CNS Parasitology

1. *Toxoplasma gondii*:

It is a coccidian, which is a member of the apicomplexa group of protozoa.

Remember: **Apicomplexa:** a group of protozoa that have a specialized organelle (apparatus) on their anterior aspect, which allows the parasite to go into the inside of cells, producing intracellular infections. Another example of this group is Plasmodium. Another feature of apicomplexa is that they have 2 ways of dividing:

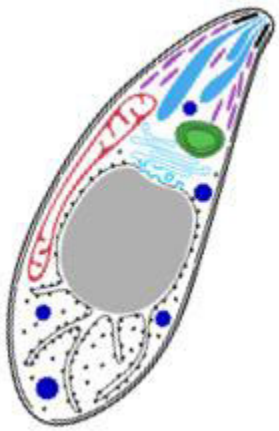
- Asexual: occurs in the intermediate host (humans for example).
- Sexual: occurs in the primary host (mosquito in the case of Plasmodium, as you remember).

As a rule, for *Toxoplasma gondii*, the primary host is a member of the feline (cats) family. These are the source of infection.

As for the intermediate host, normally, they are the animals eaten by the cat (usually a mouse or a rat). But there are no rules when the intermediate host is concerned, since *Toxoplasma gondii* can infect many animals (including human beings) and can affect many tissues. There is NO SPECIFICITY as far as the animal or tissue concerned.

Morphology of *Toxoplasma gondii:*

- Pear-shaped parasite.
- Has an organelle at the anterior end which allows it to go inside cells.
- Single mitochondrion.
- Has a nucleus.
- Has Golgi apparatus.
- 7-8 microns in length, so they can fit inside cells.



Life cycle of *Toxoplasma gondii:*

The asexual division in the intermediate host is a bit peculiar (abnormal). It is NOT by binary fission (which normally involves division of the cytoplasm into two until the daughter cells separate). In this case, there will be development of two cells inside the mother cell, which separate, and this is followed by breakdown of the plasma membrane of the mother cell, allowing the two new cells to move away from one another. This type of asexual reproduction is known as **endodyogeny**. It is a special form of binary fission restricted to *Toxoplasma gondii*.

As for the sexual reproduction, this takes place in the cat (the primary host). The result of the sexual reproduction is an **oocyst.** The oocyst comes out with feces and matures outside. Each mature oocyst normally contains 2 sporocysts and each sporocyst contains 4 sporozoites. This is the infective agent for the intermediate host.

If the rat, for example, eats something contaminated by the cat's feces or other animals eat grass contaminated by cat's feces, they become infected. Indeed, they can also infect human beings, for example children playing with cats can contaminate their hands with the feces or even if they play in sand pits, as cats like to defecate there, and also by food (lettuce for example) contaminated by cat feces.

In the intermediate host, the sporozoites are released in the gastrointestinal tract, they penetrate the walls of the intestines and then they develop into trophozoites. These trophozoites then enter inside the cells, where they divide very quickly and actively (by endodyogeny) and they eventually fill up the whole cell. The cell then ruptures, releasing the trophozoites which then go on to infect more cells, and the cycle goes on and on. These trophozoites that are actively and quickly dividing inside the cells are known as **tachyzoites** (tachy=fast, as in tachycardia). Remember they infect any type of cell or tissue non-specifically.

At some stage, some of these trophozoites will fill up the cell but they don't rupture it. Instead, they go into a dormant (resting) stage in a cell somewhere in the body. These become known as **bradyzoites**, because they are no longer dividing. This collection of bradyzoites inside a cell is known as a **cyst** (Toxoplasma cyst).

DO NOT get confused between Toxoplasma oocyst and Toxoplasma cyst:

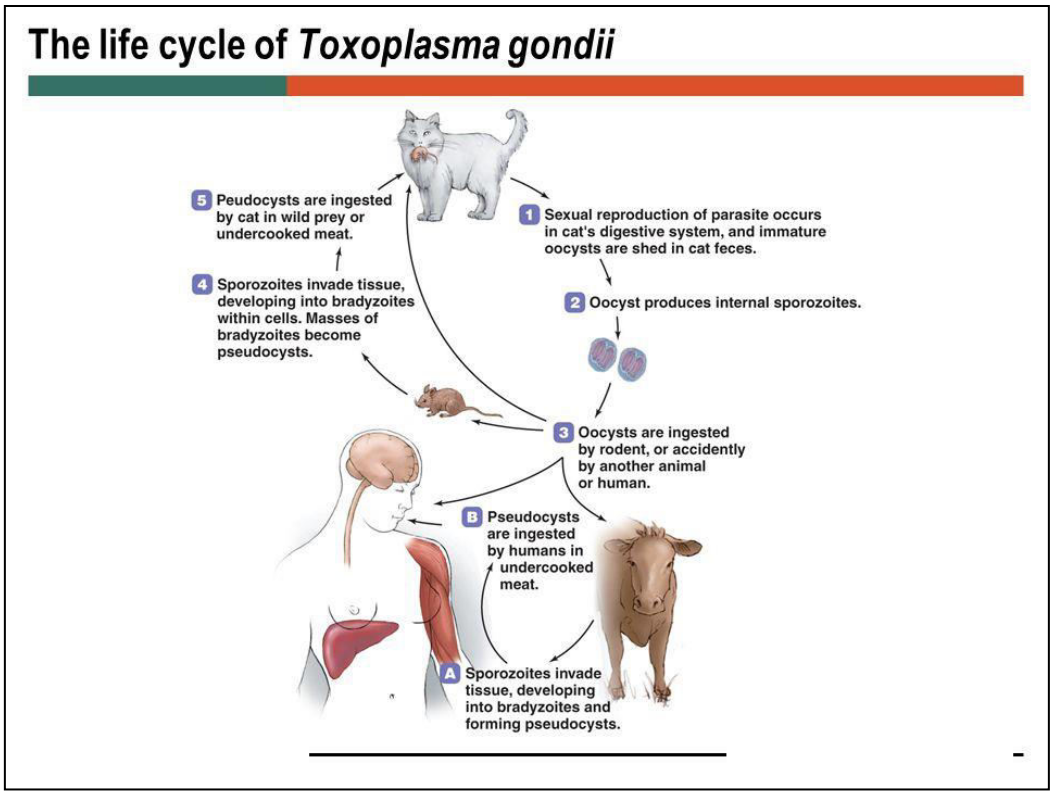
- Oocyst: the result of sexual reproduction, present in the cat's feces.
- Cyst: the result of binary fission (endodyogeny), present in the tissues of the intermediate host.

Both cysts and oocysts are infective to humans:

- Oocysts: in cat's feces (contaminated food, sand pits, etc…).
- Cysts: by eating meat of infected animals (cows and sheep for example and other intermediate hosts), without cooking it well. Cysts will then establish infection in human beings.

Human beings are intermediate hosts, but they are also **dead-end hosts**; they do not transmit the infection anymore, because it is very unlikely to be eaten by a pet cat. Infection can occur if a human is eaten by a wild cat (for example a tiger), but this is very rare.

As for infected rats (intermediate hosts), the cysts eaten up by the cat will release the bradyzoites, which will then develop into gametocytes (macrogametocytes and microgametocytes), which will fuse, giving rise to the zygote and the zygote will divide, eventually giving rise to the oocyst, which will then be shed with the cat's feces. This is the whole cycle.



Infection in humans:

INFECTION IS VERY COMMON. Wherever you have cats, you have Toxoplasma. In fact, there are studies done in certain areas of the world where the rate of infection with Toxoplasma is about 70%.

They get the infection by ingestion of the oocysts or the cysts.

Usually the infection is asymptomatic. If there are any symptoms they will be very mild (aches, malaise, etc…).

Eventually, the patient will end up with cysts containing bradyzoites, spread somewhere in the body.

There will be a CONTROLLED INFECTION because the patient will develop some immunity against the cysts, in the form of IgG. IgG will be formed against the Toxoplasma antigens and the cysts are kept under control and there will be no problem, infected people can live normal lives.

To find out whether a person has been previously infected by Toxoplasma and has cysts, IgG (anti-Toxoplasma antibodies) can be detected in blood samples. If there is no IgG against Toxoplasma (seronegative), this means that the person has never been exposed to Toxoplasma.

Disease in humans:

DISEASE IS VERY RARE. There are 2 situations where humans get the disease:

First: If a woman is infected by Toxoplasma for the first time, during pregnancy.

The Toxoplasma will pass through the placenta and will infect the fetus.

Effects on the fetus:

- First trimester: fetus is aborted, most likely.
- Second and third trimesters: there will be birth, but the baby will suffer from several problems, such as: visual field defect, neurological (sensory and motor) deficits, and mental retardation.

About 1/1000 pregnancies in America will end up with toxoplasmosis. This disease is known as **congenital toxoplasmosis**.

To confirm if a baby has congenital toxoplasmosis, take a blood sample from the baby and we detect the antibodies against Toxoplasma. In this case however, we need to measure BOTH IgG and IgM anti-Toxoplasma antibodies:

- IgG on its own: Not significant, because probably the mother had the infection a long time ago and has formed IgG against the Toxoplasma which has passed from her blood to the fetus, through the placenta.
- IgM present: Infection of the baby during pregnancy is confirmed, as IgM cannot cross the placenta, so anti-Toxoplasma IgM antibodies must have been produced by the baby.

It is recommended that a pregnant woman should not be around cats, to avoid this disease. Also, to encourage all little girls to play with cats, so that they get the infection when they are little and become immune, so there will be no chance for infection of the fetus during pregnancy. Remember, a baby is infected only if the mother is infected for the first time during her pregnancy. If a child is born with congenital toxoplasmosis, the second, third, etc… babies will be ok, because by that time the mother will be immune and there is no chance for the Toxoplasma to pass through the placenta.

***Second:* If a person becomes immunodeficient later in life.**

If a patient becomes immunodeficient (for example: HIV infection), cysts that are already there will no longer be controlled; they will become activated and will start producing tachyzoites, which will infect more cells. There will be reactivation of the disease (so the patient must be infected with toxoplasmosis a long time ago and have controlled infection, until his immunity is compromised).

Patients will suffer from problems with their eyesight and neurological deficits (sensory or motor).

END OF THE FIRST PART

Good Luck

-Ala'a Farkouh

Dedication to SQUAD

2. Trypanosoma:

The sleeping sickness or **African trypanosomiasis**

This is caused flageolet protozoa that belong to trypanosomatidae there are 2 kinds leishmania (which we took before) and Trypanosoma.

- Trypanosoma exists in two forms, one in the intermediate host (an insect) & another form in the primary host.
- Trypomastigote: found in primary host (humans)
- Epimastigotes: found in intermediate host
    - Kinetoplast (a dense granule of DNA within a large mitochondrion at the base of the flagellum).

The difference between them is in their undulating membranes (projection of plasma membrane that undulates causing some movement to the protozoan). It either extends the whole length in Trypomastigote or only in the anterior aspect in epimastigotes.

***Trypanosoma brucei*:** There are two types that infect humans, *Trypanosoma brucei (after Bruce who named it) gambiense* and *Trypanosoma brucei rhodesiense, the parasites cause similar diseases the main difference is that rhodesiense is present in east Africa (Rhodesia is the previous name of Zimbabwe) , yet the eastern type caused by rhodesiense tends to be more pathogenic causing a more severe case of the disease thus it develops faster and leads to death of the patient within few months up to a year while the case with gambiense is less severe and the patient can live up to a year and a half if not treated.*

The intermediate host in this case is the: tsetse fly.

In the case of rhodesiense it infects animals, so there is a wild reservoir (zoonosis) . The wild animals (like deers) are usually resistant to the disease and might be asymptomatic however with domesticated animals (pets; birds cats) the disease tends to be fatal. So it kills you and your dog ☹ .

So the tsetse fly would bite someone injecting it's the epimastigotes into the blood, which will change into trypomastigotes that will circulate in the blood & Go to the lymph nodes, here we have **the Acute stage** of the disease, where the patient doesn't feel well , he has fever ,headache, nausea he's a bit lethargic and it lasts for several months. If the disease was caused by the rhodesiense then it will take 3-4 months to involve the CNS, while it can take up to 8 months with the gambiense variant.

If not treated, the infection will carry on & after several months, trypanosomes (in the blood) will invade the CNS, through crossing the BBB, however, they won't invade the brain itself, but rather will invade the CSF, causing meningoencephalitis & this is the **late stage(chronic)** of the disease; which includes symptoms such as: drowsiness, patient detached from his environment, laziness, doesn't want to do anything (study for his exams) and eventually lay down and go into a coma which leads to death.

When these trypanosomes reach the CSF the patient is in a critical condition and the treatment probably wouldn't help, so they should be treated before the parasite reaches the CNS.

The patient produces lots and lots of IgM antibodies against these Ags but ineffectively; since that by the time IgM is produced the antigen changes and this is known as **antigenic variability** so a new IgM should be formed yet again the antigen changes thus the trypanosomes wouldn't be affected by the antibodies. This helps the organism to persist in the host for a long time evading the immune system. So you have a high IgM level but for nothing.

The diagnosis:

By taking a blood smear and staining it, trypomastigotes are stained and seen under the microscope.

Or in the later stages we can check the CSF for their presence.

There is a sign known as Winterbottom's sign: it's a sign that's seen in the early stages of trypanosomiasis, when you may suspect the infection, the sign includes mainly the enlargement of the posterior cervical lymph nodes in the basal occipital.

3. Taenia:

Now we're going to talk about a disease called **Cysticercosis;** if you remember when we talked about taenia we had 2 kinds taenia solium and taenia saginata, affecting pigs and cows.

We have 2 important forms of taenia which are:

1) The egg (– which have striated outer covering and in the middle we have hexacan, the same as taenia saginatum eggs)
2) Cysticercus: A single cysticercus is a cyst measuring 1–2 cm in diameter, and contains an invaginated protoscolex. The central space is filled with yellow fluid like a bladder; hence it is also called bladder worm.

Eggs are released with the feces of the primary host (Human), and then the eggs are eaten by the intermediate host (the pig or cow). Here cysticerci are produced, so if you eat the infected undercooked meat you get taenia solium or saginata (***the worm not the cysticerci***) in your GIT..

What happens if you eat the eggs through contaminated meat, feces… or by the tape worm itself?

In the case of saginata eggs get digested. Only in the case of the solium these eggs will disintegrate and release their hexacans Inside the GIT. Produce cysticeri, damage the intestinal wall and infect other tissues; distribute throughout the body developing into cysticerci around which there will be an inflammatory process, fibrosis that will lead ultimately to calcification.

So in this case with T.solium the human can actually become an intermediate host rather than having the worm, cysticerci are produced and the reason is thought to be due to the resemblance of humans with the actual intermediate host (pigs and chimpanzees). These cysticerci can live in muscles, skin, and tissues of the infected human but for a limited time as the inflammatory process takes over, the thing is here the intermediate host is a dead-end intermediate host unless cannibalism occurs.

Very commonly we find these cysticerci under the skin or as nodules in muscles which cause a reaction that's not so serious.

If the t.solim cysticerci reach the eyes (we can find them in the retina causing **retinitis**) it can cause blindness or just damage the vision (partial blindness or a blind-spot in the visual field) of the patient so it varies, the most serious condition is when the cysticeri reach the CNS it varies to the location giving rise to neurological deficits that can be motor or sensory... one peculiar deficit is the focal epilepsy.

Focal epilepsy is epilepsy affecting only a certain part of the body causing it to move involuntary.

The occurrence of focal epilepsy an adult patient with no history of brain disorders should make you suspect Cysticercosis especially in endemic areas.

We can see this in east Europe and Japan as they eat a lot of pig meat so it's common to see children with cysticercosis as well.

Diagnosis:

1) Suspect it from the signs and history of the patient.

2) CT scans to look for calcified nodules/ lesions.

3) Muscle/skin biopsy: look for cysticerci under the microscope.

Treatment: we give anti-helminthic drugs with steroids

4. **Amoeba: (mentioned in section two).**

We have 2 pathogenic kinds, one we mentioned before **nalgeria** and ***Acanthamoeba.***

The infection by these is very rare yet severe (serious).

They live in ponds (fresh water) and that's the main way of infection if you swim in the pond , drink from the water… actually if you wear contact lenses the ***Acanthamoeba*** this can cause keratitis as they reach the cornea and damage it.

Both amoebas can reach the CNS, get to the subarachnoid space and cause **meningoencephalitis** it's a very serious and dangerous disease only a few amoebic cases have been reported.

THE END.

You're only given a little spark of madness ….. You must lose it

Dedicated to SB.

Rajai Zurikat

(Dedicated to GB)