



Microbiology | Final 2

Common protozoal Infections

Written by:

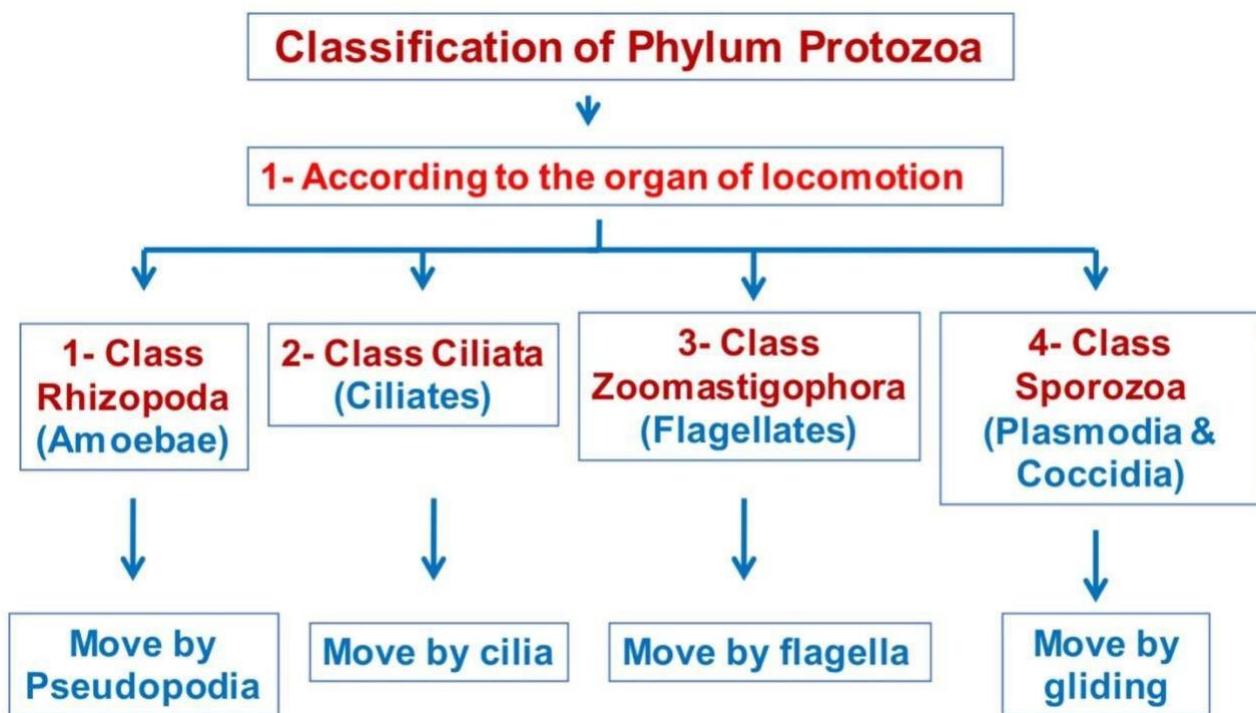
**DST & NST
Members**

Reviewed by: NST Member

Before diving into this lecture, keep in mind that it may present a significant amount of new information, which can feel overwhelming at first. However, for our current level, the key focus should be on understanding the **causative agents of protozoal infections, the clinical manifestations of the diseases they cause, and a few additional important details about each medically significant protozoan.**

Protozoal Phyla Classification (2 methods)

- 1) Locomotion organ.
- 2) Method of reproduction (sexual or asexual).

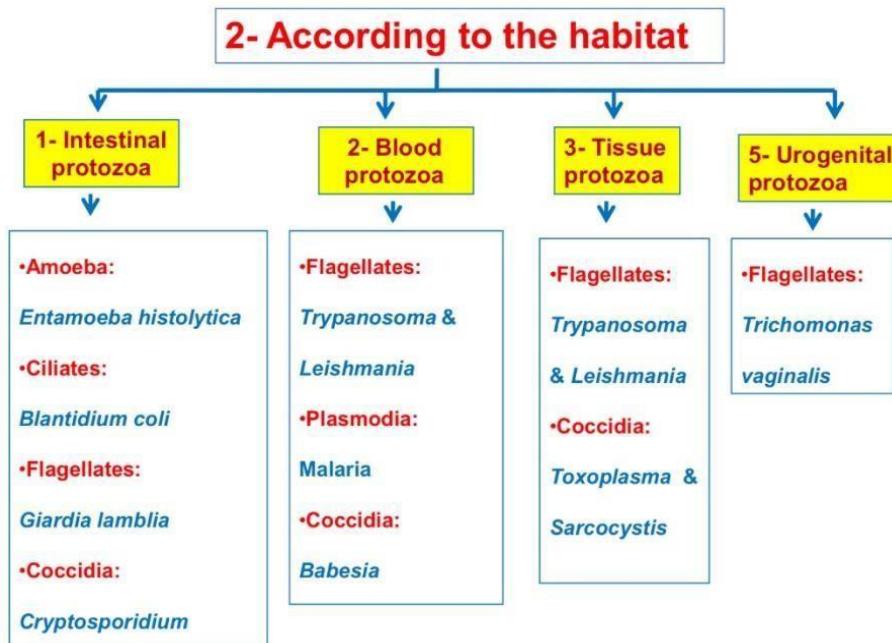


This scheme was explained also in the last lecture, but now we will dive into more detail.

1) Classifying Protozoa according to their organ of locomotion divides them into four classes:

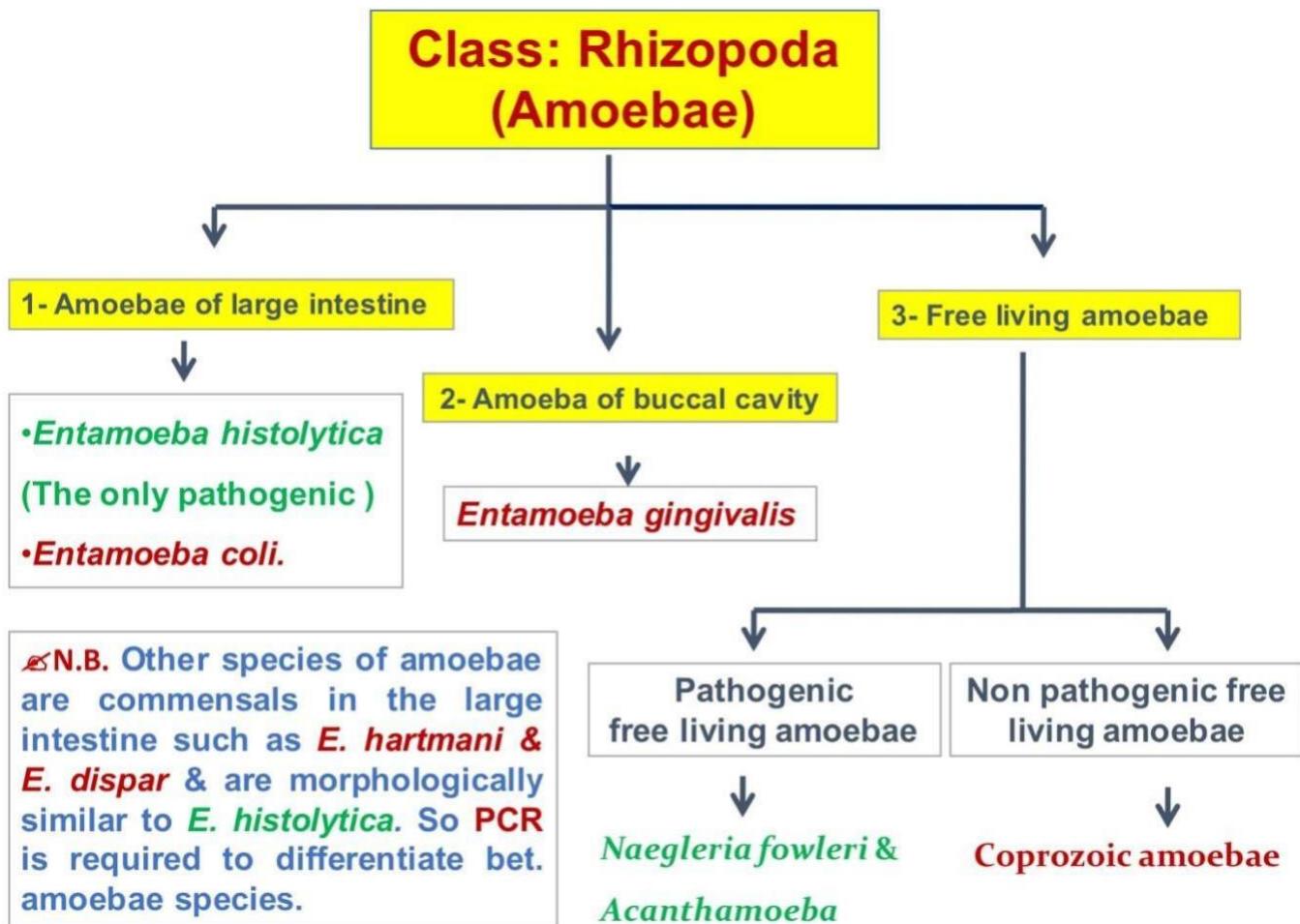
- 1- **Class Rhizopoda (Amoeba):** Amoebas move using **pseudopodia** (temporary extensions of the cytoplasm, often called “false feet” or الأرجل الوهمية/الكافحة). This group includes the parasite *Entamoeba histolytica*, which causes amoebiasis. They multiply asexually through **binary fission**.
- 2- **Class Ciliata (Ciliates):** Ciliates are **covered with cilia** (which are microscopic hair- like structures used for locomotion and feeding) This group includes the protozoan *Balantidium coli*, which causes the disease Balantidiasis (balantidial dysentery, رباء الأمعاء). **They reproduce asexually through binary fission.**
- 3- **Class Zoomastigophora (Flagellates):** They move using **flagella** (whip-like cellular appendages responsible for locomotion through wave-like or rotary motion (دوران الأسواط)). The intestinal parasite *Giardia lamblia* causes giardiasis. Flagellates multiply asexually by **binary fission**.
- 4- **Class Sporozoa (Plasmodia & Coccidia):** It includes *Plasmodium* species, the causative agents of malaria, one of the most significant protozoal diseases globally. They are motile, but members of this class **lack defined locomotory organelles** and instead **move by gliding** motility (الانزلاق). **They alternate between sexual and asexual reproduction phases.** They are **obligate intracellular parasites**, requiring host cells to complete their life cycles.

2) We can also classify Protozoa 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:

More than 200 species of amoeboid protozoa inhabit the large intestine, **but the only intestinal pathogen among them is *Entamoeba histolytica***, which causes **amoebiasis**, also known as amoebic dysentery (الرُّحَارُ الْأَمْبِيَّ).

Other amoeboid species in the large intestine, such as *Entamoeba coli*, *Entamoeba dispar*, *Entamoeba hartmanni*, and *Entamoeba moshkovskii*, are nonpathogenic commensals and part of the normal intestinal microbiota. These nonpathogenic species are clinically significant because they can be mistaken for *E. histolytica* during diagnosis. Among these, *E. coli* is most frequently confused with *E. histolytica*. A key distinguishing feature is that *E. coli* cysts have eight nuclei, while the cysts of *E. histolytica* are quadrinucleate (contain four nuclei).

2- Amoeba of the buccal (oral) cavity:

Entamoeba gingivalis is a protozoan that is a part of the **Rhizopoda** class. It resides in the oral cavity and is commonly associated with **periodontal** diseases, but it is not proven to cause them.

3- Free living amoeba:

Most amoebas are free-living in nature, with only a small proportion being parasitic or pathogenic to humans. Fewer than 70 species of amoebas are known to infect humans. Rarely, humans can become accidentally infected with free-living amoebas, which include both pathogenic and nonpathogenic species.

- **Nonpathogenic Species:** These are also referred to as **coprozoic amoebas**, meaning they pass through the intestinal tract without causing disease and are excreted in feces.
- **Pathogenic Free-Living Amoebas:** Notable pathogenic species include ***Naegleria fowleri***, which causes **primary amoebic meningoencephalitis (PAM)**. Another group, the genus ***Acanthamoeba***, primarily causes keratitis (corneal ulcers), particularly in individuals who improperly use or store contact lenses. Additionally, ***Acanthamoeba*** can cause granulomatous amoebic encephalitis (GAE). Swimming in contaminated water is a well-known exposition to cause these 2 diseases (very rare diseases but 100% fatal).

1) ***Entamoeba histolytica***

- Intestinal protozoal infections are typically associated with **poor sanitation** and **inadequate personal hygiene**, with the primary route of transmission being the **fecal-oral route**.
- **Geographical distribution:** Worldwide (cosmopolitan distribution) **especially in the temperate zone, being more common in areas with poor sanitary conditions** and especially 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 (where faeces stay there) due to faeces staying longer time in these areas this gives *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/healthy carriers) → which occurs when the *Entamoeba histolytica* protozoa only live in the lumen of the intestine without invading the tissue.
- **D.H. (Definitive Host):** Man.
- **R.H. (Reservoir Host):** Man (and other primates), dogs, pigs, rats, and monkeys.
- **Disease:** Amoebiasis or Amoebic dysentery.

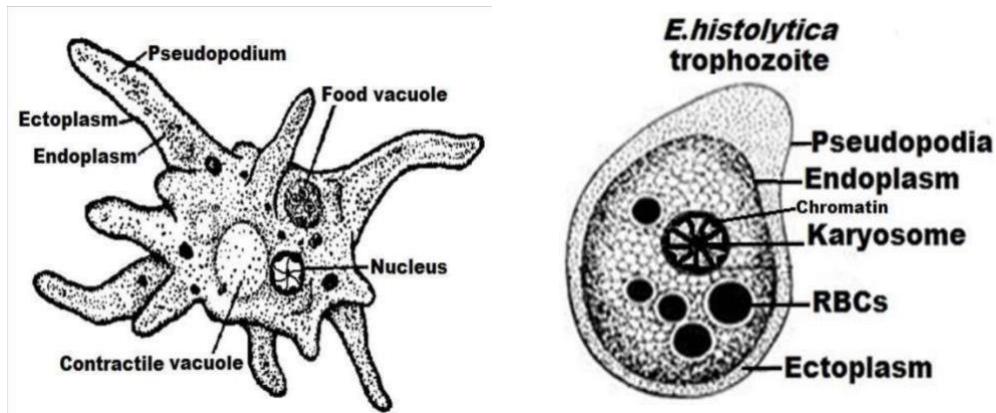
Morphological characteristics (of *Entamoeba histolytica*):

In general, protozoa have two principal morphological forms in their life cycle: the Trophozoite and the Cyst forms.

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

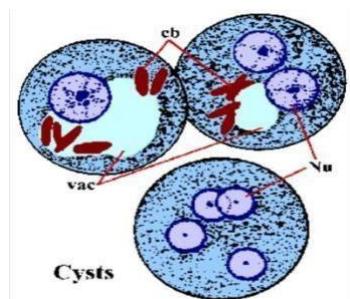
The plasma membrane of *E. histolytica* is trilaminar (a bilayer). The protoplasm of the trophozoite form of *Entamoeba histolytica* (the active, tissue-invasive stage of the amoeba) contains a **central nucleus characterized by a karyosome surrounded by a ring of fine chromatin (cigar shaped chromatin bodies)**. The trophozoite also has a **distinct ectoplasm and a granular endoplasm**, which typically **contains food vacuoles and ingested red blood cells (RBCs)**.

The presence of red blood cells (RBCs) inside the cytoplasm of these protozoa, observed under the microscope, is a pathognomonic sign of *Entamoeba histolytica* trophozoites. This distinguishes them from other commensal species such as *Entamoeba coli* and *Entamoeba dispar*, which lack the ability to phagocytose RBCs.



2- The **Cyst stage** represents the quiescent and hardened phase of a protozoan's life cycle, occurring in response to unfavorable environmental conditions, such as low temperature or low humidity (when it gets outside the body). During this stage, protozoa encyst to protect themselves and ensure survival in harsh environments.

If amoebas remain confined to the lumen of the large intestine without invading the mucosa, they will be excreted in their cystic (luminal) form. These cysts may be either immature or mature.



Immature cysts are either **uninucleate** or **binucleate**, whereas **mature cysts** are **quadrinucleate**, containing **four nuclei per cyst**. Only the mature cysts excreted in feces are infectious to other hosts. Exposure to immature cysts does not result in infection, as they lack the ability to establish a new infection in the host.

Mode of Infection:

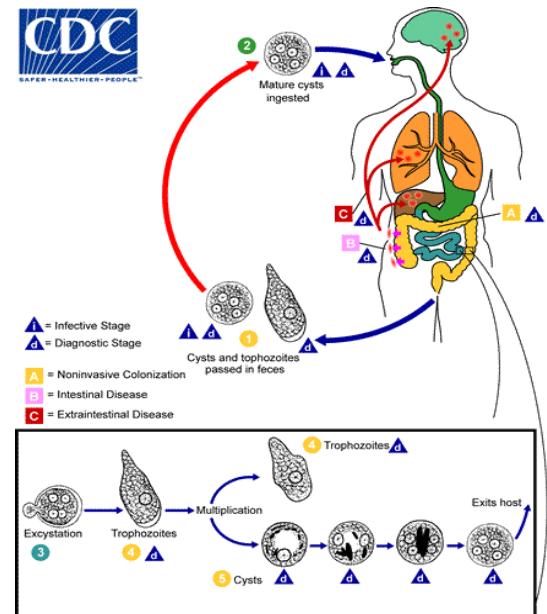
- 1- Contaminated foods (ex. green vegetables), drinks, or hands with human stool-containing mature cysts.
- 2- Handling food by infected food handlers such as cookers and waiters.
- 3- Flies and cockroaches that carry the cysts from contaminated feces to exposed food.
- 4- External or Internal Autoinfection (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).

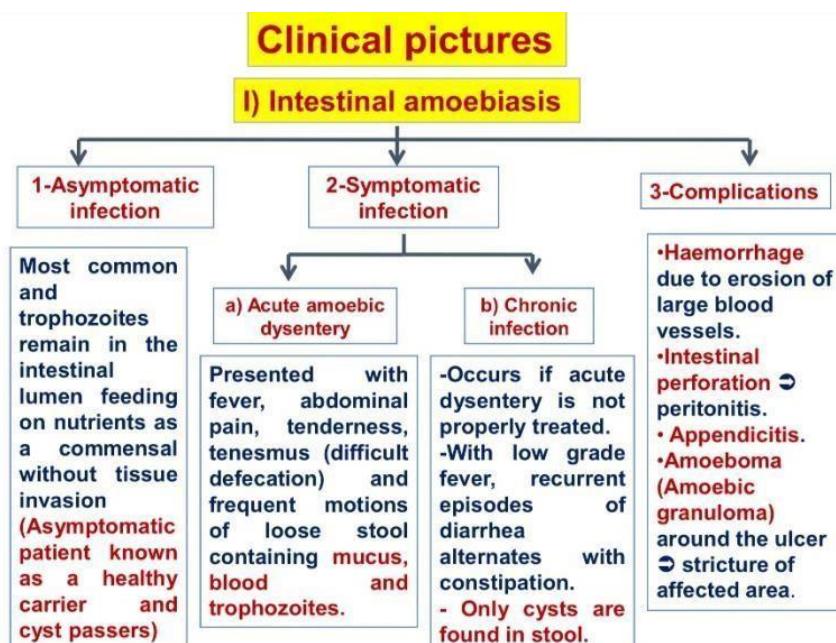
Each mature cyst excysts in the small intestine under favorable conditions, releasing **eight trophozoites**. These trophozoites multiply by binary fission.

After excystation, the trophozoites may remain confined to the lumen of the large intestine and re-encyst, leading to **asymptomatic carriers or “cyst passers” of *E. histolytica* (most common form of intestinal amoebiasis)**. In other cases, trophozoites invade the mucosa and submucosa of the intestinal tract, causing acute or chronic amoebic dysentery. In severe cases, this can progress to extra-intestinal amoebiasis, typically starting with right lobe **liver infection (hepatic amoebiasis)** and potentially spreading to the **lungs, brain (causing secondary amoebic encephalitis)**, or **skin** in untreated cases.



Clinical pictures:

I. Intestinal Amoebiasis



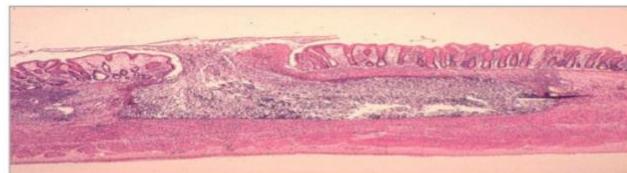
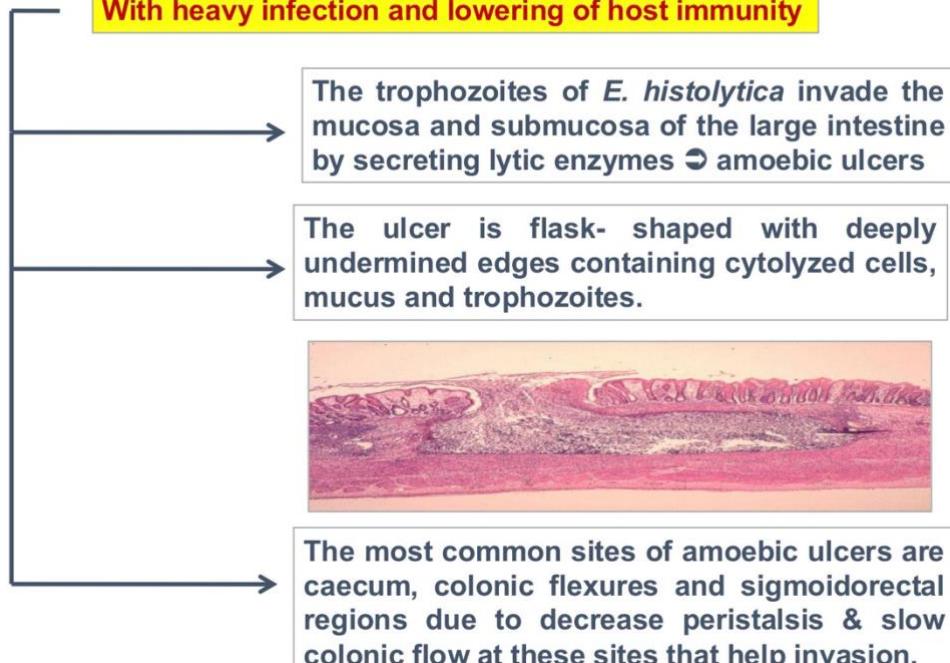
- Most people affected by *E. histolytica* are asymptomatic healthy carriers and keep the cycle of infection ongoing in the society (most people exposed to this parasite are **cyst passers**).
- **Tenesmus** is the recurrent attempt (urgent feeling) to empty bowels although them being empty.
- People 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 cytolized cells, mucus, and trophozoites**.



With heavy infection and lowering of host immunity



The most common sites of amoebic ulcers are caecum, colonic flexures and sigmoidorectal regions due to decrease peristalsis & slow colonic flow at these sites that help invasion.

II. Extra-Intestinal Amoebiasis:

Due to invasion of the blood vessels by the trophozoites of the intestinal ulcer → reach the blood → 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, removal by incision and drainage) or **diffuse amoebic hepatitis**.
- The most common site to get affected by Extra-Intestinal infection of *E. histolyticais* 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 (enlargement of the liver), 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 occurs 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 **secondary amoebic encephalitis** (secondary relative to the intestinal infection. A very serious and **fatal** condition) and **brain abscess.**

4- The Skin:

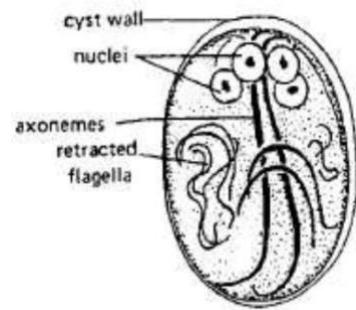
- **Cutaneous amoebiasis (*Amoebiasis cutis*)** occurs due to either extension of acute amoebic colitis to the perianal region or through **rupture** (through ulcers & direct extension) on the abdominal wall from hepatic, colonic, or appendicular lesions (mainly infects the skin near the colonic flexures).

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.

2) *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, without blood).
- Another name for **giardiasis** in Canada is “**Beaver Fever**”, an informal term linked to the association of beavers and other rodents as potential reservoir hosts of the parasite *Giardia lamblia*. However, the name is somewhat misleading, as fever is not a hallmark symptom of giardiasis.



Giardia lamblia cyst

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**.

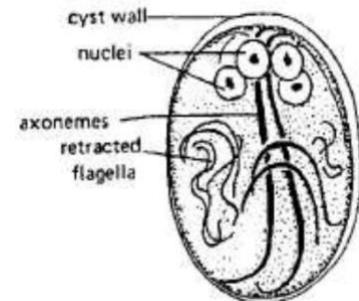
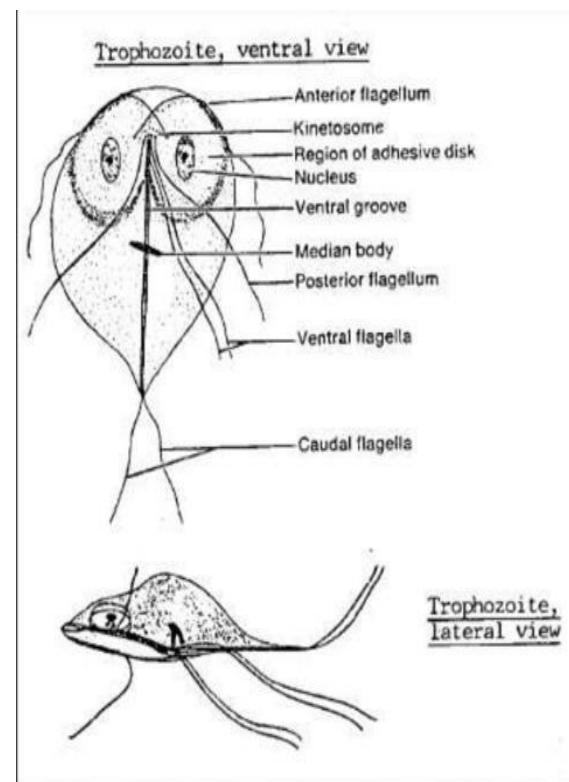
- Along with the flagella of this protozoa, each of the two nuclei is surrounded by a ventral adhesive disk (which is used for attachment), giving the organism the look of a face that is wearing goggles and has whiskers.

- The large concave sucking disks on the ventral surface **help the organism to adhere and attach to intestinal villi** (without tissue invasion).

- *Giardia lamblia* has a characteristic motility which is called “falling-leaf motility”, “tumbling motility” or “dancing motility”. And this motility is **quite important in distinguishing *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.



Pathology and Pathogenesis

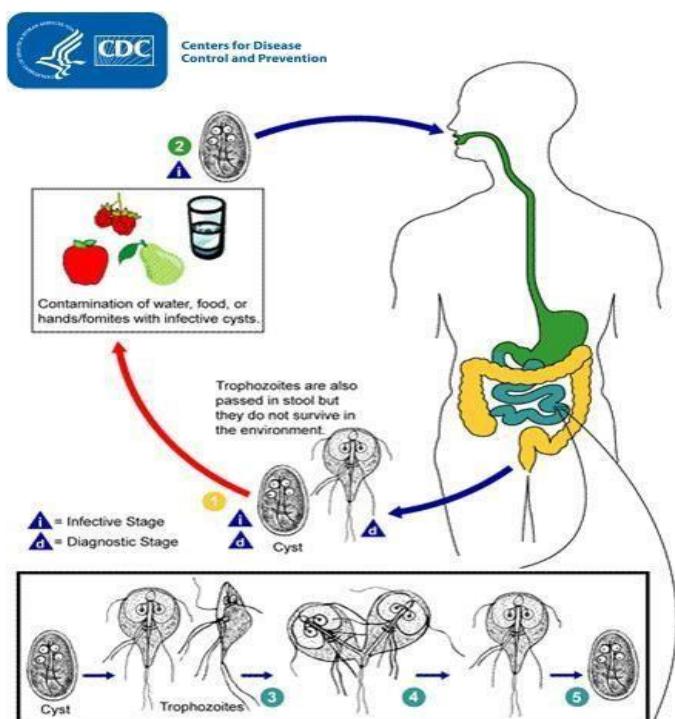
- *Giardia lamblia* is usually only weakly pathogenic for humans. Like *Entamoeba histolytica*, the majority of people infected with *Giardia lamblia* are asymptomatic cyst passers (since it only attaches to the walls of the intestines without invasion).
- Cysts may be found in large numbers in the stools 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, **they cause fatty bulky greasy stool (stratereo) caused by lipid malabsorption, which give their stool a bad odor** (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.

Transmission

- Transmission of Giardia cysts is similar to that of amoeba cysts and is associated with **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**.
- 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.
- **Amoebicidal:** targets amoebas & kills them.



- If we increase the chlorine concentration in the pool to get rid of Giardia & *Entamoeba histolytica*, **the pool becomes unsafe for human use.**
- The **infective stage** of Giardia lamblia is the **cyst stage**, as ingestion of cysts leads to infection.
- The diagnostic stage includes **both the trophozoite and cyst stages**. While both can be detected, **cysts are more commonly observed in stool samples**, as **trophozoites are fragile and typically found in fresh, watery stool (diarrhea)**.
- Each Giardia **cyst releases two trophozoites** upon excystation in the small intestine, and each trophozoite contains 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).
- The **String test (Enterotox)** is a diagnostic method involving the ingestion of a **gelatin capsule tied to a string**. After 4–6 hours, the capsule reaches the duodenum and is retrieved using the string, carrying a sample for examining Giardia trophozoites. However, this method is inconvenient as the patient must fast during the procedure, leading to its replacement by stool antigen tests in most cases.

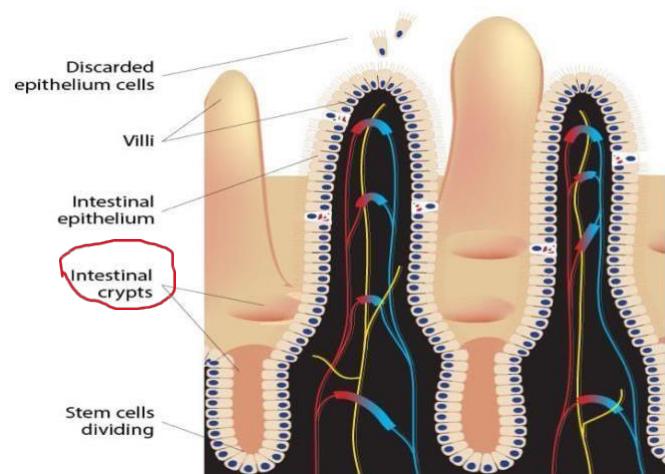
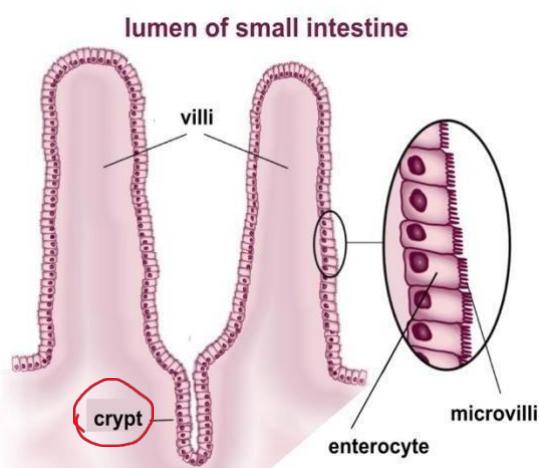
Remember:

- 1) *Cryptosporidium* species & *Cyclospora* species are of the class "Sporozoa" and i. 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 all AIDS patients; cancer; cortisone-suppressed**) and cause self transient gastritis or self transient diarrhea or 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 called it a intracellular extra cytoplasmic**
- *Cryptosporidium* derives its name from its "hidden spores," which reside in the crypts of the villi within the epithelial cells of the small intestine.

Extra Images

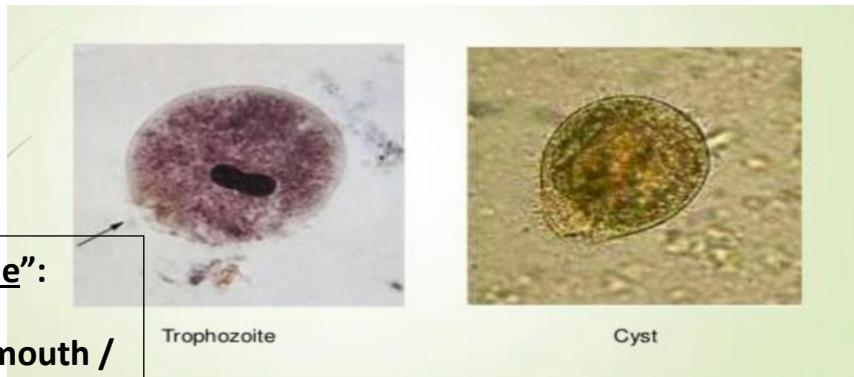


Clinical Aspects:

- 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**.
- Nitoxoxanide, a synthetic drug, has been approved for use in all patients over 1 year of age in the US and is reported to have a cure rate of 72% to 88% by the CDC. (الدكتور حكى بالمحاضرة انه مش مطلوب بالليقىل تبعنا نعرف العلاج ())

4) *Balantidium coli* (Intestinal Ciliated Protozoa)

- The protozoan with the largest size among all protozoa that infect humans.
- *Balantidium coli* is called the giant protozoan.
- Recall that they are ciliates.
- It causes Balantidiasis or Balantidial dysentery, and is the largest intestinal protozoa of humans.
- They **cause self limited gastritis**.
- 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



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.

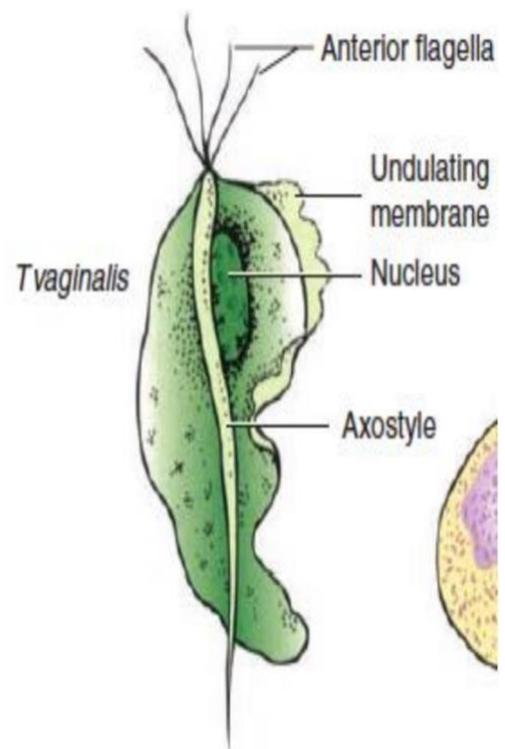
Sexually Transmitted Protozoan Infections: Trichomonas (Urogenital Flagellated Protozoa)

- 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 (pain or burning felling after urination), dyspareunia (pain after sex) and low-grad inflammation limited to the vulva, vagina, and cervix causing frothy yellow-green or creamy discharge.
- The vaginal discharge in females suffering from this condition is described as clear or thick, has a yellow or white color, and is also described as malodorous.
Usually, white vaginal discharge is clinically linked with Trichomoniasis.
- Trichomonas infection of the lower genital tract in females results in vulvovaginitis.
- 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 (4 morphological forms) in their life cycle (as can be seen in the image):

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

الدكتور حكى
أنهم للذكر وأنه ما بدء
يعقدنا ☺
المطلوب باللبيق تبعنا
الي بنلاقيهم بالإنسان :
Amastigote
Trypomastigote
الثنتين الثانيات بال
Vectors

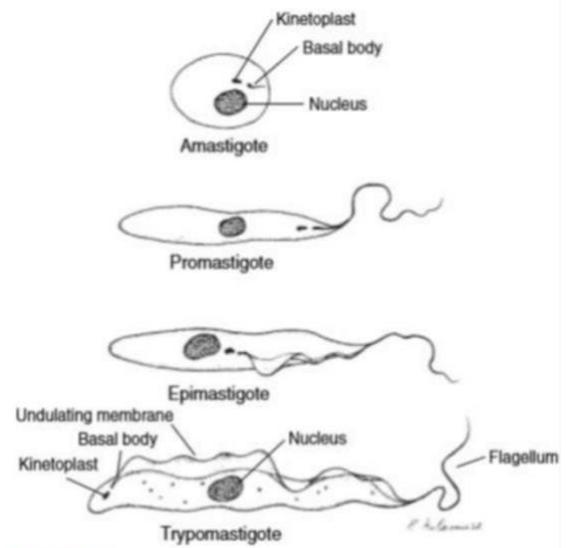


Figure 49-8 Characteristic stages of species of *Leishmania* and *Trypanosoma* in human and insect hosts. (Illustration by Nobuko Kitamura.)

These are of a class called **Kinetoplastida**; due to the presence of an extranuclear DNA-containing structure, which is typically the origin of the flagella.

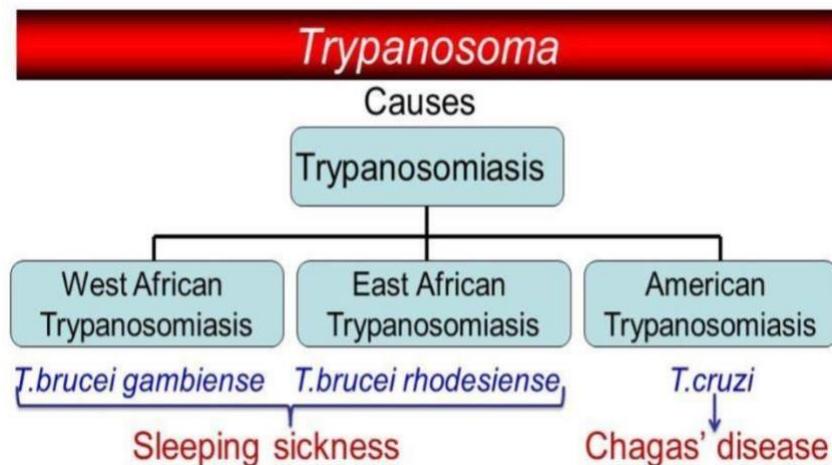
1) Trypanosoma

- Trypanosoma, leishmania, and malaria agents are vector-borne.
- The general microbiological term for the infection with Trypanosoma is Trypanosomiasis.

- ⇒ **African trypanosomiasis: African sleeping sickness**
- ⇒ **American trypanosomiasis: Chagas' disease**

- The causative agent of:

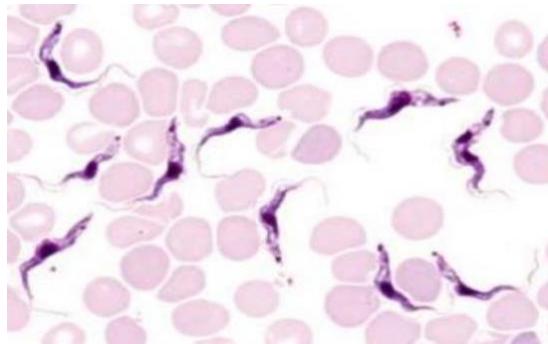
- ⇒ **African Trypanosomiasis: *Trypanosoma brucei* complex**
- ⇒ **American Trypanosomiasis: *Trypanosoma cruzi***



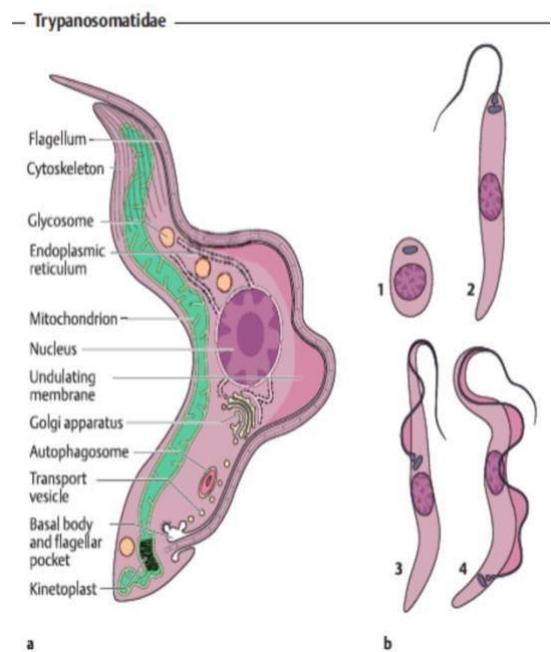
- In the end-stage of the African sleeping sickness, the patients have an uncontrollable urge to sleep (the CNS is affected; it is fatal).
For example, an African Trypanosomiasis patient might fall asleep on the side of the road while they are in the middle of a walk.
- From their name, American & African trypanosomiasis have certain geographical distributions according to the presence or absence of specific vectors for each type (details coming).

(غير مطلوب باليقل تبعنا حسب كلام الدكتور) Morphology

- African sleeping sickness **doesn't cause an intracellular infection** and is confined to blood and lymph, unlike the **American** counterpart which is also **capable of initiating intracellular infection**.



African Trypanosoma: extracellular as you see.



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*



©Warren Photographic

Tsetse fly

American trypanosomiasis

- Another name: **Chagas' disease**
- The causative agent: ***Trypanosoma cruzi***
- **Zoonosis**

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



The Reduviid 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 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 wound, other skin breaks, or even the conjunctiva of the eye due to the rubbing.

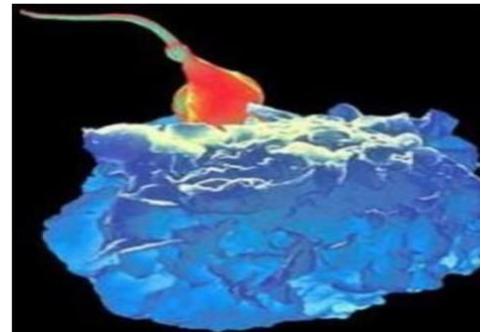
- **Definitive host: Human, dog, cat, rats...etc. Habitat in the Definitive host:**
 - ⇒ **Trypomastigote in blood.** (extracellular; Like the African trypanosomiasis)
 - ⇒ **Amastigote in tissue.** (intracellular; unique to American trypanosomiasis)

American trypanosomiases are present in hollow organs, such as the esophagus, colon, or the heart causing cardiomegaly; it can cause cardiac arrhythmias, even after a long time from the initial exposure to the pathogen.

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.
- 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.
- **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)
- **Is an obligate (completely) intracellular organism (once it enters the body it becomes obliterated intracellular)** → thereby their diagnostic stage is the Amastigote stage.

- **Infects primarily phagocytic cells and macrophages** (as soon as it enters the body)
- 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).

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 & Aleppo button 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.
- ❖ Visceral leishmaniasis are **mainly manifested in abdominal distension.**



Cutaneous
Leishmaniasis



Nasopharyngeal
Leishmaniasis
/Espundia



Visceral
Leishmaniasis

Plasmodium (blood sporozo)

General Characteristics

- **Classification:** Plasmodium is a genus of parasitic alveolates belonging to the Class Sporozoa (Blood Sporozoa).
- **Global Impact:** Malaria is considered the most significant protozoal infection worldwide.
- **Host Requirements:** The parasite requires two hosts:
 1. Vertebrate Host: Humans.
 2. Insect Host (Vector): The female Anopheles mosquito.
- **Note:** Only the female transmits the disease because she requires a blood meal to mature her eggs; males feed on nectar.

Clinical Classification: Fever Cycles

The terms "Tertian" and "Quartan" describe the frequency of fever episodes, which align with the time required for the parasite to replicate and rupture Red Blood Cells (RBCs).

- **Tertian (Malignant & Benign):** A 48-hour cycle where fever appears on Day 1, skips Day 2, and returns on Day 3.
- **Quartan:** A 72-hour cycle where fever appears on Day 1, skips two days, and returns on Day 4.

The Five Causative Species of Malaria

1. **Plasmodium falciparum**

- Disease: Malignant Tertian Malaria.
- Significance: This is the most dangerous species. It is associated with the highest mortality rates and severe complications, such as cerebral malaria.

2. **Plasmodium vivax**

- Disease: Benign Tertian Malaria.
- Significance: It is the most common and widespread species globally.
- Relapse: It is famous for having a dormant liver stage (hypnozoites) which can reactivate and cause a relapse of the disease months or years later.

3. **Plasmodium ovale**

- Disease: Benign Tertian Malaria.
- Significance: Similar to *P. vivax*, it also maintains dormant liver stages (hypnozoites) that can lead to relapse.

4. **Plasmodium malariae**

- Disease: Quartan Malaria.
- Significance: This species is rarer than the others.

5. **Plasmodium knowlesi**

- Disease: Simian Malaria (also known as the "Fifth human malaria").
- Originally a parasite of apes (monkeys). It is now recognized as a zoonotic cause of malaria in humans who live near ape populations.

The Fever Cycle

- Tertian (Malignant & Benign): **The cycle takes 48 hours. Fever occurs on Day 1, disappears on Day 2, and returns on Day 3.**
- Quartan: **The cycle takes 72 hours. Fever occurs on Day 1, disappears for two days, and returns on Day 4.**

The parasite **alternates between sexual reproduction in the mosquito and asexual reproduction in humans**.

A. Exogenous Phase (In Mosquito): Sexual Reproduction

- Process: Sporogony (produces Sporozoites).
- Mechanism:
 1. The mosquito **ingests male** (Microgametes) and **female** (Macrogametes) Gametocytes from an infected human.
 2. **Fertilization in the mosquito stomach forms a Zygote \rightarrow Ookinete \rightarrow Oocyst.**
 3. The oocyst **bursts**, releasing the **infective stage (Sporozoites)**, which **migrate to the salivary glands**.

B. Endogenous Phase (In Humans): Asexual Reproduction

Phase 1: The Exo-erythrocytic Cycle (Liver Phase)

- **Infection:** Sporozoites are injected into the human bloodstream via a mosquito bite and reach the liver within an hour.
- **Multiplication:** Inside liver cells (hepatocytes), sporozoites undergo asexual division (Schizogony).
- **Outcome:** The parasite (now a schizont) produces thousands of Merozoites.
- **Relapse (Hypnozoites):** In *P. vivax* and *P. ovale*, some sporozoites become dormant "Hypnozoites" in the liver. They can reactivate 1–5 years later, causing a relapse.

Phase 2: The Erythrocytic Cycle (Blood Phase)

- Invasion: Merozoites leave the liver to invade RBCs and reticulocytes.
- Development:
 1. **Ring Stage:** The merozoite becomes a vacuolated, ring-shaped trophozoite.
 2. **Trophozoite:** The growing form feeds on hemoglobin, creating "Malarial Pigment" from protein and hematin byproducts.
 3. **Schizont:** As the nucleus divides, it becomes a developing schizont.
- **The Attack:** The mature schizont ruptures the RBC, releasing toxins and merozoites. This rupture coincides exactly with the clinical fever spike.
- **Gametogeny:** Some merozoites differentiate into sexual Gametocytes to infect new mosquitoes.

Diagnosis

- **Method:** Thick and thin blood smear examinations to visualize stages (rings, trophozoites, gametocytes) within RBCs.
- In Jordan:
 - There is no local transmission because the *Anopheles* vector is not present in Jordan.
 - Diagnosed cases are typically imported by travelers or UN Peacekeepers returning from endemic regions like Africa.

Summary of Stages

- **Sporozoite:** Infective stage (enters human).
- **Merozoite:** Pathogenic stage (destroys RBCs).
- **Gametocyte:** Transmissive stage (enters mosquito).

Toxoplasma gondii (Tissue Sporozoa)

Not Required

- **Description:** A coccidian protozoa with worldwide distribution.
- **Hosts:**
 - **Definitive Host:** Cats and their relatives (where the sexual cycle and oocyst production occur).
 - **Intermediate Hosts:** Humans, animals, and birds (asexual reproduction).
- **Transmission:** Humans can be infected by ingesting oocysts (from cat feces) or tissue cysts (from infected undercooked meat).
- **Pathology:**
 - Parasites invade cells (especially macrophages) forming tachyzoites which spread infection.
 - Latent infections involve tissue cysts containing bradyzoites.
 - Infections can be congenital (in non-immune pregnant mothers) or postnatal.

كانت ليلةً كباقي الليالي،

امتلأت السماء بالنجوم مختلفة الألوان، وارتسمت ابتسامةً على وجه كلٍّ من يسيرُ في شوارع عمان، كانَ الريح الباردةَ تلمسُ وجوهَهم، وبينَ حينٍ وآخر تهُبْ نسمةً قويةً تُلَاعِبُ مِعْطَفَةً الأبيضَ الطويلَ فوقَ قميصِه الأسود.

رائحةُ المطر كانت حاضرةً، بعدَ أن ذرفَت عيونُ السماءِ دُمْوَعاً كثيرةً، والأشجارُ كانت جميعُها تبتسُم وَتُغْنِي، حتى لو لم يسمعها البشر.

كانت تُغْنِي دائمًا، وكان "زين" يجلسُ لِيسمعُها...

تُغْنِي كما لو كانت تُواسي السماء، تُواسي الليلَ على قدوم النهار، وتُواسي النهارَ على رحيله واستقبالِ قافلةِ الليل.

لم يسمعها أحدٌ.

لم يسمعوا أغنيةَ الأشجار للسماء، ولا نشيدَ السماء للنجوم، ولا هجاءَ الليل للنهار، ولا شكوى النهار من الليل...

وكان "زين" يتساءل دائمًا:

"ألا يسمعون؟ ألا يسمعون السماء، والأشجار، والنجوم؟!"

جلس على مقعدٍ خشبيٍّ، لم يكن مبتلاً، فقد كانت مظلَّةً صغيرَةً تعلوَه.

أغمض عينيه، وجلس يتفكر.

حاولوا إعرفوا المقصود من الخاطرة هاي واحكولي بمنشور على قروب "دكتور 24"



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