Chapter 8 - Phylum Apicomplexa: Gregarines and Coccidia

Taxonomy

P. Apicomplexa
   C. Gregarinea
      O. Eugregarinida
         S.O. Aseptina
            G. Monocystis
         S.O. Septatina
            G. Gregarina

C. Coccidia
   O. Eimeriida
      G. Eimeria, Toxoplasma
   O. Haemosporida
      G. Plasmodium

General Characteristics

All are parasitic and include a variety of parasites of medical importance
Possess a single type of nucleus, no cilia or flagella
Characterized by complex apical organelles - the apical complex, found in the sporozoite and merozoite stages of the life cycles of these organisms

Merozoites and Sporozoites

Asexual Reproduction

In apicomplexans, asexual reproduction is via multiple fission or shizogony
The multinucleated cell is called the shizont or meront

During the process of merogony, daughter nuclei of the shizont arrange themselves peripherally and a membrane forms around each nucleus
After cytoplasmic division, each nucleus with its attendant cytoplasm forms a separate organism - merozoite, which usually breaks away from the aggregate to infect a new host cell
Once a merozoite enters a new host cell, it may either enter another schizogonic cycle or becomes a macro- or microgametocyte via gametogamy
Sexual Reproduction

Syngamy initiates the sexual cycle
The resulting zygote undergoes sporogony (multiple fission of zygote) which results in the production of sporozoites (usually the infective stage)

The Apical Complex

At the anterior end, immediately beneath the cell membrane, are 1 or 2 electron dense structures call **polar rings**
Among some members, a truncated cone of spirally arranged fibrillar structures - **the conoid** - lies within the polar rings

In most members of the phylum, **subpellicular microtubules** radiate from the polar rings parallel to the long axis of the cell
Serve as support elements and possibly have a locomotive function

Located within the polar rings (and conoid if present) are electron dense bodies called **rhoptries** (singular, **rhoptry**)

A group of smaller, more convoluted structures, called **micronemes**, lies parallel to the rhoptries and appears to merge with them at the apex of the cell
Both rhoptries and micronemes appear to be secretory organelles that may facilitate the parasite’s penetration into the host cell

Located at the lateral edges of the parasite are one or more **micropores**
They seem to be sites for endocytosis of nutrients during the intracellular life of the organism

Once transformation from the sporozoite or merozoite to the trophozoite stage has occurred following incorporation into a host cell, all the aforementioned organelles lose their physical integrity and disappear - except the micropores which persist through all succeeding stages

Class Gregarinea

Parasitic of invertebrates, mainly annelids and arthropods
Parasitize the body cavity, intestine, or reproductive system of their hosts
Most members produce a resistant spore or oocyst (sporocyst containing sporozoites)
Hosts typically become infected by ingesting spores
Locomotion is by body flexion, gliding, or undulations of longitudinal ridges
O. Eugregarinida

Monocystis lumbrica

Lives in the seminal vesicles of the earthworm Lumbricus terrestris and other related worms
Worms become infected by ingesting mature spores (e.g. spores containing sporozoites)

Spores hatch in the gizzard and the released sporozoites penetrate the gut wall and enter the circulatory system via the dorsal vessel
They move forward to the hearts where they leave the circulatory system and enter the seminal vesicles
Here the sporozoites enter into tissue cells and mature to become trophozoites (= sporadins or gamonts)

The gamonts attach to cells in the region of the sperm tunnel and undergo syzygy - a permanent end to end association
After syzygy the gamonts secrete a wall around themselves, becoming a cyst (=gametocyst) with gametocytes

Each gamont undergoes numerous nuclear divisions with the nuclei subsequently moving to the periphery of the cytoplasm
The nuclei then bud off to become gametes (anisogametes); the subsequent fusion of the gametes yield the zygote
After a spore or oocyst membrane forms around the zygote it undergoes sporogony to yield 8 sporozoites

A new host may become infected from ingesting a gametocyst or an oocyst

Gregarina cuneata

This is a common parasite of the mealworm (Tenebrio spp.)

After ingestion, spores hatch and sporozoites penetrate the epithelial cells of the host’s gut
They undergo considerable growth as trophozoites; the growth of the anterior end eventually slows down and growth of the posterior region increases
Organism becomes divided into the protomerite and deutomerite

The trophozoites (gamonts or sporadins) then become separated from the host cell, pair and undergo syzygy
Trophozoites then encyst and form a thick gelatinous wall around themselves they are technically called gametocysts
During this time the protomerite and deuteromerite have fused to form a gametocyte which form anisogametes
Anisogametes conjugate forming zygotes
Zygotes form resistant spore coats and their contents divide (sporogony) to form sporozoites within a sporocyst

These are shed in the host feces
Under humid conditions, spore tubes eventually develop and spores are released

Class Coccidia

Primarily parasites of vertebrates, occurring in the epithelium of the digestive tract, liver, kidneys, blood cells
They have a prevalent intracellular reproductive phase

The life cycle has 3 major phases: **merogony** (produces merozoites), **gametogony** (produces gametocytes which yield gametes), and **sporogony** (produces sporozoites)

Thus, the coccidian life cycle includea the following stages:
**Sporozoites** the infective stage that enter host cells becoming trophozoites
These eventually multiply be merogony to yield **merozoites**
Generations of merozoites grow within and destroy host cells
Merozoites can enter other cells, undergo further merogony, and produce more merozoites

Some of the merozoites undergo gametogony and transform into gamonts in host cells
The gamonts produce "female" **macrogametocytes** and "male" **microgametocytes**
The macrogametocyte develops into a **macrogamete** and the microgametocyte undergoes multiple fission to yield biflagellated **microgametes**

Fertilization takes place to form a zygote
The zygote forms a protective wall around itself and sporogony yields a sporozoite-filled **oocyst**
Within oocysts are sporocysts, and within these are sporozoites which contain spores
The sporozoites containing spores are released when the sporulated oocyst is eaten by another host

In monoxenous life cycles, all stages occur in a single host
In some heteroxenous life cycles, merogony and a portion of gametogony occur in the vertebrate host
Sporogony occurs in the invertebrate host and sporozoites are transmitted via the bite of this host
In some heteroxenous life cycles, sporozoites are infective to a vertebrate intermediate host, which then produces zoites that are infective to a vertebrate that eats this intermediate host
Order Eimeriida

Macrogamete and microgamete develop independently without syzygy
Contains both heteroxenous and monoxenous species

F. Eimeriidae

Many species within this family are of veterinary importance

The wall of the oocysts consist of 2 layers; serves a protective function - it is comprised of resistant material that is protective against external environmental conditions

Many species of *Eimria* form sporocysts, which contain the sporozoites within the oocyst When the sporocysts reach the intestinal tract of their hosts, the sporocyst wall breaks down and the sporozoites are released

*Eimeria tenella*

A common parasite in the epithelial cells of the ceca of chickens, causing an extensive amount of tissue damage and death among young chickens

Life Cycle

Chickens become infected when they consume food or water that is contaminated with sporulated oocysts
Oocysts rupture in the gizzard and the sporozoites escape from the sporocyst in the small intestine making their way to the cecum
Here they penetrate and pass through epithelial cells

Within the epithelial cells the sporozoite become a trophozoite and undergoes considerable growth
Merogony occurs giving rise to 1st generation merozoites which eventually break out into the lumen of the cecum
Some of these merozoites enter cecal epithelial cells producing a 2nd merozoite generation
These can ultimately give rise to a third generation of merozoites

Some of the 2nd and 3rd generation merozoites enter epithelial cells of the cecum and undergo gametogony
Both macro- and microgametocytes are produced, with the microgametes eventually entering cells containing macrogametes, allowing for fertilization and the formation of a zygote
The oocyst wall then forms and oocysts are released from host cells, pass from the ceca to the large intestine and then out with the feces. Newly passes oocysts contain a single celled sporont, which undergoes sporogony to produce sporocysts and sporozoites.

Infections with *Eimeria* are self-limiting. That is, asexual reproduction in the chicken does not continue indefinitely.

**Pathogenesis**

Infection with *Eimeria* cause bloody diarrhea. There can be extensive damage to blood capillaries and as a result hemorrhaging. Cecum often becomes filled with clotted blood and plugs causing necrosis.

Many drugs are available to prevent the infection. But once it has established chemotherapy is usually non-effective.

**Family Sarcocystidae**

Members of this family are heteroxenous. Vertebrates serve as intermediate hosts; definitive hosts are mainly carnivorous birds and mammals.

**Life Cycle**

Oocysts, with their sporozoites, are passed with the feces of the definitive host and are ingested by an intermediate host. The merozoites (tachyzoites or bradyzoites) multiply asexually in various tissues and eventually form cysts. These tissue cysts contain infective merozoites.

Merozoite multiplication in the intermediate host is by merogony. When the carnivorous host has ingested its infected prey, some of the tissue merozoites develop into gametes. This sexual development leads to oocyst formation and sporogony leads to sporozoites.
Merozoites: Tachyzoites vs. Bradyzoites

The term tachyzoites has been coined for the first, actively multiplying merozoites that develop within the intermediate host, irrespective of whether infection is from oocysts or tissue cysts. Metrocytes (noninfectious) and bradyzoites (infectious) are merozoites that develop within tissue cysts.

Toxoplasma gondii

Causes human toxoplasmosis; originally discovered in the desert rodent.

The primary means of acquiring the parasite is either ingestion of inadequately cooked meat (e.g., beef, pork, and lamb) containing tissue cysts or contact with feral or domestic cats with oocysts. Congenital toxoplasmosis is a very serious disease, and for this reason pregnant women should avoid contact with litter boxes used by cats. Flies and roaches have been implicated as carriers of the infective stages from cat feces to food.

The parasite can attack a wide variety of tissue cells, but seems to favor muscle, lymph nodes and intestinal epithelium.

Infection of intestinal epithelium cells occurs only in felines and this developmental pathway is termed the enteric or enteroepithelial phase. It is during this stage that sporozoite-containing oocysts are formed that serve as the primary source for human infection.

In other hosts, including many species of carnivores, insectivores and primates, only the tissue or extraintestinal phase occurs.

The bradyzoites are released from the oocyst in the lumen of the host’s small intestine. In cats, some bradyzoites penetrate intestinal epithelial cells to begin the enteric phase, while others penetrate the mucosa and develop in cells of underlying tissues, including lymph nodes and leukocytes.

In the enteric phase, the bradyzoites enter the host cell, become trophozoites and undergo merogony. Each trophozoite produces from 2-40 merozoites. Some of these invade host cells and develop into micro- and macrogametocytes; undergo gametogony to yield gametes. The microgametes then invade cells with macrogametes to allow for fertilization and gamete formation.

The zygote develops in an oocyst that breaks out of the cell into the lumen of the cat’s intestine to be passed out with the feces.
The oocyst undergoes sporogony, forming 2 sporocysts each containing 4 sporozoites

In extraintestinal development, the sporozoites invade cells other than those of the intestinal epithelium, reproduce, and form merozoites - tachyzoites

In acute infections, an increase in the number of tachyzoites causes the cell to disintegrate, releasing the parasites to invade new cells
As the disease becomes chronic, parasites infecting the cells of the brain, heart, and skeletal muscle reproduce more slowly than during the acute phase
At this time they are bradyzoites and they accumulate in large numbers within a cell

Gradually thick walls develop around the masses to form pseudocysts, which may persist for years
Therefore, all animals, except cats can be considered paratenic hosts, since the parasite never completes its sexual phase in them

**Epidemiology**

*T. gondii* is cosmopolitan in distribution
All mammals, including humans are capable of transmitting toxoplasmosis transplacentally

Sporulated oocysts, tachyzoites and bradyzoites all serve as infective agents
Sources of infection vary, ranging from direct contamination to ingestion of inadequately cooked food or raw milk

Immunological surveys reveal that humans throughout the world carry antibodies to *Toxoplasma*
Clinical toxoplasmosis is rare, and infections are generally asymptomatic

The level of pathology can be affected by a number of factors:

- age of the host, with older hosts being more resistant to disease
- virulence of the strain of *T. gondii* involved
- natural susceptibility of the host
- degree of acquired immunity of the host
Symptomology and Diagnosis

Symptomatic or clinical toxplamosis may be classified as acute, subacute, chronic, or congenital.

*Acute* toxoplasmosis in humans is characterized by parasitic invasion of the mesenteric lymph nodes and liver parenchyma. The most common symptom is painful swollen lymph glands, especially in the cervical region. It is accompanied by fever, headache, anemia, muscle pain and sometimes lung complications.

*Subacute* toxoplasmosis is merely a prolongation of the acute stage.

Normally, the duration of the *chronic* stage is limited by the host’s immunological system. However, if immunity develops slowly, the course of clinical toxoplasmosis can be protracted. During this period, there can be extensive lesions to the lungs, heart, liver, brain and eyes (caused by the tachyzoites). The onset of the chronic phase occurs when immunity in the host becomes sufficient to suppress tachyzoite proliferation, which coincides with the formation of cysts.

Cysts may remain intact for years, producing no clinical symptoms. A cyst wall may occasionally rupture, releasing bradyzoites, most of these are killed by host responses. Death of bradyzoites elicits a hypersensitive reaction.

In the brain, nodules of glial cells gradually form at the sites of such reactions. And as a consequence, the victim may develop symptoms of chronic encephalitis, sometimes accompanied by spastic paralysis.

Congential toxoplasmosis results from fetal transplacental infection. Such infection may result in stillbirth.