmosis can cause severe neurological disorders and pneumonia in AIDS patients.
Congenital Toxoplasmosis

• 1° infection must occur during pregnancy
  • can only occur once
  • 1/3 will pass infection to fetus
• incidence ~1 per 1000 births
• severity varies with age of fetus
  • move severe early in pregnancy
  • more frequent later in pregnancy
• infection can result in: spontaneous abortion, still birth, premature birth, or full-term ± overt disease
Diagnosis

- seldom by direct parasite demonstration
  - biopsy
  - inoculation into mice or cell culture (only acute stage)
- various serological tests
- active (acute) vs chronic infection
  - compare samples at 2 week intervals
  - $\text{IgM} > \text{IgG}$; ↑ Ab titers
Prevention

Raw Meat

- Cook meat thoroughly (66 C, 150 F)
- Cook lamb, beef, and pork until well done.
- Wash fruits and vegetables and cutting boards thoroughly before eating.
- Wear gloves when handling.
- Wash hands after.

Cat Feces

- No cats in home
- Clean litter box promptly (<24 hr)
- Wear gloves
- Keep cat in house
- Cover sand box
- Control strays
- Feed cats commercial cat food.
- Don't let cats eat wild rodents, birds or raw or undercooked kitchen scraps.

Wash hands thoroughly after working with soil, cleaning litter boxes, before and after handling foods, and before eating.

Persons with weakened immune systems and pregnant women should be particularly careful to avoid contact with cat feces and soil and to avoid ingestion of undercooked meats.
Figure 28.1 General life cycle of Sarcocystis sp.
Carnivores ingest infected tissues
Merozoites released from the small intestine- invade cells
Form gamonts- micro/macro gametes
Sporulation of oocysts occurs within cells. Sporocysts and some oocysts appear in feces ~14 days later

Intermediate host ingests sporocysts
Bradyzoites digested- move from intestine to circulation
Merogony I occurs in organs/capillaries
Merogony II occurs in capillaries, second generation merozoites enter striated muscle, develop within myocytes
Bradyzoites ~3 month process

Sarcocystis programmed genetically to go through series of stages
Once Bradyzoites are formed in muscle- development stops
Must be ingested
Rice-grain sized cysts of *Sarcocystis* sp. evident in parallel streaks in A, breast muscle fibers of a mallard and B, thigh and leg muscle of an American black duck.
Clinical Signs:

In the definitive host, the parasite is not very pathogenic. However, the intermediate host's brain, muscle, and kidney tissues may be damaged by infection.

Infection of the intermediate host causes a loss of appetite, fever, weight loss, anemia, and death in severe infections. It also cause gait abnormalities, weakening of the limbs, muscle wasting, and head tilt. The animal may also move in circles. It has been known to cause abortion in pregnant animals. The number of clinical signs that appear is proportional to the number of Sarcocystis organisms parasitizing the host.
Intestinal coccidia:

*Eimeria, Isospora, Cryptosporidium*

Genetically programmed number of asexual cycles-
sexual reproduction-oocysts- exit with feces

Extra Intestinal coccidia:

*Toxoplasma, Sarcocystis*

Genetically programmed number of asexual cycles-
sexual reproduction-oocysts- exit with feces some stages enter muscle or other tissues- transmitted via predation