

LECTURES #7 & #8: APICOMPLEXA 2  
**Apicomplexa of Systemic Pathology**  
*Toxoplasma, Neospora, Sarcocystis*

***Toxoplasma gondii***

**Feline coccidian of zoonotic importance**

A. Morphology

- Oocyst
  - small, sub-spherical, smooth coat, no polar cap, single embryo when passed
  - Sporulated oocyst contains 4 sporocysts with 2 sporozoites each = 8 sporozoites total
- Intracellular parasite of intestinal epithelium and various host tissues.

B. Life Cycle Rather Complex

1. Cat to Cat

- a. Direct Life Cycle (homoxenous) --- Definitive host – Felids only
- b. Transmission -- fecal-oral, ingestion of oocyst – felid hosts only
- c. Invasion -- Sporozoites excyst from oocyst and invade enterocyte
- d. Asexual reproduction (in intestinal cells)
  - i. Endodyogeny [single division forming 2 daughter cells] and schizogony [multi-nuclear division followed by cytoplasmic division forming multiple daughter cells]
  - ii. Approximately 5 cycles of endodyogeny and / or schizogony
  - iii. Causes none to mild pathology in the cat.
- e. Sexual reproduction (only occurs in the Felids)
  - i. Final generation of “zoites” exit the enterocyte, infect other enterocytes, and go through gametogony (production of gametes)
  - ii. Macrogamete (egg)
    1. Some final zoites remain a single cell and become a macrogamete (egg), within a macrogamont.
  - iii. Microgametes (sperm)
    1. Other final zoites go through multi-nuclear division, cytoplasmic division, and develop 2 flagella (bi-flagellate) on each gamete; thus forming a microgamont
    2. Exflagellation – when microgametes exit the microgamont in search of a macrogamete.
  - iv. Fertilization – a microgamete fuses with a macrogamete forming a zygote
  - v. A cyst wall forms around the zygote and the immature oocyst exits the macrogamont into the lumen of the host’s gut and is passed in the feces.
- f. Dissemination
  - i. Oocysts (unsporulated) exit the host in the feces and contaminate the environment.
    1. Felids are the only hosts to pass oocysts.
    2. Prepatent period (oocyst ingestion to oocyst passing): 19 - 48 days
    3. Oocysts highly resistant and remain infectious for many months

2. Cat to Paratenic Host
  - a. Facultative Indirect Life Cycle (heteroxenous) -- Paratenic host – Any warm blooded animal, including felids
  - b. Transmission
    - i. ingestion of an oocyst from the feces of a felid (the definitive host)
  - c. Invasion -- “Zoites” enter intestinal cells and lymph cells and transform in to tachyzoites.
    - i. Tachyzoites - rapidly dividing zoites via endodyogeny (2 daughter cells / division)
  - d. Asexual reproduction – extra-intestinal cells
    - i. Tachyzoites are dispersed throughout the body of the paratenic host
      1. The rapid destruction of host cells during the tachyzoite phase causes the acute/ severe disease
    - ii. Eventually tachyzoites transform into bradyzoites
      1. Bradyzoites
        - a. Slowly dividing zoites via endodyogeny (2 daughter cells / division)
        - b. Stationary (= non-disseminating) and form tissue cysts.
      2. Tissue cysts
        - a. Cause more chronic pathology in the paratenic (and human) hosts
        - b. Occur in and cause damage to the brain, liver, striated muscles
        - c. Remain viable for the life of the paratenic host.
  - e. General Notes
    - i. Tachyzoites may be transplacentally transmitted.
    - ii. Thus mother ingestion of oocyst from cat feces – Toxoplasmosis in fetus
3. Paratenic Host to Paratenic Host
  - a. Transmission
    - i. ingestion of a tissue cyst from a paratenic host (any warm blooded animal) = carnivorousism
  - b. Invasion and Asexual reproduction is the same as “Cat to Paratenic Host” above
  - c. General Notes
    - i. Tachyzoites may be transplacentally transmitted.
    - ii. Thus mother ingestion of raw meat with tissue cyst – Toxoplasmosis in fetus
4. Paratenic Host to Cat
  - a. Transmission
    - i. ingestion of a tissue cyst from a paratenic host (any warm blooded animal) = carnivorousism
  - b. Invasion, Asexual Reproduction, Sexual Reproduction and Dissemination is the same as “Cat to Cat” above.
  - c. General Notes:
    - i. Prepatent period (Ingest tissue cyst from paratenic host to passing oocysts) = 3 to 10 days  
V/S
    - ii. Prepatent period (Ingest oocyst from cat feces to passing oocysts) = 19 to 48 days

- C. Pathogenesis
  - 1. Intestinal Phase in Felids -- minimal.
  - 2. Systemic Disease (Extra-Intestinal Phase) in felids or paratenic hosts or humans – Explosive multiplication of tachyzoites cause massive destruction of host cells, also acute immune response. Tissue cysts cause tissue damage, and a source for recrudescence of acute disease.
- D. Clinical Disease (Cat only, see DZ in paratenic hosts below)
  - 1. Intestinal Disease – no complaint - oocysts found on routine fecal
  - 2. Systemic Disease -
    - a. Fever, anorexia, vomiting, diarrhea, enlarged lymph nodes, pneumonia (especially for FIV+ cats), encephalitis, nephritis, death.
- E. Diagnosis (Cat only, see DZ in paratenic hosts below)
  - 1. Intestinal Disease – oocysts in feces – use Zinc Sulfate as oocysts may distort in other solutions
  - 2. Systemic Disease – serologic tests
- F. Treatment
  - 1. Pyrimethamine plus triple sulfa drugs used against intestinal phase and acute phase.
  - 2. Clindamycin and Ponazuril also used.
  - 3. No good treatment for tissue cysts
- G. Control
  - 1. Sanitation
    - a. Clean litter box daily (sporulation in 1-3 days).
    - b. No raw meat for cats
    - c. Don't let cat outside to defecate or hunt
- H. Non-felid paratenic hosts
  - 1. Dogs -- Systemic toxoplasmosis, ingest oocyst from cat feces or tissue cyst from prey.
    - a. Fever, respiratory signs
  - 2. Sheep & Goats -- Systemic toxoplasmosis & Congenital toxoplasmosis, ingest oocyst from cat feces
    - a. Systemic – CNS signs
    - b. Congenital – abortion
    - c. Toxovac S48 – vaccine
  - 3. Cattle -- Congenital toxoplasmosis (abortion, but very rare), ingest oocyst from cat feces.
  - 4. Horse -- Systemic toxoplasmosis, low pathology, ingest oocyst from cat feces
  - 5. Swine -- Systemic toxoplasmosis, ingest oocyst from cat feces or tissue cyst from prey.
    - a. Fever, respiratory signs
    - b. Highly prevalent in free-range pigs
    - c. Important source of infection for humans
  - 6. Poultry -- Systemic toxoplasmosis, ingest oocyst from cat feces.
    - a. Prevalent in free-range and back-yard chickens
    - b. Important source of infection for humans
  - 7. Rodents -- Systemic toxoplasmosis, ingest oocyst from cat feces or tissue cyst from prey.
    - a. Decreased fear of cats
    - b. Major source of infection for cats.
- I. Zoonosis (Human infections)
  - 1. Systemic Toxoplasmosis and Congenital Toxoplasmosis
  - 2. Ingestion of oocysts from cat feces, unwashed vegetables, or unclean hands
  - 3. Ingestion of tissue cyst from undercooked meat (mainly mutton, goat, free-range pork, free-range chicken)
  - 4. Transplacental Transmission (Congenital Toxoplasmosis)
  - 5. Immunocompetent (systemic toxoplasmosis)
    - a. 1<sup>st</sup> exposure – “flu-like” illness that may last for weeks (Fever, myalgia, sore throat, lymphadenopathy)
    - b. Future exposures -- immune-protected, no issues.
  - 6. Immuno-deficient Adult (systemic toxoplasmosis)
    - a. Elderly & those with Immunosuppressive diseases
    - b. Severe disease (Respiratory, CNS, etc.)
    - c. 1<sup>st</sup> exposure prior to immune-suppression, then recrudescence may cause severe DZ
    - d. 1<sup>st</sup> or future exposure after immune-suppression may cause severe acute DZ
  - 7. Immuno-deficient Fetus (Congenital toxoplasmosis)

- a. Severe DZ (congenital malformation, mental retardation, death)
- b. If mother's 1<sup>st</sup> exposure occurs during pregnancy.
  - i. Transplacental transmission is greatest in 3<sup>rd</sup> trimester.
  - ii. But more severe defects if transplacental transmission occurs in the 1<sup>st</sup> Trimester.
- c. 1<sup>st</sup> exposure prior to pregnancy, then immune system controls toxoplasmosis, unless mother is immune-deficient. – can get antibody tested.
- d. Avoid cat feces, have someone else clean litter box daily (sporulation in 1-3 days)
- e. Avoid uncooked meat, unclean hands, unclean vegetables, unclean knives and cutting boards.

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### *Neospora caninum*

#### Canine coccidian of bovine abortions

##### A. Morphology

- Oocyst
  - small, subspherical, smooth coat, no polar cap, single embryo when passed
  - Sporulated oocyst contains 4 sporocysts with 2 sporozoites each = 8 sporozoites total
- Intracellular parasite of intestinal epithelium and various host tissues.

##### B. Life Cycle Rather Complex

1. Intermediate Host to Dog
  - a. Obligate Indirect Life Cycle (heteroxenous)
    - i. Definitive host – Canids only (Dog, Coyote, Wolf, etc.)
    - ii. Intermediate Host – Cattle and other animals
  - b. Transmission -- carnivorism, ingestion of tissue cysts
  - c. Invasion -- Zoites excyst from tissue cyst and invade enterocyte
  - d. Asexual reproduction (in intestinal cells)
    - i. Endodyogeny [single division forming 2 daughter cells] and schizogony [multi-nuclear division followed by cytoplasmic division forming multiple daughter cells]
    - ii. Causes no pathology in canids.
  - e. Sexual reproduction (only occurs in the Canids)
    - i. Final generation of “zoites” exit the enterocyte, infect other enterocytes, and go through gametogony (production of gametes)
    - ii. Macrogamete (egg)
      1. Some final zoites remain a single cell and become a macrogamete (egg), within a macrogamont.
    - iii. Microgametes (sperm)
      1. Other final zoites go through multi-nuclear division, cytoplasmic division, and develop 2 flagella (bi-flagellate); thus forming a microgamont
      2. Exflagellation – when microgametes exit the microgamont in search of a macrogamete.
    - iv. Fertilization – a microgamete fuses with a macrogamete forming a zygote
    - v. A cyst wall forms around the zygote and the immature oocyst exits the macrogamont into the lumen of the host's gut and is passed in the feces.
  - f. Dissemination
    - i. Oocysts (unsporulated) exit the host in the feces and contaminate the environment.
      1. Canids are the only hosts to pass oocysts.
      2. Oocysts highly resistant and remain infectious for many months.
2. Dog to Intermediate Host
  - a. Transmission
    - i. ingestion of an oocyst from the feces of a canid (the definitive host)
  - b. Invasion -- “Zoites” enter intestinal cells and lymph cells and transform into tachyzoites.
    - i. Tachyzoites - rapidly dividing zoites via endodyogeny (2 daughter cells / division)

- c. Asexual reproduction – extra-intestinal cells
    - i. Tachyzoites are dispersed throughout the body of the intermediate host
      - 1. The rapid destruction of host cells during the tachyzoite phase causes the acute/ severe disease
    - ii. Eventually tachyzoites transform into bradyzoites
      - 1. Bradyzoites
        - a. Slowly dividing zoites via endodyogeny (2 daughter cells / division)
        - b. Stationary (= non-disseminating) and form tissue cysts.
      - 2. Tissue cysts
        - a. Cause more chronic pathology in the intermediate hosts
        - b. Occur in and cause damage to the CNS, lungs, heart, striated muscles, etc.
        - c. Remain viable for the life of the intermediate host.
  - d. General Notes
    - i. Tachyzoites may be transplacentally transmitted.
    - ii. Pregnant dog ingestion of oocyst to in utero puppies
    - iii. Pregnant cow ingestion of oocyst to in utero calf
3. Intermediate Host to Intermediate Host’s Offspring
- a. Congenital Neosporosis -- Transplacental transmission
  - b. Transmission
    - i. “Re-activated” bradyzoites invade the placenta and fetus
    - ii. Tissue cyst of pregnant dog to in utero puppies
    - iii. Tissue cyst of pregnant cow to in utero calf
  - c. General Notes
    - i. Trans-generational infection
      - 1. A cow that was infected in utero will in-turn infect their calves, without reinfection with oocyst from dog feces.
4. Dog to Dog (via oocysts has not been reported, oocyst ingestion does not result in oocyst production).

#### C. Pathogenesis

- 1. Intestinal Phase in Canids -- none.
- 2. Systemic Disease (Extra-Intestinal Phase) in canids or intermediate hosts – Explosive multiplication of tachyzoites causes massive destruction of host cells, also acute immune response. Tissue cysts cause tissue damage, and is source for transplacental transmission.

#### D. Clinical Disease

- 1. Intestinal Neosporosis – no complaint - oocysts found on a routine fecal (Canids only)
- 2. Systemic Neosporosis
  - a. Dogs
    - i. Multi-system DZ due to tachyzoites and bradyzoites throughout the body and the immune reaction and inflammation that follows
    - ii. Neurologic signs, nodular dermatitis, pneumonia, urine incontinence, fecal incontinence, nephritis, myocarditis, polymyositis (inflammation (and pain) of several muscles).
- 3. Congenital Neosporosis
  - a. Dogs
    - i. Puppy litter-mates dying with signs of polyradiculitis (inflammation of the nerve roots, especially of the hind limbs)
    - ii. Puppy with signs of paralysis of the rear limbs at 3 weeks post-birth
    - iii. Puppy with flaccid hind limb paresis
  - b. Cattle
    - i. Abortions (10-20% of abortions caused by *N. caninum*)
      - 1. Abortions usually occur with 1<sup>st</sup> post-infection pregnancy
      - 2. Later pregnancies usually go to term, but calves are infected.
    - ii. Trans-generational infections (Seropositive calves give birth to seropositive calves –without reinfection via oocyst ingestion)
    - iii. Effects on milk production is unresolved

E. Diagnosis

1. Dogs
  - a. Puppy – classic flaccid hind limb.
  - b. Serology, molecular tests
  - c. Organism on biopsy, necropsy of litter mates
2. Cattle
  - a. Diagnostic arrays, immunological and molecular tests
  - b. Antibody tests for whole milk

F. Treatment

1. Dogs
  - a. No drugs available to kill tissue forms.
2. Cattle
  - a. No drug therapy available
  - b. Treatment of lactating cows is problematic (check withdrawal times)

G. Control

1. control wild and domestic canid populations
2. cull seropositive cows

H. Zoonosis --- Is not zoonotic

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***Sarcocystis cruzi***

**Canine coccidian of bovine deaths**

A. Morphology

- Sporocyst
  - Thin-walled oocyst sporulates and ruptures before exiting in the feces, thus sporocysts are seen in the feces
  - small, oval, smooth coat, no polar cap; 4 sporozoites

B. Life Cycle Rather Complex

1. Dog to Cattle
  - a. Obligatory Indirect Life Cycle (heteroxenous) --- Definitive host – Dog
  - b. Transmission -- carnivorism, ingestion of sarcocyst in cattle muscle
  - c. Invasion -- Bradyzoites from sarcocyst from muscle invades intestinal cells
  - d. (Asexual reproduction – none occurs in the dog.)
  - e. Sexual reproduction (only occurs in Dogs)
    - i. Zoites go through gametogony (production of gametes)
    - ii. Macrogamete (egg)
      1. Some final zoites remain a single cell and become a macrogamete (egg), within a macrogamont.
    - iii. Microgametes (sperm)
      1. Other final zoites go through multi-nuclear division, cytoplasmic division, and develop 2 flagella (bi-flagellate); thus forming a microgamont
      2. Exflagellation – when microgametes exit the microgamont in search of a macrogamete.
    - iv. Fertilization – a microgamete fuses with a macrogamete forming a zygote
    - v. A cyst wall forms around the zygote and the immature oocyst exits the macrogamont into the lumen of the host's gut
    - vi. The oocyst sporulates within the gut lumen, then ruptures, releasing its 2 sporocysts into the gut lumen.

- f. Dissemination
  - i. Sporulated sporocysts exit the host in the feces and contaminate the environment.
    - 1. Dogs are the only hosts to pass sporocysts.
    - 2. Sporocysts are infectious when shed, are very resistant and remain infectious for several months if kept cool and moist.
- 2. Cattle to Dog
  - a. Intermediate host – Cattle
  - b. Transmission
    - i. ingestion of a sporocyst from the feces of a dog (the definitive host)
  - c. Invasion -- Sporozoites enter vascular endothelial cells
  - d. Asexual reproduction – vascular endothelial cells and muscle cells
    - i. Zoites go through a few cycles of schizogony, then disperse throughout the body to muscle cells.
      - 1. The destruction of host cells during the tachyzoite phase causes the acute/ severe disease with immune reaction and inflammation.
    - ii. Bradyzoites go through schizogony
      - 1. Sarcocysts (muscle cysts), full of bradyzoites develop within muscle cells and remain viable for the life of the paratenic host.
  - e. Transmission -- carnivorous, ingestion of Sarcocyst in cattle muscle
- C. Pathogenesis
  - 1. Intestinal Phase in Canids -- none.
  - 2. Systemic Disease (Endothelial and Muscle Phase) in cattle – Zoites cause destruction of host cells, also acute immune response.
- D. Clinical Disease
  - 1. Intestinal Sarcocystosis – no pathology in the dog
  - 2. Systemic Sarcocystosis -- cattle only
    - a. Multi-system DZ due to zoites throughout the vascular endothelium and muscles, w/ immune reaction and inflammation that follows
      - i. Protracted fever, lymphadenopathy, anorexia, cachexia, muscle spasms, myositis, hyper-excitability, diarrhea, hyper-salivation, weakness, hair loss around eyes, neck and tail switch,
      - ii. Pregnant cows – abortions, still births
      - iii. Condemnation of carcass at inspection due to Sarcocysts
    - b. Pathology in cattle begins about 4-6 weeks post-ingestion of sporocyst
- E. Diagnosis
  - 1. Dogs –sporocysts found on a routine fecal exam
  - 2. Cattle – serology, necropsy
- F. Treatment
  - 1. Dogs
    - a. No drugs available to kill tissue forms.
  - 2. Cattle
    - a. Amprolium may provide some prophylactic protection.
    - b. Treatment against sarcocysts is ineffective
- G. Control
  - 1. control wild and domestic canid populations
  - 2. don't let dogs have access to raw meat or offal or dead animals
- H. Zoonosis --- Is not zoonotic

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## *Sarcocystis neurona*

### Opossum coccidian of horse neuropathy

#### A. Morphology

- Sporocyst
  - Thin walled oocyst sporulates and rupture before exiting in the feces, thus sporocysts are seen in the feces
  - small, oval, smooth coat, no polar cap; 4 sporozoites

#### B. Life Cycle

##### 1. Sylvatic Life Cycle

- a. Obligatory Indirect Life Cycle (heteroxenous)
  - i. Opossum -- definitive host; sexual / intestinal stages, passes sporocysts
  - ii. Bird – intermediate host, asexual / muscle stages, sarcocysts in muscles
  - iii. Bird ingests sporocysts from opossum feces and opossum ingests sarcocyst in bird muscle.

##### 2. Accidental Host -- Aberrant, dead-end host

- a. Horse
  - i. ingests sporocyst from opossum feces (contaminated food or water)
  - ii. Asexual stages / systemic stages
  - iii. Organism disseminates throughout body., especially to neural tissue, and muscle tissue

#### C. Pathogenesis

- 1. Systemic Disease but with a predilection for neural tissue (neurons and leukocytes of the brain and spinal cord) in horses – Zoites cause destruction of host cells, and acute immune response / inflammation.

#### D. Clinical Disease

##### 1. Equine Protozoal Myeloencephalitis (EPM)

- a. Spinal Cord involvement
  - i. Gait abnormalities, unilateral muscle atrophy (gluteal), myopathy, asymmetric weakness, and ataxia of limb
  - ii. Demarcated spontaneous sweating, loss of reflexes, cutaneous hyper-sensation.
- b. Cranial nerve involvement
  - i. Seizures, visual deficits, behavioral abnormalities
- c. Brain involvement
  - i. Depression, head tilt, facial paralysis, muscle atrophy (masseter), dysphagia
- d. Without treatment, may progress to recumbency and death

#### E. Diagnosis

##### 1. Horses

- a. Observation of Clinical Signs, mostly neurologic and muscle atrophy.
  - i. Unfortunately there is a broad spectrum of disease agents that induce similar clinical signs
- b. Serology
  - i. Serum for antibodies provides evidence of current or recent exposure; but may also give a false-positive due to exposure to another non-pathogenic *Sarcocystis* species.
  - ii. Western Blotting uses *S. neurona* specific antigens. Parasite antigen or antibody in spinal fluid is diagnostic.
  - iii. Molecular techniques such as PCR for demonstration of *S. neurona* DNA.
- c. Post-mortem demonstration of organism in CNS lesions.



F. Treatment

1. Horses

- a. Ponazuril, diclazuril, pyrimethamine, sulfadiazine.
- b. Long treatment period. Be vigilant of side-effects.
- c. Improvement in 60-70%, complete recovery in up to 20%, relapse in 20%.

G. Control

- 1. Prevent access of opossums to horse-feeding / watering areas
- 2. Prevent access of opossums to stored horse feed
- 3. Fallen fruit should be removed from horse pastures. Why?

H. Zoonosis --- Is not zoonotic

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