Sheet n.15

Doctor 22

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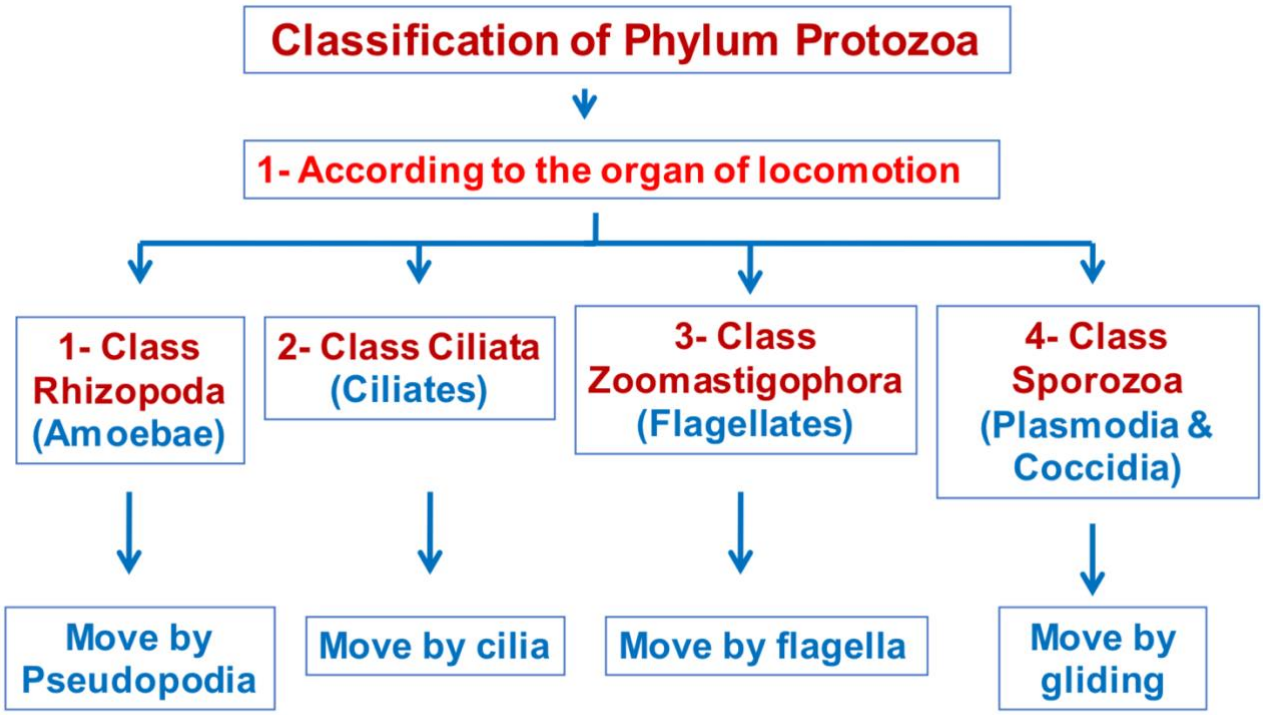
Protozoal Infections

Just a quick heads up before studying for this lecture.
This lecture may be full of new information, which could be slightly overwhelming, but what's actually important for our current level concerning protozoal infections, is understanding the different causative agents of these infections, the manifestations of the subsequent diseases, and some extra facts about each type of medically significant protozoan.

Classification of Phylum in Protozoa

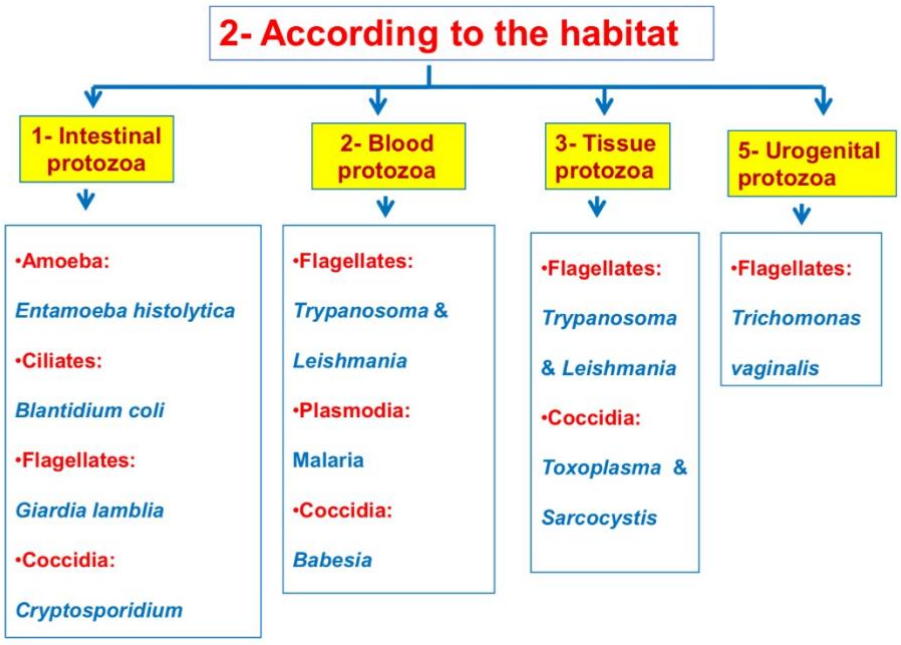
In microbiology, Protozoa can be categorized in two ways, they are either categorized according to their mechanism/organ of locomotion or according to their habitat/infection site in the human body, and we can also classify them according to their ability to reproduce sexually or asexually.



1) **Classifying Protozoa according to their organ of locomotion divides them into four classes:**
   1- **Class Rhizopoda (Amoeba) prossess pseudopods as an organ of locomotion (move by pseudopodia الأرجل الوهمية/الكاذبة). They include the parasite *Entamoeba histolytica*, an amoebozoan that causes amoebiasis.**
   2- **Class Ciliata which includes ciliates such as the Giant protozoa Balantidium coli that causes the disease Balantidiasis. The organ of locomotion of Cilitiates is their cilia (move by cilia/الشعيرات).**
   3- **Class Zoomastigophora also known as the Flagellates. They possess flagella as their organ of locomotion (move by flagellar rotation/دوران الأسواط).**
   4- **Class Sporozoa is an extremely important class of protozoa in medicine. They include Plasmodia which is the causative agent in Malaria, Babesia which is the causative agent in Babesiosis, and Coccidia which include Cryptosporidium, Cyclospora, and Isospora (all of which infect the gastrointestinal tract). Although being motile, the members of this class lack a defined organ of locomotion (they move by gliding/الانزلاق والتزحلق).**

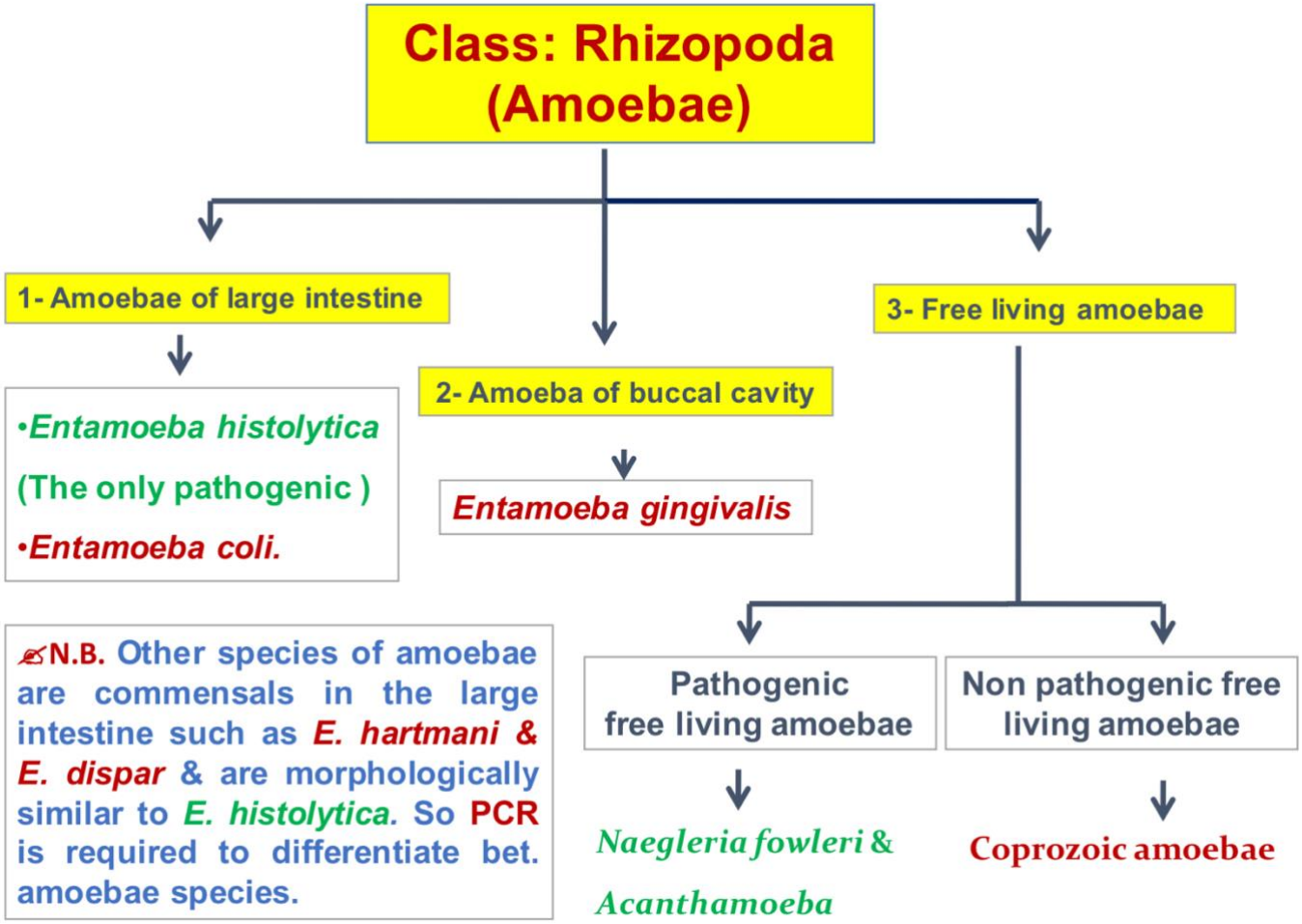
-The three classes of Rhizopoda, Ciliata, and Zoomastigophora all reproduce by binary fission.
-In contrast, Sporozoa have a sexual part in their life cycle, meaning that they alternate between sexual and asexual reproduction in their lifetime.
-Another special feature of Sporozoa is that they are all obligate intracellular parasites.

2) **The other classification of Protozoa involves categorizing them according to their habitat (the place they reproduce and reside in during an infection). This method divides Protozoa into four groups as well:**



Intestinal Protozoan Infections

Rhizopoda (Amoeba) is a broad group of protozoa that includes many members and species.



1- Amoeba of the Large Intestine:

It is known that the only pathogen of the Rhizopoda group that affects the intestinal tract is the species *Entamoeba histolytica*. Intestinal infection due to *E. histolytica* causes the disease known as Amoebiasis or Amoebic dysentery (دوسنطاريا/الزحار الأميبي). Dysentery is the infection of the intestines that results in severe diarrhea accompanied by the presence of blood and mucus in the stool/feces (the blood may be seen macroscopically with the naked eye or may require microscopic inspection to be observed, therefore it is easy to misdiagnose dysentery as normal diarrhea).

Other species of the Rhizopoda group including *Entamoeba coli*, *Entamoeba dispar*, *Entamoeba hartmanni*, and *Entamoeba moshkovskii*, all of which are considered nonpathogenic commensals that inhabit the large intestines and are part of the normal flora.

These species of the normal microbiota are important in medical microbiology because they could be easily mistaken for the pathogenic species *Entamoeba histolytica* when trying to reach a diagnosis. The most species to be confused with *E. histolytica* is *E. coli*, with one of the differences between the two is that *E. coli* has eight nuclei while the infective cyst of *E. histolytica* is *quadrinucleate* (has 4 nuclei).

For more definitive and accurate identification, PCR probes are required to differentiate between the pathogenic and nonpathogenic (commensal) amoeba species.

2- Amoeba of the buccal (oral) cavity:

***Entamoeba gingivalis* is a species of the Rhizopoda group that is also part of the normal flora. It is found to be associated with periodontal diseases but doesn't have a causation relationship with them.**

3- Free living amoeba:

It is very rare to encounter such amoeba and they include pathogenic and nonpathogenic species.

-The nonpathogenic species are also known as Coprozoic amoeba. This means that they only pass through the intestinal tract and exit along with feces without causing any disease in the host (the species of Sappinia were previously thought to be Coprozoic but recent studies reveal otherwise).

-Pathogenic free living amoeba include the species *Naegleria fowleri* that causes primary amoebic encephalitis (a very fatal condition with bad prognosis) and the genus Acanthamoeba that mainly cause keratitis (corneal ulcers), and it especially infects people that frequently use contact eye lenses. Acanthamoeba also causes GAE (Granulomatous Amoebic Encephalitis).

Entamoeba histolytica

-Generally, intestinal protozoal infections are related to poor sanitation & poor personal hygiene, and their main route of transmission is the feco-oral route. Furthermore, their geographical distribution is described as cosmopolitan distribution (which means worldwide or everywhere), but of course they are more common & prevalent in developing countries & temperate regions than in developed countries.

-Geographical distribution: Worldwide (cosmopolitan distribution) especially in the temperate zone and more common in areas with poor sanitary conditions and in people with poor personal hygiene (which is more commonly found in developing countries).

-Habitat: Large intestine (cecum, right and left colonic flexures, and sigmoidorectal region all in which fecal stasis takes place due to less peristalsis, giving *E. histolytica* a greater chance to infect and invade the mucosa and submucosa of the large intestine, resulting in dysentery).

-Important: we must know the microorganisms that cause dysentery & we must relate the pathophysiology of the microorganism to the resulted dysentery.

➔ Microorganisms that invade the intestinal mucosa & submucosa cause dysentery (bloody diarrhea)

-*Entamoeba histolytica* is also known for invading the intestinal tissue.

-*Entamoeba histolytica* infections are most commonly asymptomatic (we call the infected people in this case cyst passers) ➔ which occurs when the *Entamoeba histolytica* protozoa only live in the lumen of the intestine without invading the tissue.

-Cyst passers (people infected with asymptomatic amoebic infection) are actually healthy, but they still shed cysts in their stool ➔ so they may infect others directly or indirectly.

-When the *Entamoeba histolytica* protozoa invade the intestinal tissue ➔ they cause the typical amoebic dysentery (acute & chronic).

-D.H. (Definitive Host): Man

-R.H. (Reservoir Host): Man (and other primates), dogs, pigs, rats, and monkeys

-Disease: Amoebiasis or Amoebic dysentery

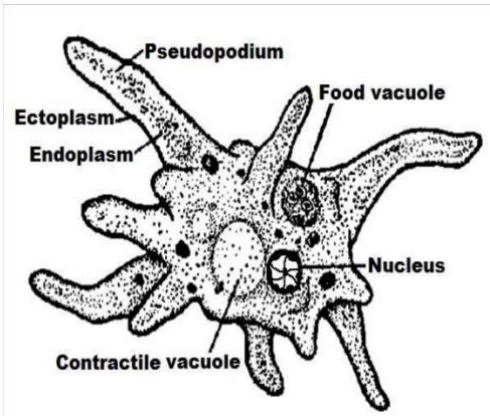
Morphological characteristics (of *Entamoeba histolytica*):

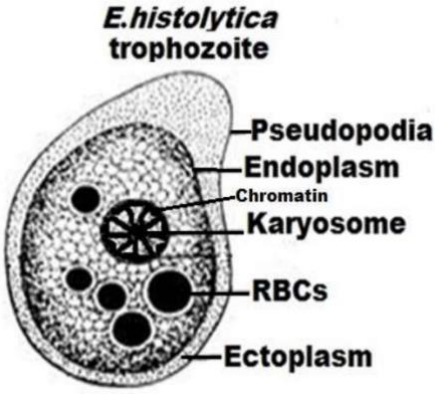
In general, protozoa have two principal morphological forms: the Trophozoite and the Cyst forms.

1- The Trophozoite stage is also known as the Tissue, Vegetative, Active, Motile, and Feeding form.

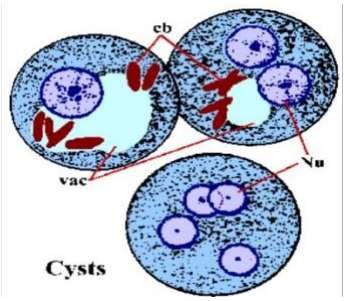
   The protoplasm of *E. histolytica's* Trophozoite form (the form the Amoeba takes on after invading tissue) contains a central nucleus that has a karyosome surrounded by fine chromatin, and it also has an ectoplasm and a granular endoplasm that contains food vacuoles and RBCs.

The presence of RBCs in these protists under the microscope is a pathognomonic sign indicating that these cells are definitely *E. histolytica* Trophozoites, differentiating them from other similar species such as *Entamoeba coli* and *Entamoeba dispar* (because these commensals can't perform phagocytosis on RBCs).

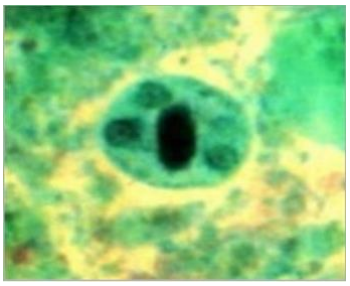




2- The Cyst stage appears during the quiescent and hardened stage of the protozoa's life cycle (such as during low temperature and low humidity conditions). Protozoa become encysted in order to protect themselves in harsh environments.



If the Amoebas have only been present in the lumen of the large intestine's tract without invading its mucosa, they will exit in their Cyst/Luminal form, which could either be immature or mature cysts.



Immature cysts are Uninucleate or Binucleate while the mature cysts are Quadrinucleate consisting of four nuclei per cyst. Only the mature cysts that exit with feces are capable of infecting another host (meaning that even if one was exposed to an immature cyst, they wouldn't get infected).

Mode of Transmission

1- Contaminated foods (ex. green vegetables), drinks, or hands with human stool containing mature cysts.

2- Handling food by infected food handlers such as cookers and waiters.

3- Flies and cockroaches that carry the cysts from contaminated feces to exposed food.

4- External or Internal Autoinfection (the feco-oral route or hand to mouth infection).

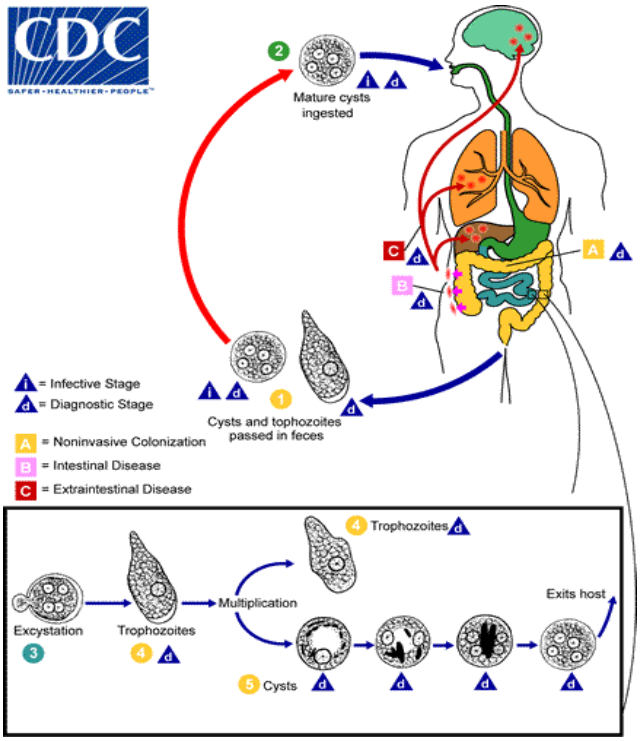
5- Homosexual transmission after getting exposed to contaminated fecal matter.

❖ **It is very important to distinguish between the infective stage and the diagnostic stage in the life cycle of a parasite.**

The mature Quadrinucleate Cyst is the infective stage of *Entamoeba histolytica*. The diagnostic stage however, can either be the cyst form of the amoeba or its Trophozoite form (which can only be observed when observing stool in cases of acute dysentery/diarrhea because the Trophozoites didn't have enough time to change into the Cyst form).

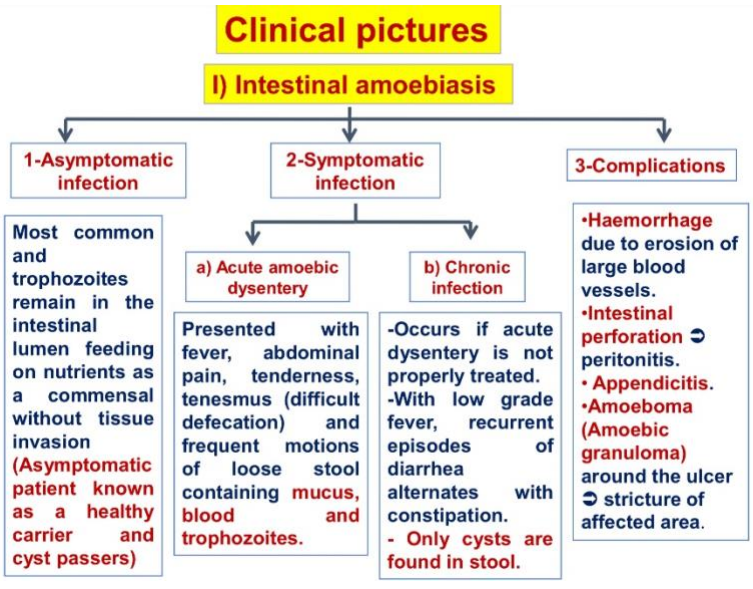
Each mature Cyst can become a Trophozoite (in the right conditions / after they invade the large intestinal mucus) and each Trophozoite can multiply into eight new Trophozoites.

After the mature Cysts enter the large intestine, they may remain confined to the intestinal lumen without changing into Trophozoites (these cases are known as Cyst passers or Asymptomatic carriers of *E. histolytica*). They may also invade the mucosa and submucosa of the intestinal tract (which causes acute or chronic amoebic dysentery), which could progress and result in extra-intestinal amoebiasis (infecting the liver, the lungs, the brain, and even the skin).



Clinical pictures:

I) Intestinal Amoebiasis:



-Intestinal amoebiasis includes a wide spectrum of manifestations (most common category) including asymptomatic infections, symptomatic infections, and other complications.

-Most people affected by *E. histolytica* are asymptomatic healthy carriers and keep the cycle of infection ongoing in the society (the majority of people exposed to this parasite are cyst passers).

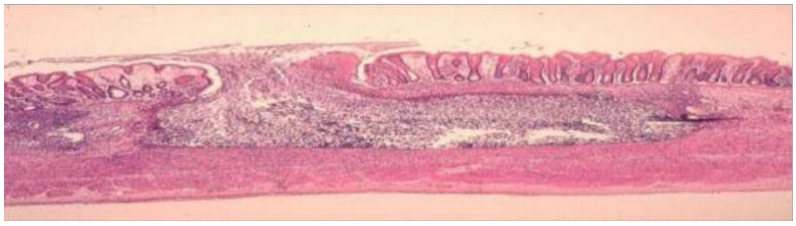
-Tenesmus is the recurrent attempt (urgent feeling) to empty bowels although them being empty.

-People suffering from invasive amoebiasis, whether acute or chronic, can also suffer from other complications including Hemorrhage formation, Intestinal perforation (which could lead to peritonitis), Appendicitis, and Amoeboma (Amoebic granuloma mass) around the ulcers formed by the invasion of the parasite.

*With heavy infection and lowering of host immunity

- The trophozoites of *E. histolytica* invade the mucosa and submucosa of the large intestine by secreting lytic enzymes resulting in amoebic ulcers. These ulcers usually occur at sites of slow colonic flow due to decreased peristalsis, especially in the cecum, in the colonic flexures, and in the sigmoidorectal region.

- Ulcers associated with Amoebiasis typically have a special histopathologic appearance described as flask shaped or inverted flask shaped with deeply undermined edges containing cytolyzed cells, mucus, and trophozoites.



II) Extra-Intestinal Amoebiasis:

Due to invasion of the blood vessels by the trophozoites in the intestinal ulcer ➔ reach the blood ➔ to spread to different organs such as:

1- The Liver:

- This type of Amoebiasis affecting the liver results in Amoebic liver abscess (giving off an Anchovy paste appearance) or diffuse amoebic hepatitis.
- The most common site to get affected by Extra-Intestinal infection of *E. histolytica* is the right lobe of the liver, either due to spread via the portal vein or direct extension from a perforating ulcer in right colonic flexure.

- **Clinical Presentation: includes fever, hepatomegaly, and pain in right hypochondrium.**

2- The Lungs:

- **Resulting in lung abscess, which causes pneumonitis with chest pain, cough, and fever.**
- **Amoebic lung abscess usually occur in the lower part of the right lung due to either direct spread from the liver lesions through the diaphragm or very rarely trophozoites may reach the lung via blood (circulation).**

3- The Brain:

- **The infection may continue to spread hematogenously (through blood circulation) and eventually reach the brain, which if infected results in encephalitis (a very serious and fatal condition) and brain abscess.**

4- The Skin:

- **Cutaneous amoebiasis (Amoebiasis cutis) occurs due to either extension of acute amoebic colitis to the perianal region or through rupture (through ulcers & direct extension) on the abdominal wall from hepatic, colonic, or appendicular lesions (mainly infects the skin near the colonic flexures).**

***Note: Immunocompromised individuals may suffer from the progression of the infection to become systemic amoebiasis. This can result in damage to any organ as well as the ones already mentioned.**

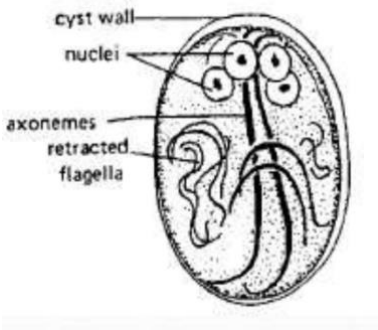
Patients afflicted by these diseases require medication and treatment, but most importantly, the contamination source must be cut off to prevent recurrent infections.

Giardia lamblia (an Intestinal Flagellate):

- ***Giardia lamblia* (also referred to as *Giardia duodenalis* or *Giardia intestinalis*) is the causative agent of Giardiasis and is the only common pathogenic protozoan found in the duodenum and jejunum of humans.**

- **Giardia exists in two forms: the trophozoite and the cyst forms.**

- **Unlike intestinal amoebiasis caused by *E. histolytica*, *Giardia lamblia* resides in the upper part of the small intestine's lumen (duodenum & jejunum, unlike the large intestine for *E. histolytica*) and is a noninvasive pathogen (and therefore only results in watery diarrhea without dysentery).**

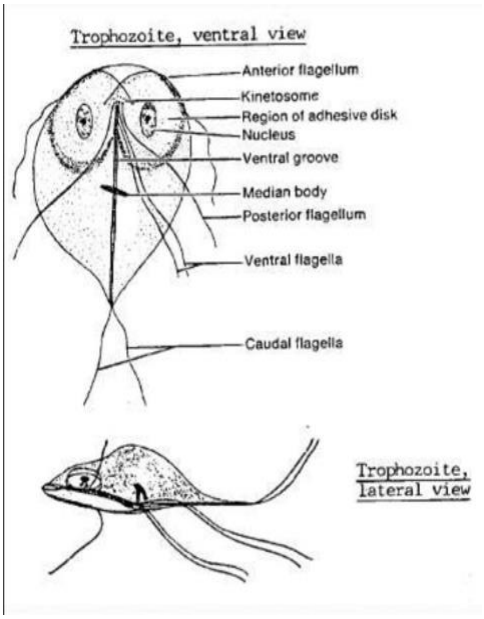


- **Another name for Giardiasis is Beaver fever (حمّى القندس).**

  (This means that there are reservoir hosts other than humans, such as beavers and other rodents. Nonetheless, Beaver fever is a controversial name for the condition because fever is not a symptom commonly associated with Giardiasis.)

Giardia lamblia: Morphology

- **The trophozoite of *G. lamblia* is a heart-shaped organism, has four pairs of flagella, 2 nuclei with prominent central karyosome, 2 axostyles (separating the two nuclei and dividing the organism into two halves), and is approximately 15 µm in length.**
- **They are flagellates which possess 4 pairs of flagella.**



- **Along with the flagella of this protozoa, each of the two nuclei is surrounded by a ventral adhesive disk (which is used for attachment), giving the organism the look of a face that is wearing goggles and has whiskers.**
- **The large concave sucking disks on the ventral surface helps the organism to adhere and attach to intestinal villi (without tissue invasion).**

- **The swaying or dancing motion of the trophozoites in fresh preparations is unmistakable.**

- ***Giardia lamblia* has a characteristic motility which is called "falling-leaf motility" or "tumbling motility" or "dancing motility". And this motility is quite important in order to distinguish *Giardia lamblia* in the diagnosis of giardiasis.**

- **Cysts are found in the stool –often in enormous numbers. As the parasites pass into the colon, they typically encyst, and the cysts are passed in the stool.**

- **They are ellipsoid (elliptical in shape), thick-walled, highly resistant, and 8–14 µm in length; they contain two nuclei as immature forms and four as mature cysts.**

- **The infective stage: the cyst stage.**

- **The diagnostic stage: the trophozoite & the cyst stages (& usually in giardiasis we observe the trophozoites).**

Pathology and Pathogenesis

- ***Giardia lamblia* is usually only weakly pathogenic for humans. Similar to *Entamoeba histolytica*, the majority of people infected with *Giardia lamblia* are asymptomatic cyst passers.**

- **Cysts may be found in large numbers in the stools of entirely asymptomatic persons.**

- **In some persons, however, large numbers of parasites attached to the bowel wall may cause irritation and low-grade inflammation of the duodenal or jejunal mucosa (with abdominal pain, below-grade fever, nausea & vomiting), with consequent acute or chronic diarrhea associated with crypt hypertrophy, villous atrophy or flattening, and epithelial cell damage.**

- **The attachment of the Giardia Trophozoites to the intestinal villi lining the brush border of the small intestine <u>prevents the absorption of many digested nutrients, including lipids</u>, leading them to <u>get excreted with feces</u> in what's known as <u>steatorrhea</u> (fat rich, greasy, foul, and smelly stool). Note that although stool is lipid-rich in the case of Giardiasis, it normally doesn't contain blood.**

Transmission

- **Transmission of Giardia cysts is very similar to that of Amoeba cysts, and is related to poor sanitation and hygiene.**

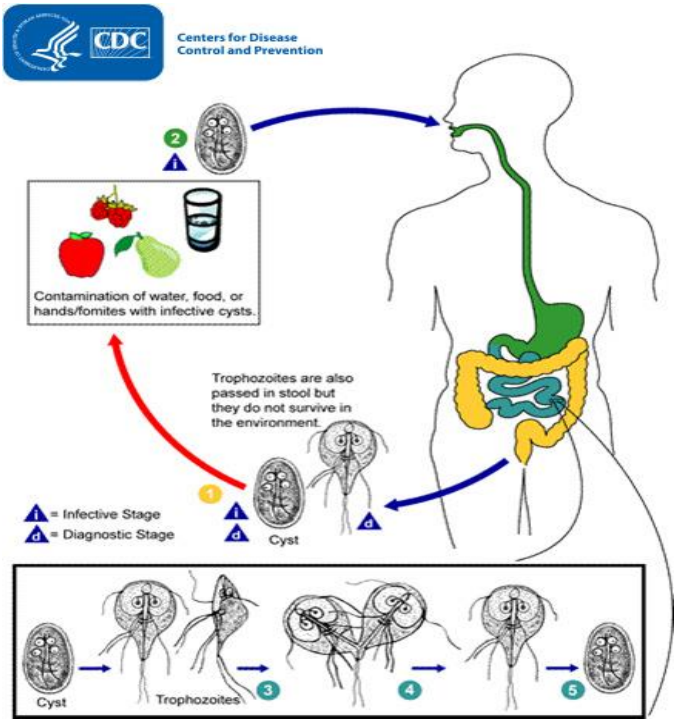
- **Giardiasis tend to be an outbreak, as humans are infected by ingestion of fecally contaminated water or food containing giardia cysts or by direct fecal contamination, as may occur in day care centers, refugee camps, and institutions (such as in prisons and in military camps), or during oral–anal sex (homosexual acts).**

- **Epidemic outbreaks have been reported at resorts, where overloading of sewage facilities or contamination of the water supply has resulted in sudden outbreaks of giardiasis.**

- **The cysts of *Entamoeba histolytica* can survive in water as well as in the environment for up to weeks, meanwhile the cysts of Giardia can survive in water for up to 3 months (the infection is mainly water borne and transmission can occur even in chlorinated water).**

- **Water chlorination is neither cysticidal nor amoebicidal.**

- **Cysticidal (targets cysts and kills them) while amoebicidal (targets amoebas & kills them)**



- **If we increase the chlorine concentration in the pool in order to get rid of Giardia & *Entamoeba histolytica*, the pool becomes unsafe for human consumption.**

- **The infective stage of *G. lamblia* is their mature Quadrinucleate cyst form, while the Trophozoite form mainly (as well as the cyst form) is the diagnostic stage of the parasite.**

- **Each Giardia cyst gives two Trophozoites (each of which has two nuclei).**

Giardiasis: Clinical Aspects

- The spectrum varies from asymptomatic carriage to severe diarrhea and malabsorption. Subclinical infections common in endemic areas.

- In acute outbreaks, stools may be watery, semisolid, greasy, bulky, and foul smelling at various times during the course of the infection, described as steatorrhea (typical diarrheal stool in giardiasis patients).

- The diagnosis of giardiasis is made by finding the cyst in formed stool or the trophozoite in diarrheal stools samples, duodenal secretions, or jejunal biopsy specimens.
- Commercially available, enzyme immunoassays (EIAs) contain antibodies that detect Giardia antigen in stool (fecal/stool antigen test) ➔ Enzymatic reaction or color change indicates the presence of the antigen in the tested sample.

- Another method of diagnosis is known as the String test or the Entero-test which makes use of a gelatin capsule that's tied to a string and is ingested. After almost 4-6 hours of the capsule getting swallowed, the capsule reaches the duodenum, and the string is used to pull out the capsule that now carries material (a sample) representing the duodenum in order to search for Giardia Trophozoites. The downside of using such a method of diagnosis is that the patient will be required to remain fasting for the entire duration through which the capsule remains in their body. Because of the inconvenience of the method, fecal/stool antigen test replaces this method & many other tests most of the time.

- Frequent testing is usually required to reach a diagnosis. This is because tests may be done at times when the parasite is present in the body but not necessarily apparent (as when there is no shedding of the trophozoites and cysts with stool). In Amoebiasis for example, when the patient has a severe fever (which occurs only in acute amoebic dysentery), the trophozoites and cysts of E. histolytica are extremely likely to be found compared to other times that have intermittent shedding (as in chronic amoebiasis)

Giardiasis Treatment

- Quinacrine and Metronidazole are effective (70%-95%) and are preferred for patients capable of ingesting tablets.

- Tinidazole.

- Furazolidone is used by pediatricians.

Close contacts should be examined.

- **Remember:**
  1) **Cryptosporidium species & Cyclospora species are of the class "Sporozoa" and of the subclass "Coccidia".**
  2) **Sporozoa can sexually reproduce in their life cycle as they alternate between sexual & asexual reproduction.**

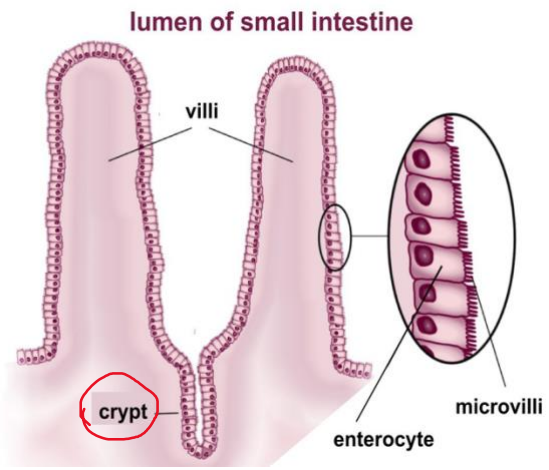
3- CRYPTOSPORIDIUM (INTESTINAL SPOROZOA)

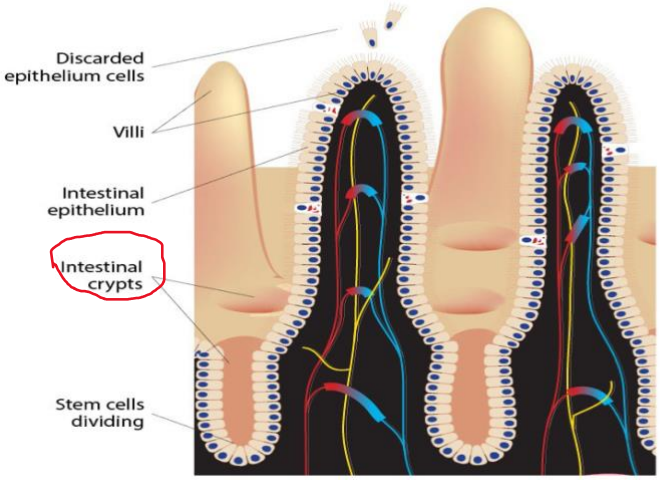
- **The disease caused by Cryptosporidium is called Cryptosporidiosis.**

- **Cryptosporidium species, typically *C. hominis* and *C. parvum* can infect the intestine of immunocompromised persons (eg, those with AIDS, as it occurs in almost every AIDS patient) and cause severe, intractable diarrhea (prolonged chronic diarrhea) ➔ the patient may die due to dehydration caused by the diarrhea.**

- **Cryptosporidium inhabits the brush border of mucosal epithelial cells of the gastrointestinal tract, especially the surface of villi of the lower small bowel.**

- **They are spores (hidden spores) which are present in the crypts of the intestinal villi (of the small intestine), hence the name "Crypto"-"sporidium").**





Extra images

- **Cryptosporidium species have a sexual part in their life-cycle (a reason as to why they are classified as Sporozoa), and because of this, their cysts is called oocysts.**

- **They are also an example on internal autoinfection, as they can continue their life cycle in the same host.**

- They have long been known as parasites of rodents, fowl, rhesus monkeys, cattle, and other herbivores and have probably been an unrecognized cause of self-limited, mild gastroenteritis and diarrhea in humans.

Clinical Aspects:

- Clinically, range from self-limited, mild and transient watery diarrhea (immunocompetent) to chronic, severe, non-bloody diarrhea with nausea, vomiting, abdominal pain, and anorexia resulting in weight loss and death, which is why the infection can be dangerous to certain people (immunocompromised).

- Diagnosis depends on detection of oocysts in fresh stool samples.

- Stool concentration techniques using a modified acid fast stain are usually necessary (the oocysts stain red using acid fast stain). Stool antigen detection by direct fluorescent antibody or EIA tests are now commercially available.

- Nitozoxanide (in addition to HAART -Highly Active Anti-Retroviral Therapy- treatment given to HIV patients), a synthetic drug, has been approved for use in all patients (immunocompromised patients) over 1 year of age in the United States and is reported to have a cure rate of 72% to 88% by the CDC.

- Immunocompetent individuals don't get treatment because the disease they acquire has mild symptoms (mild & transient gastroenteritis).

4- CYCLOSPORA (INTESTINAL SPOROZOA)

- The infection caused by Cyclospora is called Cyclosporiasis.

- Just like Cryptosporidium, Cyclospora infection causes mild & transient gastroenteritis in immunocompetent individuals.
  On the other hand, Cyclospora infection causes severe intractable diarrhea in immunocompromised individuals (like HIV-patients).

- The life cycle of Cyclospora is similar to that of Cryptosporidium and appears to involve only a single host (internal autoinfection). Cyclospora, however, differs from Cryptosporidium in that Cyclospora oocysts are not immediately infectious when passed in stools.
- Their oocysts need time in the environment (about 4-5 weeks) before they become infectious ➔ So, person to person transmission is less likely in Cyclosporiasis.

- **Pathogenesis: Altered mucosal architecture with shortening of intestinal villi due to diffuse edema and infiltration of inflammatory cells leads to diarrhea, anorexia, fatigue, and weight loss.**

- **When examining stools for oocysts while trying to reach a diagnosis (8–10 µm), keep in mind that the oocysts are acid-fast positive (reddish).**

- **Cyclospora infections are treatable with trimethoprim-sulfamethoxazole (TMP-SMZ).**

- **To reemphasize: an important difference between Cryptosporidium and Cyclospora:**

  In Cryptosporidium ➔ their oocysts are immediately infectious once they are passed in the stool, so person to person transmission is possible whether directly or indirectly.

  In Cyclospora ➔ their oocysts need about 5 weeks for them to become infectious.

- **Important note: Cryptosporidium & Cyclospora are acid-fast protozoa along with Isospora ➔ So we can use acid-fast stain to diagnose them (we observe acid-fast oocysts).**
  (Their oocysts can't be seen by the wet mount test -by mixing a stool specimen with saline and then looking at it under the microscope- we must use the acid-fast stain test to detect them & they are stained red.)

5- *Balantidium coli* (Intestinal Ciliated Protozoa)

- **The protozoan with the largest size among all protozoa.**

- ***Balantidium coli* is called the giant protozoan.**

- **It causes Balantidiasis or Balantidial dysentery, and is the largest intestinal protozoa of humans.**

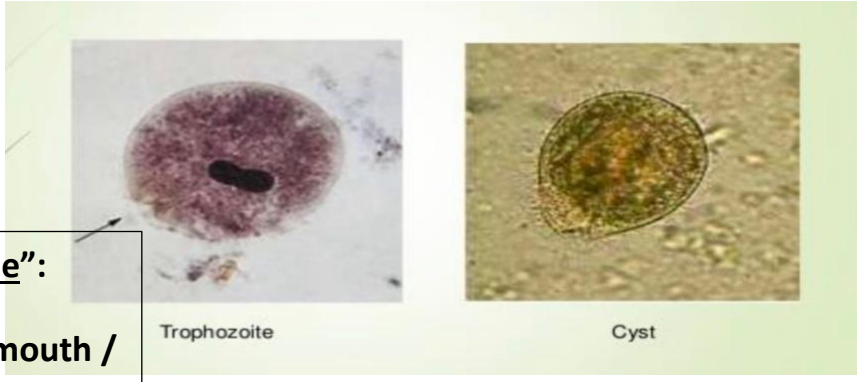
- **In Balantidium coli infections, there could be:**

⇨ **Only attachment: which causes watery diarrhea.**
⇨ **Invasion: which causes bloody diarrhea (dysentery).**

- **The trophozoite is ciliated oval organism 60 X 45 µm or larger. It has a steady progression and rotation around the long axis motion.**

- **Most infections are apparently harmless (asymptomatic). However, rarely, the trophozoites invade the large bowel and terminal ileum causing erosions and ulceration (resulting in Balantidial dysentery).**

- **Treatment: Oxytetracycline, may be followed by Iodoquinol or Metronidazole.**



A "Cytosome":

It acts as a mouth / food apparatus.

Balantidium coli

- ***Balantidium coli* is characterized by having two nuclei:**

  1) **The first one is called Macronucleus: which is sausage-shaped, and it can be seen in the image above.**
  2) **The second one is called Micronucleus: which is nested into the macronucleus, and it is not clear in the image above.**

Sexually Transmitted Protozoan Infections:

Trichomonas (Urogenital Flagellated Protozoa)

- **Trichomonas are flagellated protozoa.**

- **IMPORTANT: Don't have a cyst stage, as they are only found in the trophozoite form. ➔ Require direct contact to cause infection (a sexually transmitted disease).**

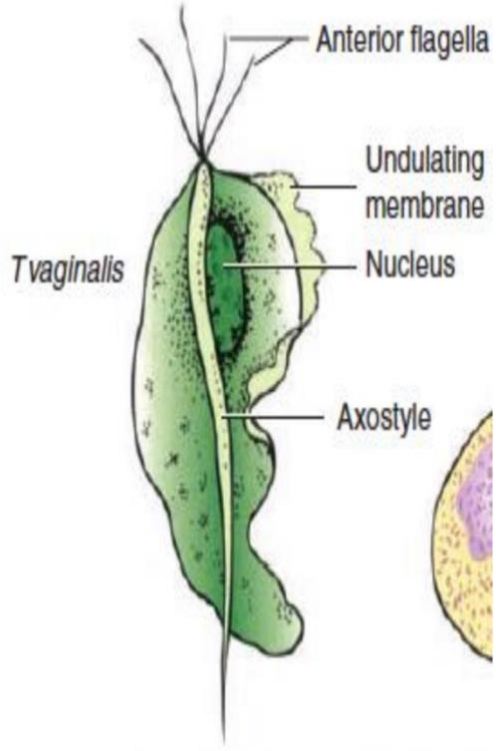
  ➔ They can't survive outside the body (as only the cyst form can usually survive outside the body, but there are exceptions of course regarding the fact that they can't live outside the body).

- **Its shape is described as "pyriform" (pear-shaped).**

- **IMPORTANT: Its name "Trichomonas" might cause confusion & might be misleading, as one may think that the prefix "Tri" refers to Trichomonas having three flagella, while it actually has 5 flagella: 4 anterior flagella & 1 running along the undulating membrane.**

- **IMPORTANT (past paper question): how many flagella does Trichomonas have? (Pay attention & don't let the name mislead you!)**

  Answer: It has 5 flagella.



- **Three members (species) of the genus Trichomonas parasitize humans (they are of high medical importance): *Trichomonas hominis*, *Trichomonas tenax*, *Trichomonas vaginalis*. Only T. vaginalis is an established pathogen however.**

- **Trichomonas vaginalis inhabits the urogenital tract of females & the urethra of males.**

- **Trichomonas tenax inhabits the oral cavity.**

- **Trichomonas hominis inhabits the intestine.**

- **Trichomonas tenax & Trichomonas hominis are part of the normal flora, and usually they don't cause confusion in the diagnosis of *Trichomonas vaginalis* infection because of the specificity of the habitat they live in.**

  So, when you take a specimen from the urogenital tract of an infected person and you find it containing Trichomonas, you know for sure that it is the pathogenic *Trichomonas vaginalis* because the other Trichomonas species (tenax & hominis) inhabit other parts of the body.

- **Trichomonas vaginalis causes trichomoniasis in human.**

- **It is pear-shaped with an undulating membrane lined with a flagellum along with 4 other anterior flagella. It is about 5-30 X 2-14 µm.**
  It moves with wobbling or rotating motion.

- **Direct contact of *T. vaginalis* with the squamous epithelium of the genitourinary tract results in destruction of the involved epithelial cells and the development of a neutrophilic inflammatory reaction and petechial hemorrhages (petechial hemorrhages: ruptures of the microscopic capillaries).**

- **Usually, females are more susceptible than males to be infected with Trichomoniasis when exposed to *Trichomonas vaginalis*.**

- **In females, it causes dysuria, dyspareunia and low-grad inflammation limited to the vulva, vagina, and cervix causing frothy yellow-green or creamy discharge.**
  - **Dysuria: the sensation of pain or burning in association with urination.**
  - **Dyspareunia: pain during sexual intercourse.**

- **The vaginal discharge in females suffering from this condition is described as clear or thick, has a yellow or green color, and is also described as malodorous (having a very unpleasant odor).**
  Usually, green vaginal discharge is clinically linked with Trichomoniasis.

- **Trichomonas infection of the lower genital tract in females results in vulvovaginitis.**

- **Strawberry cervix is a characteristic sign of Trichomoniasis (we will study it in more depth in OB/GYN) ➔ the cervix becomes strawberry-like.**

- **In males, it may infect the prostate, seminal vesicles, and the urethra.**

- **In the case of Trichomonas infection in males, the protozoan is usually found in the urethra ➔ so, the most usual symptom is dysuria.**

- **Wet mount examination for motile trophozoites is sufficient in most symptomatic cases.**
- **The type of motility of *Trichomonas vaginalis* in wet samples seen under the microscope is known as "corkscrew motility" which is typical for Trichomonas vaginalis.**

- **It is important to note that the type of motility of a microorganism is significant for identification & diagnosis and can be specific for certain microorganisms.**

- **Treatment: Topical and Systemic Metronidazole.**
  Tinidazole, Ornidazole are equally effective with fewer side effects

- **Always remember that: as a doctor, when you diagnose a person with Trichomoniasis, you never actually cure them from Trichomoniasis unless you cure their partner as well ➔ if you don't cure their partner; they will get reinfected with Trichomoniasis.**
  So, in STD's (Sexually Transmitted Diseases) you need to cure the patient & their partner to prevent reinfections.

Blood and Tissue Protozoan Infections

They are a bit different from intestinal and urogenital protozoa ➔ as we are not going to refer to their life-cycle stages as "trophozoites" & "cysts".

Haemflagellates

- **Trypanosoma ➔ Causes Trypanosomiasis (is further divided into African Trypanosomiasis & American Trypanosomiasis).**

- **Leishmania ➔ Causes Leishmaniasis.**

- **They have 4 stages in their life cycle (as can be seen in the image):**

  1) **Amastigote**
  2) **Promastigote**
  3) **Epimastigote**
  4) **Trypomastigote**

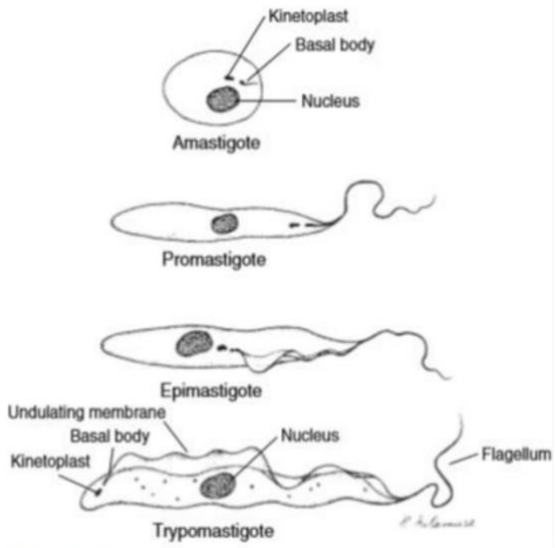


Figure 49-8 Characteristic stages of species of *Leishmania* and *Trypanosoma* in human and insect hosts. (Illustration by Nobuko Kitamura.)

- **Both Promastigote & Epimastigote stages are only found in vectors carrying these protozoans.**

- **Trypanosoma, Leishmania, and even the causative agent of malaria require a vector to transmit the infection to other reservoir hosts.**

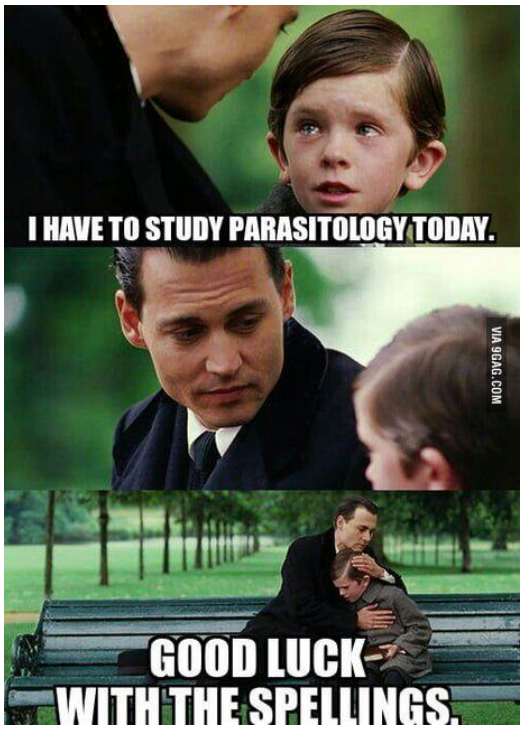
- **However, in the host (human), they are present in their Amastigote or Trypomastigote stages.**

- **Amastigote stage is unique ➔ as it is round in shape and it is the intracellular form. So, if the disease involves an intracellular infection ➔ these protozoans will be in the Amastigote stage.**

- **Generally, the diagnostic stage of Trypanosoma & Leishmania:**

⇨ **Can never be their Promastigote or Epimastigote stages.**
⇨ **They can be however, in their Amastigote or Trypomastigote stage, depending on the nature of the particular disease they cause.**

- **Therefore, if asked about the diagnostic appearance of Trypanosoma or Leishmania when they cause an extracellular infection, the only possible answer is that they are in their Trypomastigote stage.**
  The Amastigote stage must be ruled out because the infection isn't intracellular. Furthermore, the "Promastigote" & "Epimastigote" stages must be ruled out as well since these stages only appear in their vectors but not in infected hosts (humans).



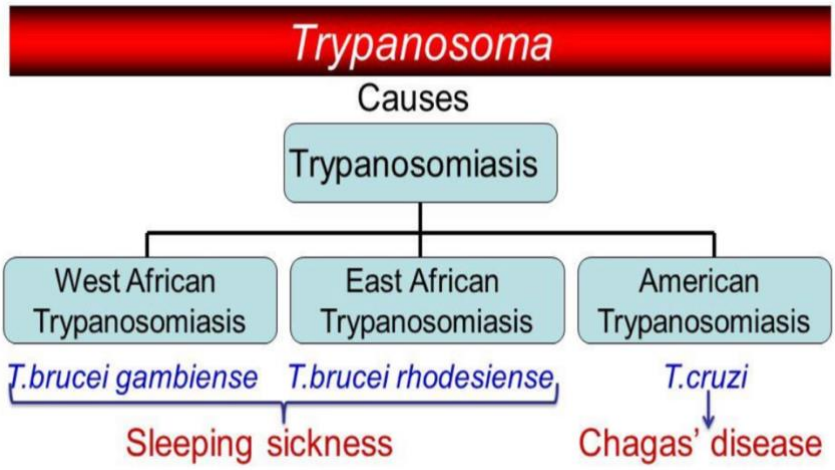
1- Trypanosoma

- **The general microbiological term for the infection with Trypanosoma is <u>Trypanosomiasis.</u>**

⇨ **<u>African</u> trypanosomiasis: <u>African sleeping sickness</u>**
⇨ **<u>American</u> trypanosomiasis: <u>Chagas' disease</u>**

- **The <u>causative agent</u> of:**

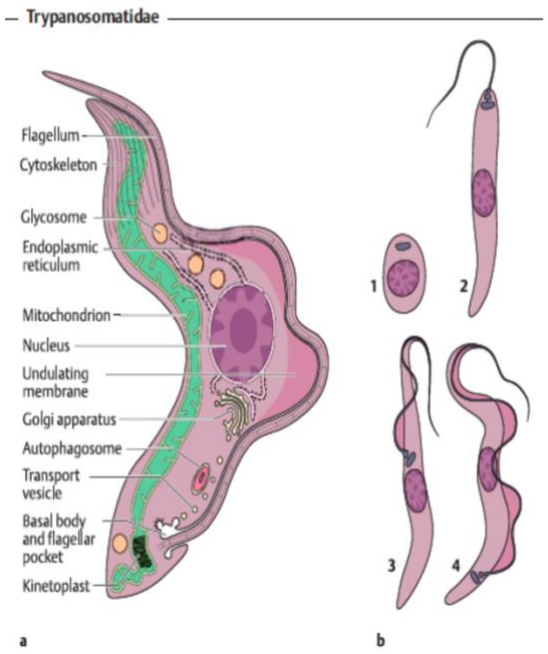
⇨ **<u>African</u> Trypanosomiasis: *Trypanosoma brucei* complex**
⇨ **<u>American</u> Trypanosomiasis: *Trypanosoma cruzi***



- **In the <u>end-stage</u> of the African <u>sleeping sickness</u>, the patients have an <u>uncontrollable urge to sleep</u>.**
  For example, an African Trypanosomiasis patient might fall asleep on the side of the road while they are in the middle of a walk.

- **From their name, American trypanosomiasis & African trypanosomiasis have <u>certain geographical distributions</u>.**
  - **Extra note for people interested in USMLE: they focus in their questions on *Trypanosoma cruzi* because it is an endemic in central & South America and is also frequently found in the immigrants of North America.**

Morphology

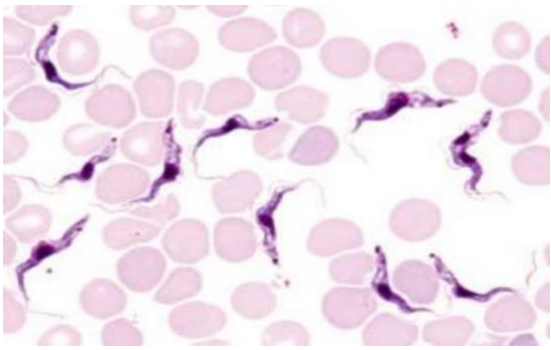


- **The morphologically differentiated forms include:**

  - Spindly, uniflagellate stages: (Trypomastigote, Epimastigote, Promastigote)
  - And a rounded, Amastigote form.

- **Remember: the Amastigote & Trypomastigote stages are the stages present in humans.**

- **<u>African sleeping sickness</u> <u>doesn't</u> cause an <u>intracellular</u> infection ➔ it is <u>impossible</u> to find their causative agent in the <u>Amastigote</u> stage ➔ their <u>diagnostic stage</u> is <u>Trypomastigote</u>.**



- **Notice the <u>blood film</u> image on the right, it contains the causative agent of African sleeping sickness. Notice that the infection is <u>extracellular</u> as the agent is outside the RBC's and it is in the <u>Trypomastigote stage</u>.**

- **However, the causative agents of <u>American Trypanosomiasis</u> cause an <u>intracellular</u> infection ➔ they can be found in the <u>Amastigote</u> stage.**

- **The causative agent of <u>American trypanosomiasis</u> (Chagas' disease) preferably lives in the <u>cardiac muscle</u> ➔ which causes <u>cardiomyopathies</u>.**

When you learn about the horrifying life cycle of some parasite and need to tell everyone

African trypanosomiasis:

- **It is caused by 2 sub spp. :**

  1) **T. brucei gambiense: West African trypanosomiasis**
  2) **T. brucei rhodesiense: East African trypanosomiasis**

- **Vector: tsetse fly (Scientific name: Glossina spp.)**

⇨ **Which is found in rural Africa.**
⇨ ***Glossina palpalis* transmits T. b. gambiense**
⇨ ***Glossina morsitans* transmits T. b. rhodesiense**

Tsetse fly

- **East African trypanosomiasis (which is caused by Trypanosoma brucei rhodesiense) is acute, rapidly progressive, fatal & more severe than the West African trypanosomiasis (which is caused by Trypanosoma brucei gambiense).**

- **Reservoir host of:**

⇨ **Trypanosoma brucei gambiense: infected humans.**
⇨ **Trypanosoma brucei rhodesiense: infected humans as well as animals, which is why it may be more severe with worse progression.**

- **When a person gets bitten by tsetse fly, it transmits the infective stage of the parasite which is the Trypomastigote stage.**

- **The site of the bite leaves a reaction which is called "chancre".**
  Medically, chancre means a painless ulcer.
  Treponema pallidum (the causative agent of syphilis) is a bacteria which also causes chancre.

- **Remember: all the stages of African trypanosomiasis are extracellular stages and the causative agent is present in the Trypomastigote stage in humans but never in the Amastigote stage.**

- **The stages of African trypanosomiasis:**

⇨ **Stage (1): Parasitemia (the presence of the parasite in the blood).**
⇨ **Stage (2): the parasites cross the BBB (Blood-Brain Barrier) and they enter the CNS. Moreover, they get access to the CSF (Cerebrospinal fluid) and that's why the hosts (patients) have an uncontrollable urge to sleep.**

- **The prognosis of the African sleeping sickness completely differs between the cases depending on the stages of the disease where treatment takes place (in stage (1) where the protozoa are present in the blood (Parasitemia) or in stage (2) where the protozoa are present in the CNS).**

American trypanosomiasis

- **Another name: Chagas' disease**

- **The causative agent: *Trypanosoma cruzi***

- **Zoonosis (transmitted from a non-human animal to humans):**

  Transmitted by vector: Reduviid bugs, a.k.a. Triatomine bug or Kissing bug.

- **The Reduviid bug is also called the Kissing bug ➔ because it targets the human face looking for a meal.**

- **Reduviid bug defecates while taking a blood meal.**

The Reduviid bug

- **The causative agent of American trypanosomiasis is not necessarily transmitted through the bite of the Reduviid bug itself.**

  The bug actually defecates on the face near the place of its bite. ➔ If the person rubs their face at the site of the bug's bite, ➔ the protozoa might get access to the bite wound, other skin breaks, or even the conjunctiva of the eye due to the rubbing. ➔ This could lead to a very famous sign associated with acute American trypanosomiasis called "Romana's sign" which describes unilateral eye swelling.

- **Definitive host: Human, dog, cat, rats...etc.**
  Habitat in the Definitive host:

⇨ **Trypomastigote in blood.**
⇨ **Amastigote in tissue.**

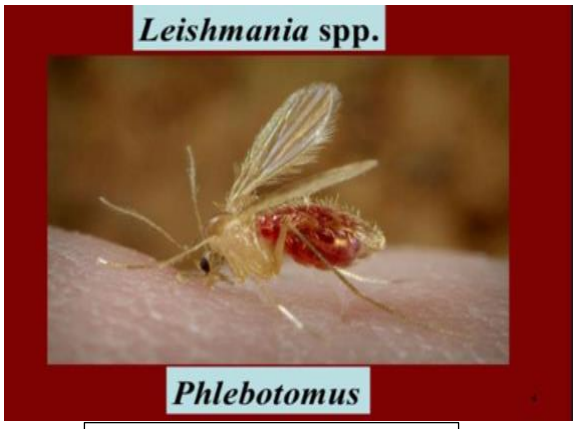
- **The diagnosis of American trypanosomiasis:**

⇨ **If *Trypanosoma cruzi* is present in the circulation ➔ the protozoan is in the Trypomastigote stage.**
⇨ **Remember that *Trypanosoma cruzi* protozoa also have an intracellular stage (the Amastigote stage) ➔ they tend to internalize into cardiomyocytes (cardiac muscles) ➔ the Amastigote of Trypanosoma cruzi can then be seen in a biopsy of the heart muscle.**

- **So, the diagnostic stage of American trypanosomiasis is the Amastigote stage & the Trypomastigote stage.**
  While the diagnostic stage of the African trypanosomiasis is only the Trypomastigote stage ➔ because all of the stages of African trypanosomiasis are extracellular.

2- Leishmania

- **Another member of the blood & tissue flagellates.**
- **It is a flagellated protozoan.**
- **The disease caused by Leishmania is called Leishmaniasis.**
- **The vector which transmits leishmaniasis is the "Sand fly" also known as the Phlebotomus.**



The sand fly (female)

- **Actually, there is a type of leishmaniasis which was considered an endemic in certain areas of Jordan (mainly in the south, Wadi Araba and Al-Quairah where the sand fly is present)**

- **The only type of leishmaniasis present in Jordan is cutaneous leishmaniasis. But now, cutaneous leishmaniasis is way less prevalent in Jordan than before.**

- **The vectors of the African & American trypanosomiasis (tsetse fly & triatomine bug respectively) are not present in Jordan الحمدُلله.**

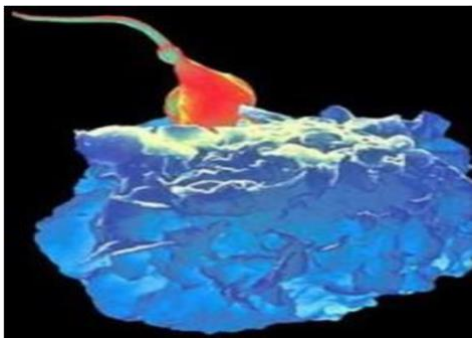
- **Life cycle requires two hosts :**

⇨ **Vertebrate; mammalian host**
⇨ **Invertebrate vector; female sand fly (female sand flies and not males because females need our blood for their egg maturation)**
(On the other hand, both sexes of the tsetse fly can transmit African trypanosomiasis.)

- **Is an obligate (completely) intracellular organism ➔ thereby their diagnostic stage is the Amastigote stage.**

- **Infects primarily phagocytic cells and macrophages (as soon as it enters the body) & then the Leishmania protozoa infect the reticuloendothelial system.**

- **It may remain only in the skin, or it may enter a lymphoid organ and cause Visceral Leishmaniasis.**



- **The incubation period ranges from 10 days to 2 years,**

- **Remember: the main route of transmission for Trypanosoma, Leishmania, & malaria parasites is through a vector carrying the infective stage of the parasite (mainly through a bite from the vector).**

- **The infective stage of Leishmania is the Promastigote stage.**

Transmission

(most of these methods of transmission can also be applied to Trypanosoma & malaria)

- **Bite of sand fly (only for the transmission of Leishmaniasis).**
- **Blood transfusion (with a contaminated product)**
- **Mother to baby (from a pregnant woman to its fetus | vertical transmission).**
- **Direct contact; from man to man through nasal secretion (only possible for the transmission of a type of leishmaniasis called the Nasopharyngeal Leishmaniasis).**
- **Organ transplantation**

Leishmania spp.

- **Leishmaniasis is divided into clinical syndromes according to what part of the body is affected most.**

⇨ **Cutaneous leishmaniasis (*Leishmania tropica*, *Leishmania major*, & *Leishmania infantum*)**

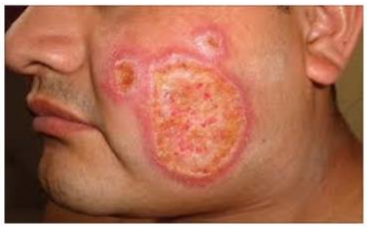
- ❖ **The infection is just confined to the epidermis & the dermis.**
- ❖ **The infection has other names: oriental sore, Baghdad boil (دمّلة بغداد) & Aleppo button (حبّة حلب), so it was prevalent in our geographical areas.**

⇨ **Mucocutaneous leishmaniasis (*Leishmania braziliensis*)**

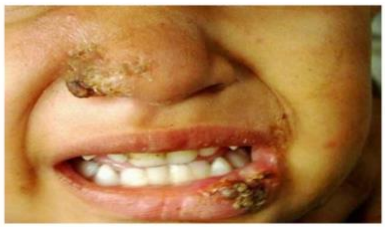
- ❖ **Other names for the infection: Nasopharyngeal Leishmaniasis & Espundia.**

⇨ **Visceral leishmaniasis (*Leishmania donovani*)**

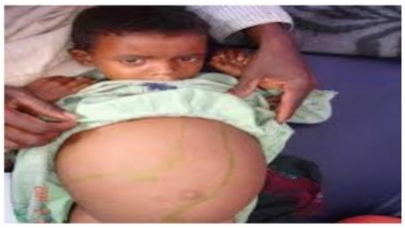
- ❖ **Occurs when the Leishmania protozoa enter secondary lymphoid organs.**
- ❖ **Another name for the infection: kala-azar (in Hindi) or the black fever (in English).**
- ❖ **The infection has a Hindi common name because it is an endemic in Southeast Asia.**
- ❖ **Viesceral leishmaniasis are mainly manifested in abdominal distension.**
- ❖ **Bone marrow biopsy is required for the diagnosis of visceral leishmaniasis in order to detect/see the Amastigote (round intracellular form).**



Cutaneous Leishmaniasis



Nasopharyngeal Leishmaniasis /Espundia



Visceral Leishmaniasis

3- Plasmodium (Blood Sporozoa)

- **Plasmodium is a genus of parasitic alveolates, many of which cause malaria in their hosts.**

- **There are specific types of malaria depending on the species of the causative agent (Plasmodium), such as: Benign Tertian malaria, Malignant Tertian malaria, Quartan malaria & other types.**

- **Species:**

  1) ***P. falciparum***
  2) ***P. malariae***
  3) ***P. vivax***
  4) ***P. ovale***
  5) ***Plasmodium knowlesi***

- **The type of malaria disease depends on the Plasmodium species:**

⇨ ***Plasmodium vivax* & *Plasmodium ovale*: cause Benign Tertian malaria**
⇨ ***Plasmodium malariae*: causes Quartan malaria**
⇨ ***Plasmodium falciparum*: causes Malignant Tertian malaria**

- **The specific types of malaria differ from each other depending on the periodicity of the fever caused by them and how severe the fever is:**

⇨ **Tertian malaria: the patient has fever on a specific day, and the next day they doesn't have fever, but on the third day the fever returns (every 48 hours).**
⇨ **Quartan malaria: the patient doesn't have fever on the second & the third day, but on the fourth day the fever returns (every 72 hours).**

- **The periodic fever is also referred to as "periodic paroxysms" at regular 48 hour or 72 hour intervals.**

- **The type of malaria caused by Plasmodium falciparum is called Malignant Tertian malaria because they cause very severe fever in the patients (higher than 41°C) and they have very broad complications.**

- **Malaria that results in less severe fever that is much easier to treat is known as Benign Malaria.**

- **The most important complication of *Plasmodium falciparum* infection is cerebral malaria.**

- **Plasmodium falciparum is the major species (the most important species) associated with deadly infections throughout the world (highest mortality of malaria).**

- **The most common plasmodium species that is associated with the highest incidences of malaria is Plasmodium vivax.**

- ***Plasmodium malariae* is the oldest one among the list.**

- ***Plasmodium knowlesi* was newly added to the list, as it used to cause malaria in monkeys, and it was discovered to cause malaria in humans in the communities living near monkeys such as Southeast Asia.**

- **Plasmodium knowlesi is also known as the fifth cause of human malaria.**

Mechanism of Infection

- **The parasite always has two hosts in its life cycle: a Dipteran insect host and a vertebrate host.**
- **The vector for malaria is the Dipteran female Anopheline mosquito.**

  - **Dipteran insect: an insect that has 2 wings.**

- **Remember that the malaria causative agents are Sporozoa ➔ which means that they alternate between the sexual & asexual reproduction.**

⇨ **The asexual production: occurs in Humans**
⇨ **The sexual production: occurs in the Anopheles mosquito**

- **Asexual reproduction sometimes in the literature is referred to as "Schizogony" or "Merogony".**

- **The sexual reproduction, which occurs in the mosquito, is also referred to as "Sporogony".**

- **The infective stage of the malaria is the Sporozoite stage.**

- **When the vector takes a blood meal, Sporozoites (the infective stage) contained in the salivary glands of the mosquito are discharged into the puncture wound.**

- **There are 2 cycles of the malaria inside the body of the infected human:**

⇨ **The exoerythrocytic cycle: which occurs in the liver**
⇨ **The erythrocytic cycle: which occurs in the RBC's**

- **Within an hour, these infective Sporozoites are carried via the blood to the liver, where they penetrate hepatocytes and begin to grow, initiating the pre-erythrocytic or primary exoerythrocytic cycle.**

- **The Sporozoites become round or oval and begin dividing repeatedly (asexually).**

- **Schizogony results in large numbers of exoerythrocytic Merozoites.**

- **Once these Merozoites leave the liver, they invade the red blood cells (RBCs), initiating the erythrocytic cycle.**

- A different, "Dormant" type of Schizogony, may occur only in P. vivax and P. ovale organisms, which remain quiescent in the Liver.

- These resting/dormant stages have been termed Hypnozoites, and they lead to a true relapse (recurrent infection of the RBC's), often within 1 year or up to more than 5 years later.

- In other words, during their exoerythrocytic cycle in the liver, *P. vivax* and *P. ovale* form dormant stages (called Hypnozoites) which might later leave their dormant stages to reestablish RBC infection (generally cause recurrent RBC infections).

- Once the RBCs and reticulocytes have been invaded (in the erythrocytic cycle), the parasites grow and feed on hemoglobin ➔ the Merozoites consume the hemoglobin in the infected RBC's, therefore causing hemolytic anemia.

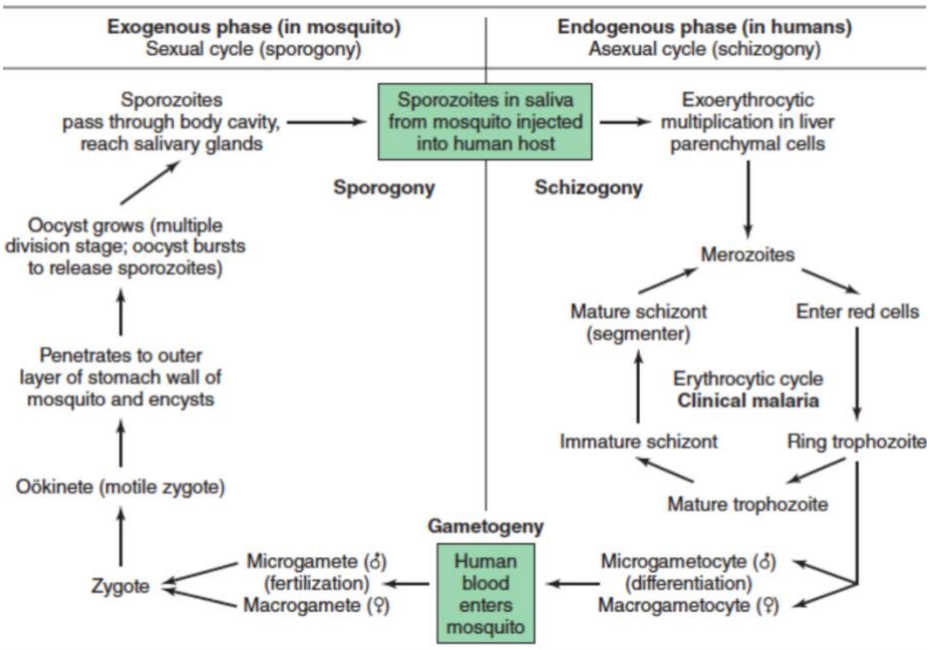
  However, in malaria patients, hemolytic anemia isn't feared, what is feared is the development of cerebrospinal malaria.

- Within the RBC, the Merozoite (or young trophozoite) is vacuolated, ring shaped, more or less ameboid, and uninucleate.

- The excess protein and hematin present from the metabolism of hemoglobin combine to form malarial pigment.

- Once the nucleus begins to divide, the trophozoite is called a Developing Schizont.
- The Mature Schizont contains Merozoites (whose number depends on the species), which are released into the bloodstream.

Malaria Life Cycle (a quick overview)



❖ **The transmission of the parasite from the mosquito to a susceptible person:**

- ⇨ **Firstly, the female Anopheles mosquito bites a susceptible human in order to get its blood meal.**
- ⇨ **While sucking the blood and getting its blood meal, the mosquito injects the infective stage of the Plasmodium (the Sporozoites) into the susceptible human's body.**
- ⇨ **The Sporozoites get carried out to the liver through the bloodstream. So, in humans there are 2 cycles of the malaria: the exoerythrocytic cycle (which occurs in the liver) & the erythrocytic cycle (which occurs in the RBC's in peripheral circulation).**

❖ **Schizogony: asexual reproduction in the exoerythrocytic cycle of the parasite:**

- ⇨ **So the first thing the parasite does is that it enters the liver, and it starts to reproduce asexually in the liver parenchymal cells (Schizogony).**
- ⇨ **Every Schizogony/Merogony (asexual reproduction) results in Merozoites (also called the "daughter cells").**

❖ **Schizogony: asexual reproduction in the erythrocytic cycle of the parasite:**

- ⇨ **These Merozoites might enter the RBC's, and once they enter the RBC's, the erythrocytic cycle starts.**
- ⇨ **The Merozoites cause the consumption of hemoglobin, and subsequently cause hemolytic anemia in the patient.**
- ⇨ **The Merozoites also multiply by Schizogony/Merogony (asexual reproduction) to produce Merozoites again ➔ (we use them in the diagnosis of malaria, not the Merozoites themselves, but the stages inside the RBC's such as the Ring Trophozoite stage and banana stage, etc…).**
- ⇨ **The Merozoites transform into ring Trophozoites in the RBCs, and these Trophozoites could either mature to eventually into Schizonts and more Merozoites, or they could differentiate into Microgametocytes & Macrogametocytes.**

❖ **Sporogony: the sexual part of the parasite's life cycle:**

- ⇨ **The Gametocytes (Microgametocytes & Macrogametocytes) are uptaken with the blood by a mosquito during a blood meal.**
- ⇨ **Inside the female Anopheles mosquito, the uptaken Microgametocytes & Macrogametocytes continue the sexual reproduction (the Sporogonic cycle).**
- ⇨ **The sexual reproduction results in Oökinete (motile zygote) and then in the later steps it forms a Sporozoite, which is the infective stage of the parasite to continue the cycle.**

Now, we are going to talk about the drugs involved in the treatment of malaria.

- **Quinolones are the first line of management for malaria patients.**

- **However, if a malaria patient is infected with *Plasmodium vivax* or *Plasmodium ovale*, the quinolones alone are not going to be sufficient to cure the patient because they don't kill the Hypnozoites which live in the liver ➔ so, recurrent RBC infections will occur when the Hypnozoites leave the dormant stage.**

- **To cure a malaria patient infected with *Plasmodium vivax* or *Plasmodium ovale*, we need a drug which is able to kill the Hypnozoites which live in the patient's liver in order to make sure there will be no more RBC infection recurrences.**

- **The drug which is given to malaria patients infected with *P. vivax* & *P. ovale* is called Primaquine. However, the Primaquine is not used to treat the erythrocytic stage of malaria, but to kill hypnozoites which live in the patient's liver in order to prevent relapse.**

- **The drugs which are given to treat malaria caused by Plasmodium falciparum are totally different from Quinolones.**

- **The drugs which are given to treat malaria caused by Plasmodium falciparum are ACT (Arteminsin Combination Therapy).**

Tissue Protozoa

Toxoplasma gondii (Tissue Sporozoa)

- They are Sporozoa ➔ which means they have a sexual part in their life-cycle.
- It is a coccidian protozoa with worldwide distribution that infects wide range of animals and birds but does not appear to cause disease in them.
- The definitive host (D.H) of the Toxoplasma: Cats (or Felidae)
- The normal final hosts are strictly cats and their relatives, the only hosts in which the oocyst-producing sexual stage of toxoplasma can develop.

- How does the human get infected with toxoplasmosis? / What is the route of transmission of toxoplasmosis?

⇨ Exposure to infected cat feces.
⇨ Consumption of food contaminated with infected cat feces.
⇨ Consumption of the meat of animals that have consumed food contaminated with infected cat feces ➔ as the animal meat contains the cysts of the Toxoplasma because it got infected from the infected cat feces.

- When oocysts are ingested, they can either repeat their sexual life cycle in a cat, or -if ingested by a human- they can establish an infection in which they can reproduce asexually. In humans, the oocysts open and release sporozoites into the duodenum which then invade various cells, especially macrophages, where they form Tachyzoites that spread the infection to lymph nodes and other organs.
- In immunocompetent individuals, toxoplasmosis may be asymptomatic or it may cause flu-like illness or as they call it "infectious mononucleosis-like".
- Toxoplasmosis is fearful & is a matter of concern when it affects a pregnant woman for the first time during her pregnancy (in Nonimmune mothers during pregnancy).

  If she had been infected with toxoplasmosis before, she would have been kind of immune to it.

  However, if a pregnant woman is infected with toxoplasmosis for the first time during the pregnancy ➔ the toxoplasmosis poses a threat and danger towards the fetus (may produce Congenital or Postnatal Toxoplasmosis).

- **The dangers & threats that toxoplasmosis poses against the fetus:**

  / Consequences (symptoms) of Congenital Toxoplasmosis:

  1) **Stillbirth (which is the death or loss of baby before or during delivery)**
  2) **Chorioretinitis**
  3) **The child will suffer from blindness, seizure and severe developmental delays.**

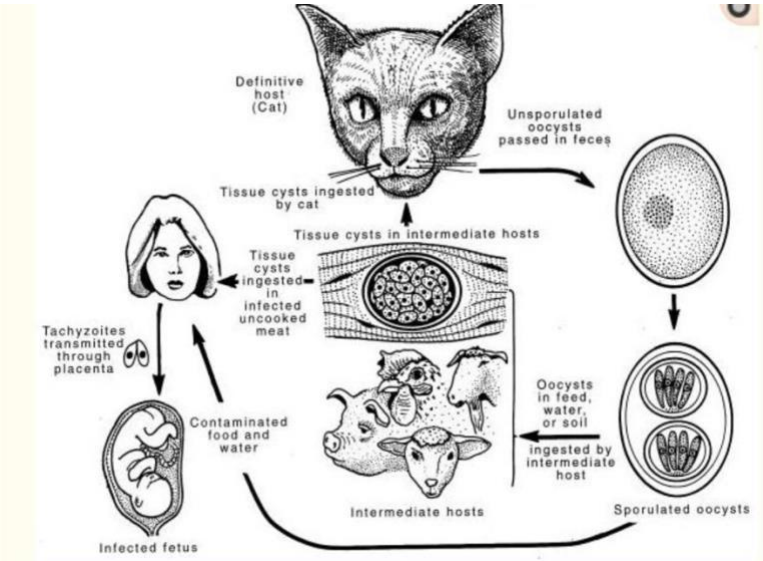
- **Toxoplasmosis is also fearful & is a matter of concern in immunocompromised individuals (like AIDS patients for example) ➔ the patients in this case may develop disseminated toxoplasmosis.**

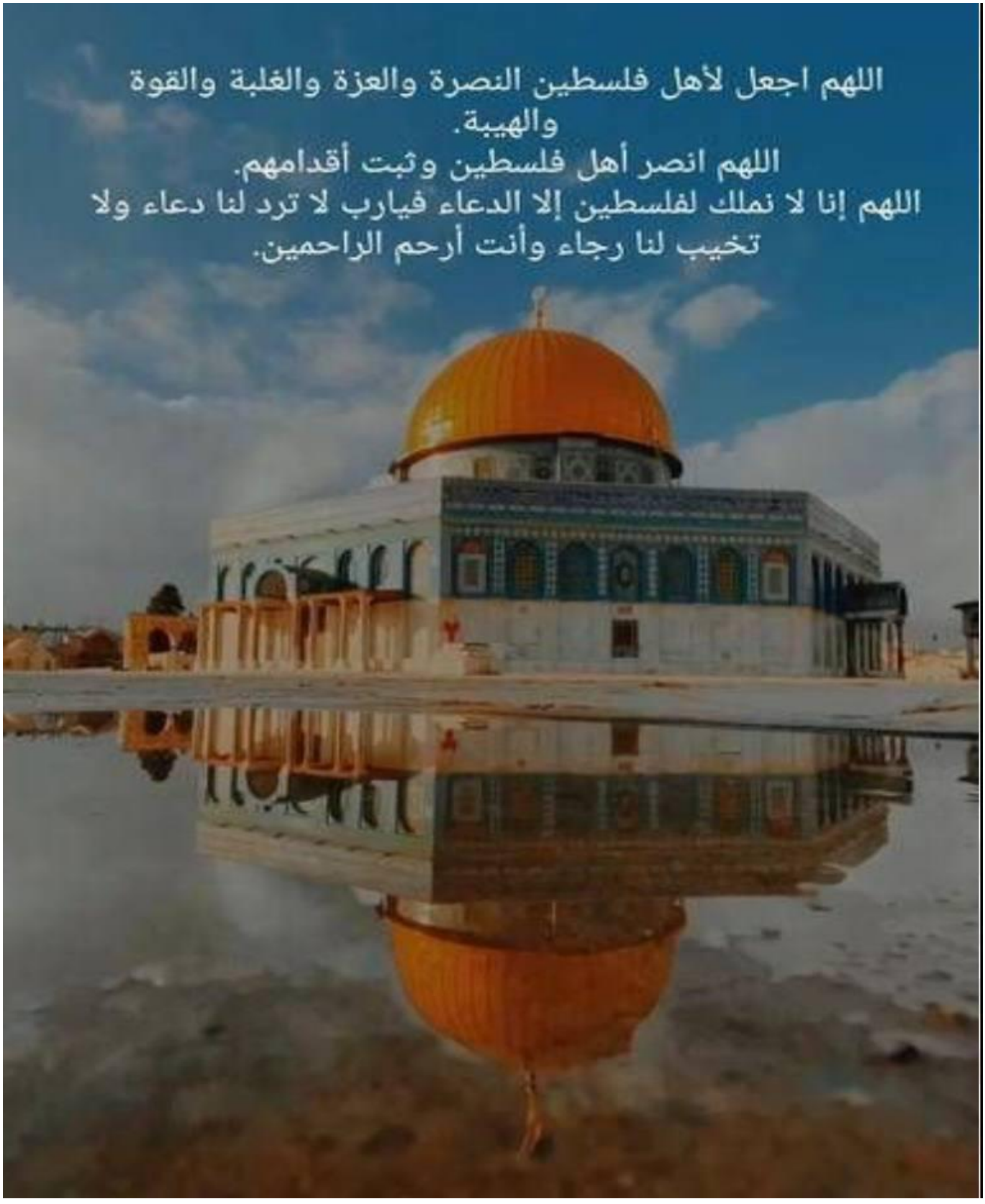
- **There are two morphological forms of Toxoplasma:**

⇨ **Tachyzoites: they are like trophozoites, as they are the active, motile and the feeding form.**
⇨ **Bradyzoites: they are similar to Hypnozoites of the malaria, they live dormantly inside the infected humans.**

- **Latent (Dormant) infections occur with Toxoplasma (parasites in tissue cysts are called Bradyzoites).**

- **Remember that the definitive hosts of Toxoplasma gondii are the cats (or Felidae), and the sexual part of the life-cycle of Toxoplasma occurs in them.**
- **Humans are accidental hosts of Toxoplasma gondii.**




اللهم اجعل لأهل فلسطين النصرة والعزة والغلبة والقوة والهيبة.
اللهم انصر أهل فلسطين وثبت أقدامهم.
اللهم إنا لا نملك لفلسطين إلا الدعاء فيارب لا ترد لنا دعاء ولا تخيب لنا رجاء وأنت أرحم الراحمين.