Systemic Apicomplexans (part 1)
Parasitic Protozoa

Grouped by Infection Site and Morphology

**Apicomplexa** (sg = Alveolates)

- **Blood apicomplexa** (piroplasmidia)
  - Babesia spp.
  - *Cytotauxzoon felis*

- **Systemic apicomplexa** (coccidia)
  - *Toxoplasma gondii*
  - Neospora caninum
  - *Sarcocystis spp.*

- **Intestinal apicomplexa**
  - Cryptosporidium parvum (gregarine)
  - *Eimeria spp.* (coccidia)
  - *Cystoisospora spp.* (coccidia)

**Flagellates** (sg = Excavates)

- **Hemoflagellates**
  - *Trypanosoma cruzi*
  - *Leishmania infantum*

- **Mucoflagellates**
  - *Trichomonas foetus*
  - *Giardia spp.*
**Toxoplasma gondii**

- Feline coccidian of zoonotic importance
- Complex Life Cycle
  - Direct and Facultative
Morphology: *Toxoplasma gondii*

- **Oocyst**
  - *small, sub-spherical, smooth coat, no polar cap, single embryo when passed = unsporulated*
  - Sporulated oocyst contains 2 sporocysts with 4 sporozoites each = 8 sporozoites total

[Images of oocysts and sporocysts]

[Link to CDC page on toxoplasmosis](https://www.cdc.gov/dpdx/toxoplasmosis/index.html)
Terminology Review: Toxoplasma gondii

- **Definitive host** – species in which the adult (or sexual) form of the parasite occurs
  - felids are definitive hosts for T. gondii
- **Facultative intermediate / paratenic** – species which supports the multiplication (asexual) stage of parasite, can carry parasites through food chains to the definitive host, but not required for life cycle of the parasite
  - any warm-blooded animal can be an intermediate host
- **Accidental host** – “dead-end” host, parasites can’t complete life-cycle
  - humans are accidental hosts when infected with T. gondii
- **Endodyogeny** – single division forming 2 daughter cells in mother cell
  - occurs in cat and intermediate/paratenic hosts (only replicative form in paratenic host)
- **Merogeny** – multi-nuclear division followed by cytoplasmic division forming multiple daughter cells
  - occurs in the cat in intestinal epithelium
- **Tachyzoite** – fast growing infective stage
  - localize in neural and muscle tissue, fast growing; will develop into tissue cyst bradyzoites
- **Bradyzoite** – slow growing infective stage
  - cysts in tissue (including neurons and skeletal muscle cells) remains semi-dormant (chronic infections)
**Toxoplasma gondii**

**Different approaches to the invasion**

*We need numbers Fred! WE NEED NUMBERS!!*

*Dude... Relax, let's just build a fort and sleep thru this... the invasion is over!*

**Tachyzoite**

**Bradyzoite**

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Growing in neural and muscle tissue
**Life Cycle: T. gondii**

**Direct Life Cycle:** (homoxenous)
- cat → cat

**Facultative Indirect Life Cycle:** (heteroxenous)
- cat → paratenic host
- paratenic host → cat

T. gondii facultative intermediate/paratenic hosts = any warm-blooded animal

Definitive Host (sexual & asexual cycles)
- Transplacental to the kittens

Facultative Intermediate hosts (asexual cycle only)
- Ingestion

Accidental Host
- Sporulated Oocyst
- Contaminated food
- Sporulation in 2-3 days
- Unsporulated Oocyst
- Ingestion
- Cat

Cat → Paratenic Host → Paratenic Host
Direct Life Cycle: *T. gondii*  
Cat to Cat

- **Direct Life Cycle** (homoxenous)
  - Definitive host = Felids only
- **Transmission** -- fecal-oral, ingestion of oocyst
- **Invasion** -- Sporozoites excyst from oocyst and invade enterocyte
- **Asexual reproduction (in intestinal cells)**
  - Endodyogeny AND Merogony
    - ~ 5 cycles
  - Causes either no or mild pathology in the cat
  - Some sporozoites invade deep tissues (CNS, muscle, viscera) multiply & disseminate as tachyzoites, and eventually form bradyzoite cysts
Direct Life Cycle: *T. gondii* in the Cat

- **Sexual reproduction** *(only occurs in the Felids)*
  - Gametogony → Fertilization → Oocyst

- **Dissemination**
  - Oocysts (unsporulated) exit the host in the feces and contaminate the environment
    - Felids are the only hosts to pass oocysts *(b/c of sexual fertilization)*
    - Prepatent period *(oocyst ingestion to oocyst passing)*: 19 - 48 days
    - **Felids usually only shed oocysts once in their life-time**
    - Oocysts highly resistant and remain infectious for many months
Facultative Indirect Life Cycle: *T. gondii*

**Cat to Paratenic host**

- Facultative Indirect Life Cycle (heteroxenous)
  - Paratenic host – Any warm-blooded animal, **including felids**

- **Transmission**
  - Paratenic host ingests a sporulated oocyst from the feces of a felid

- **Invasion** -- sporozoites enter intestinal cells and lymph cells, divide then transform into tachyzoites (fast growing).
Complex Life Cycle

**T. gondii in the Paratenic Host**

- **Asexual reproduction** (endodyogeny) – extra-intestinal cells
  - **Tachyzoites**
    - Disseminate and invade deep tissue, throughout the body
    - Fast growing → rapid destruction of host cells → **acute / severe disease**
    - Transform into bradyzoites

- **Bradyzoites** (slow dividing zoites)
  - Stationary (= non-disseminating) and form tissue cysts
  - Tissue cysts
    - Slow growing → **chronic pathology** in the paratenic (and human) hosts
    - Occur in and cause damage to the brain, liver, lungs, striated muscles
    - Remain viable for the life of the paratenic host
Complex Life Cycle

T. gondii in the Paratenic Host

- General Notes
  - Tachyzoites may be transplacentally transmitted
  - Mother’s ingestion of oocyst from cat feces could lead to toxoplasmosis in fetus
*T. gondii* in the Paratenic host

Ingestion of Sporulated Oocyst

Exystation Sporozoites

Asexual Cycle

Some sporozoites invade deep tissues

Rapid multiplication and dissemination of tachyzoites.

Tachyzoites invade brain, muscle & liver cells. Then become bradyzoites, that slowly divide & form cysts.

Transplacental transmission to fetus.

http://chiragratapp.com/bio-science.html
**Facultative Indirect Life Cycle: T. gondii**

**Paratenic host to Cat**

- **Facultative Indirect Life Cycle (heteroxenous)**
  - Infected paratenic host (bradyzoites in tissue cysts)
  - Transmission – carnivorism → cat ingests a tissue cyst from a paratenic host
  - Bradyzoites released from ingested tissue cysts, develop into merozoites in enterocytes
  - The rest of life cycle follows that of “Cat to Cat”
    - Asexual cycle in Intestinal epithelium
    - Merozoites → sexual stage resulting in an unsporulated oocyst, passed in the feces
    - Some merozoites → invasion of deep tissues to form tachyzoites then bradyzoite cysts

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Prepatent period (time from ingesting tissue cyst to passing oocysts) = 3 to 10 days vs. the 19-48 days in cat-to-cat cycle
Toxoplasma gondii in the Feline host

**Sporogony**

- **Paratenic Host**: Ingestion of Paratenic host
- **Sexual Stage**: Fertilization, Cyst Wall Formation
- **Asexual Cycle**: Bradyzoites, Microgamonts, Macrocytes
- **Tachyzoites**: Rapid multiplication and dissemination of tachyzoites
- **Toxoplasma invade brain, muscle & liver cells. Then become bradyzoites. Then slowly divide & form cysts.**

*start here*
**T. gondii**

**Paratenic host to Paratenic host**

- **Transmission**
  - Carnivorism → ingestion of a tissue cyst from a paratenic host
  - Bradyzoites released from tissue cysts develop into tachyzoites
- **Invasion** and **Asexual reproduction** is the same as “Cat to Paratenic Host”
- **General Notes**
  - Tachyzoites may be transplacentally transmitted.
    - Mother’s ingestion of raw meat with tissue cysts may lead to toxoplasmosis in the fetus
**T. gondii in the Paratenic host**

1. **Paratenic Host**
   - Ingestion of Paratenic host

2. **Asexual Cycle**
   - Bradyzoites released from tissues of paratenic host
   - Bradyzoites
   - Rapid multiplication and dissemination of tachyzoites
   - Tachyzoites invade brain, muscle, & liver cells. Then become bradyzoites that slowly divide & form cysts.

3. **Transplacental transmission to fetus**

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[NC State University](http://chriegerapps.com/bioscience.html)
Pathogenesis: *Toxoplasma gondii*

- Intestinal phase in felids → minimal

- Systemic disease (extra-Intestinal phase) in felids, paratenic hosts or humans
  - Explosive replication of tachyzoites causes:
    - massive direct destruction of host cells
    - acute immune response
  - Most often affects brain, liver, lungs and striated muscles.
  - Tissue cysts cause physical cell/tissue damage and are a source for latent disease
Clinical Disease: *Toxoplasma gondii*

**Intestinal/Acute Disease** – usually no complaint
- Oocysts noticed on routine fecal
- 10-20% of cats develop self-limiting small bowel diarrhea

**Systemic Disease** -
- **Non-specific disease**: Fever, anorexia, vomiting, diarrhea, myositis, uveitis, enlarged lymph nodes, pneumonia (especially for FIV+ cats), encephalitis, nephritis, death
- Can transmit congenitally to kittens (not common)
**Diagnosis:** *Toxoplasma gondii*
cats only

**Intestinal/Acute Disease**
- Oocysts in feces
  - Fecal float centrifugation (Zinc Sulfate)

**Systemic Disease**
- Serologic tests – measure IgG and IgM antibodies
  - good to rule-out if seronegative; not as useful at proving Toxo is cause of disease. **WHY?**
- Thoracic radiographs if lung involvement (pneumonia)
- Definitive diagnosis – detection of tachyzoites in effusions, tissue aspirates or biopsy samples
**Diagnosis:** Fecal Float Centrifugation
cats only

https://www.cdc.gov/dpdx/toxoplasmosis/index.html
**Diagnosis:** System Disease

Aspirates or Necropsy

- Tachyzoites from effusion or aspirate
- Bradyzoite cyst from Necropsy / Histology

[https://www.cdc.gov/dpdx/toxoplasmosis/index.html](https://www.cdc.gov/dpdx/toxoplasmosis/index.html)
**Treatment:** *Toxoplasma gondii*  
cats only

**Intestinal / Acute Disease (shedding oocysts)**
- Pyrimethamine plus triple sulfa drugs
- Clindamycin
- Ponazuril
- Hospitalize cat during oocyst shedding to reduce zoonosis

**Systemic Disease (clinically ill)**
- **Clindamycin** for at least 4 weeks
- Supportive treatment depending on clinical signs
- No good treatment to clear tissue cysts
Control: Toxoplasma gondii
 cats only

- Sanitation
  - Clean litter box **daily** (environmental sporulation in 1-3 days)

- No raw meat for cats

- Don’t let cat outside to defecate or hunt

https://theoatmeal.com/comics/universe_cat
Toxoplasma gondii
Non-felid paratenic hosts

- Dogs
  - Systemic toxoplasmosis, ingest oocyst from cat feces or tissue cyst from prey
    - Less commonly develop clinical disease
    - May develop nonspecific signs: fever, neurological, ocular or respiratory signs
    - Rule-out Neospora caninum infection

- Sheep & Goats
  - Systemic & Congenital toxoplasmosis, ingest oocyst from cat feces
    - Systemic – CNS signs (circling, etc.)
    - Congenital – abortion
    - Toxovac S48 live vaccine available
Toxoplasma gondii
Non-felid paratenic hosts

- Cattle
  - Congenital toxoplasmosis (abortion, but very rare), ingest oocyst from cat feces.

- Horse
  - Systemic toxoplasmosis, low pathology, ingest oocyst from cat feces

- Rodents
  - Systemic toxoplasmosis, ingest oocyst from cat feces or tissue cysts from prey
  - Decreased fear of cats
  - Major source of infection for cats and pigs
**Toxoplasma gondii**

Non-felid paratenic hosts  
*(important sources of human infections)*

**Swine**

- Systemic toxoplasmosis, ingest oocyst from cat feces or tissue cyst from prey.
  - Fever, respiratory signs
  - Highly prevalent in free-range pigs
  - **Important source of infection for humans**

**Poultry**

- Systemic toxoplasmosis, ingest oocyst from cat feces
  - Prevalent in free-range and back-yard chickens
  - **Important source of infection for humans**
Zoonosis
Systemic Toxoplasmosis

- Concern for the immunocompromised
- Transmission
  - Ingestion of oocysts from cat feces/unclean hands
  - Food-borne
    - Oocysts on unwashed vegetables
    - Ingestion of tissue cyst from undercooked meat
      - mainly mutton, goat, free-range pork, free-range chicken
Zoonosis
Systemic Toxoplasmosis

Immunocompetent Person

- 1\textsuperscript{st} exposure
  - “flu-like” illness that may last for weeks
  - Fever, myalgia, sore throat, lymphadenopathy
  - Often asymptomatic

- Future exposures
  - immune-protected, no pathology

- Can remain latently infected with cysts
Zoonosis
Systemic Toxoplasmosis

**Immuno-deficient** Adult
- Higher risk for infection and disease
- Elderly & those w/ Immunosuppressive dzs
- **Severe disease**
  - Respiratory, CNS, ocular, etc.
  - Often from recrudescence of latent infection after immune-suppression

Pyrimethamine
Zoonosis
Congenital Toxoplasmosis

**Transmission**

- Infection of Mother
  - Ingestion of oocysts or tissue cysts
- Infection of Fetus
  - Transplacental Transmission

Zoonosis
Congenital Toxoplasmosis

Fetal Toxoplasmosmosis
  - Severe Disease
    - congenital malformation
    - mental retardation
    - death

Zoonosis

Congenital Toxoplasmosis

Pregnancy, Infection & Immunity

- If mother’s 1st exposure occurs:
  - **During pregnancy** (i.e. if mother does NOT have protective antibodies from a previous exposure)
    - Transplacental transmission could occur and infect fetus
  - **Prior to pregnancy,**
    - then mother’s immune system will control toxoplasmosis, unless mother is immune-deficient
- Newly pregnant women usually tested for antibodies → if seropositive then that’s good! → mother and fetus are protected if exposed while pregnant
Zoonosis
Congenital Toxoplasmosis

Pregnancy Advice

- Get antibody tested: Mother & Cat
  - Seropositive then no worries!
  - Cats usually only shed oocysts once in their life, so seropositive cat usually = a previous exposure/infection
- Avoid cat feces (sporulation in 1-3 days)
- Avoid uncooked meat, unclean hands/vegetables/knives/cutting boards.
- Casual contact with cats is very low risk.
  - Indoor cats less risky than outdoor cats
  - Old outdoor cats less risky than young outdoor cats

"What? Did you hear me say stop? No, I didn’t think so."
http://www.ataleoftwocats.co.uk
In-Class Discussion

A pregnant client wants to get rid of their cat due to concerns about Toxoplasmosis.

How would you educate your client?
What you’re expected to know

See Review Tables:
Toxoplasma

Posted on-line at Parasitology Website:
https://parasitology.cvm.ncsu.edu/vmp930/lecture.html

The information in the review tables is basic information that you should know. You should also be able to use that information via critical thinking to answer more complex case-based questions.