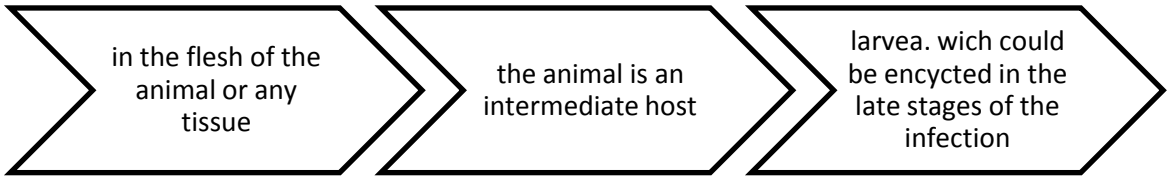
PARASITOLOGY

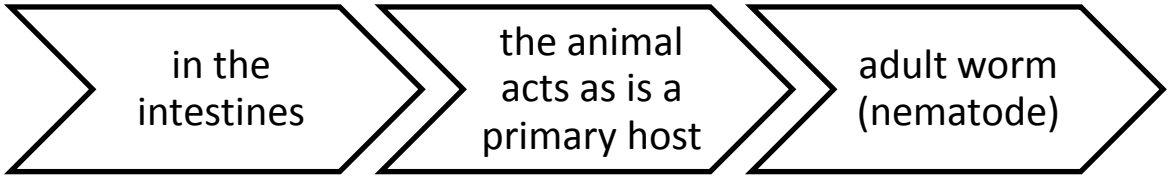
- in this lecture we will talk about parasites that affect the muscloskeletal system ,which will include mainly the skin , muscles and some subcutaneous tissues and so on .

The doctor will not go in details as we took them in the previous semester

☒Trichinella spiralis

- The first parasite, a nematode, that we will talk about is trichinella spiralis , it's called spiralis because it is spiral in shape as we will see later on, in fact it is a small nematode (round worm) usually measures about 2 to 3 millimeters in length.
- when we took the parasites last semester we talked about primary and intermediate hosts , this worm actually has two stages of existence I.e (it must have primary and intermediate hosts) , BUT What is unique about this worm is that the same animal serves both as primary and intermediate host , so this is really an exception because the normal parasites' hosts are different organisms , for example (human or animal as a primary host and vector or another animal as a secondary host) . So the animals or even humans if they are infected with this worm they will act as primary and secondary hosts, in other words this worm could exist in the intestine of the animal as an adult worm (nematode) and this stage is considered as a primary host but the intermediate stage which is the (larvea or a cycted larvea) actually happened to be in the tissues of that animal mainly the skeletal muscles.





- this type of infection (in which the organism is both primary and secondary hosts) is transmitted from organism to another by :
  1. cannibalism in the same species (a bear eats his brother :P)
  2. eating flesh (meat) from another species (when a human eats pig's or bear's meat)
  - from the points 1,2 we can conclude that the transmission of the infection is by eating the flesh (tissues) of the animals (((eating the larvae)))
  - from the second point we can conclude that trichinella spiralis is NOT very specific (it is ubiquities) as it could infect different animals or species (rats , pigs , polar bears , seals) , and this is another exception as other parasites are confined to specific kind of animals or species

✓ THE LIFE CYCLE :

- The adult worms are found in the intestinal tract, and as they are nematodes they must have separate sexes, then there will be pairing between males and females to produce fertilized eggs but again there is another exception, in fact trichinella spiralis doesn't form eggs as other nematodes do, they form larvae immediately just like the microfilaria (tremadotes) but it is not classified as microfilaria it is a nematode indeed.
- Then these larvae are deposited in the sub mucosa of the small intestine and the male usually disappears , (After fertilizing the females the males' job is done) , and they will be discarded with the faces , but the females stay in the sub mucosa of the intestine producing larvae .
- These larvae will penetrate the wall of the small intestine and then get access to lymphatics and blood vessels, then they will disseminate to the whole body (heart, lungs, liver, etc).

Although these larvae disseminate to the whole body they can't settle down, further develop, and produce cysts except in the skeletal muscles (A kind of specialization for these worms).

The presence of the worms in the intestine could give GI symptoms (diarrhea, vomiting, ...) but once they actually go to the blood stream they can produce constitutional (generalized) symptoms.

- ❖ PS: anything that reaches the blood as bacteria or viruses or even parasites cause what is called constitutional symptoms which can be manifested by malaise (feeling unwell), headache and sometimes fever. In general parasites specially worms or helminthes don't cause fever, the protozoa do. so this is again another exception as the trichinella spiralis is a worm and does produce fever (larvae in the blood do that).
- As these worms reach different parts of the body they could cause a wide variety of symptoms for example :
  - encephalitis and meningitis in the brain
  - pneumonia in the lungs

These symptoms are usually mild because the number of the larvae isn't that high and they disappears on their own, but if the load (number) of the larvae was high these symptoms could become sever and cause death.

- So what happens now is that all the larvae that were settled in the organs will dye except the ones that reach the skeletal muscles , in the muscles they will cause inflammatory reaction which will bring the macrophages , other inflammatory cells and fibroblasts . Then after the end of the inflammatory reaction around the larvae the fibrosis will take place then these lesions eventually after few months will become calcified. so the fibrosed lesion in the skeletal muscle contains the spiral encysted larvae , so this lesion will cause pain, tenderness, and swelling .Then after few months it will calcify and the pain will disappear because the inflammation had stopped and the calcification took place (could be seen on X-ray in severe cases) . so the main symptoms appear at the beginning (pain , tenderness , swelling in the muscles all over the body) and then the larvae will stay quiescent but alive for several years . so as the doctor said : " if u ganna eat your brother at least cook him to kill the larvae and prevent spreading of the infection "O.o . So if a human eats a polar bear's or seal's meat infected with larvae he/she will catch the infection BUT!! u can kill the larvae before eating the meat by cooking it or also freeze it at -21 degrees centigrade

✓ DIAGNOSIS :

There is no point of examining feces cause you will see nothing in them even the male worm won't be seen

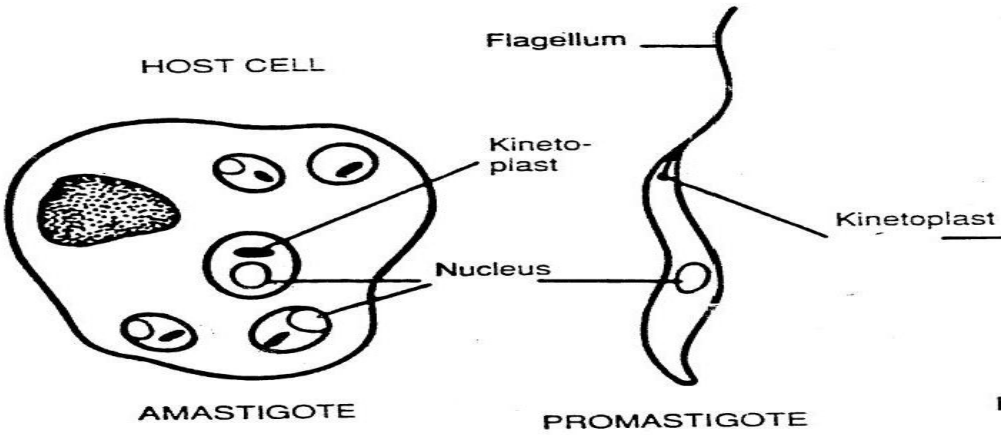
1. **Taking history** from the patient could give you a clue especially in endemic regions, actually in our country the cases are rare and that apply on most Muslim and jewish countries because mainly the infection comes from pigs , so in USA and Europe u could see some cases.
2. **Serology :** because these worms induce the formation of IgE Anti-bodies and sometimes IgG you can measure the titer of these IgE anti-bodies against the worm by serological tests , usually the concentration of IgE Abs remains high for about one year so in the early stages of the disease you can use management of specific IgE against the worm for diagnosing or even IgG titer .
3. **Eosinphilia :** in fact this namatode is peculiar in that it produces a high level of eosiphilia from 40% up to 50% (in the initial stage of infection) , so after one year or after calcification you won't see high levels of eosinphils
4. **Muscle enzymes** (in initial stages) : the injury of the muscles cause the elevation of certain muscular enzymes that could be measured for the diagnosis such as : CPK (creatine phsphokinase) and LDH (lactic dehydrogenase), these enzymes are specific

for skeletal muscles not cardiac ones .

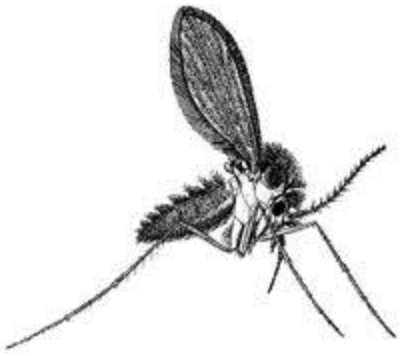
5. **Muscle biopsy**: as they say seeing is believing. This is the best way of diagnosis, you search for swellings or lesions in the muscle then a biopsy is taken and the tests are made under the microscope to see the spiral larvae , if there is an inflammatory reaction around it that means it's in the early stages if its calcified the infection is old then.

☒LEISHMANIA

- The lesion is caused by a protozoa called leishmania . This kind of protozoa belongs to a family called (flagellates / or tissue flagellates / or hemo flagellates). But why they are called hemo or tissue flagellates???Because they are tissue parasites and they are flagellated as will.
- The family itself is called Trypanosomatidae with 2 groups (genera):
    - Leishmania
    - Trypanosoma : we will talk about it later.



- This figure represents the leishmaina in its primary host (the left part) and intermediate host (the right part) . so leishmaina is a tissue dimorphic parasite as it has two different structures in the primary and intermediate hosts . The primary host could be a human, a dog or even a jerboa so really this is a zoonosis as these animals work as reservoirs for this parasite. The intermediate host is actually a vector, the sand fly. The morphological structure in the primary host is called amastigote or donovan bodies which is an intracellular structure measuring about 3 microns in diameter so the left picture in the figure is actually a macrophage with multiple amastigotes in it (5 particles) , this amastigote contains nucleus and a kinetoplast (small mitochondrial DNA) . The structure of the leishmania in the intermediate host (promastigote) is much bigger about 20 microns with an anterior flagellum, nucleus and kinetoplast at the base of the flagellum.



Considering the sand fly (the intermediate host) , as u can see in the second figure it has:

- Hairy wings.
- When it is not flying its wings project upward unlike the other kinds of flies which have horizontal (downward) wings when they land.

✓ LIFE CYCLE :

- When the sand fly bites someone it's going to pick up the lesions (amastigotes) , then inside the body of the fly it will develop and form (promastigote) . After that the fly goes and bites someone else and injects the promastigotes into the skin. then these promastigotes lose their flagellum and are taken by the macrophage by phagocytosis and become incorporated with the phagolysosome, but they are very resistant to the acidity of the lysosomes and thats why they could live for a long time in the macrophage as an amastigotes.

the only way to get rid of these amastigotes is by **chronic** infection by T helper-lymphocytes and more macrophages to site of infection, and that goes on and on for a long time .

When the human is sticked by a sand fly the site of injection will develop a lesion (usually a swelling) which becomes hard as it is made of inflammatory cells. so you will get a hard nodule which will ulcerate then become indurate chronic ulcer and after about one year it will heals leaving a nasty scar and you will get solid immunity . (Bagdad, Halab , Aleppo , Pommpe) boils are the endemic areas.

- In Jordan there are some few cases in AL-gour and Ma'an.

✓ LEISHMAINA SPECIES

- They are identical in there morphologies so they can't be differentiated depending on their shapes, for differentiation we can use **molecular methods** or by monitoring the **pattern of diseases** that they form.
  - In fact, the illness that we have talked about is called **cutaneous leishmaniosis** , and usually the leishmaina that causes it could found in the new world (America) or the old

world (Asia , Africa) as , leishmania tropica , leishmania major and leishmania aethiopica,In the new world usually the leishmania mexicana cause the cutanous leishmaneousis

- The second type of leishmaniosis is the **diffuse cutaneous leshmaniosis** (mostly associated with L.aethiopica) , its named diffuse because there is a spreading of the lesions on the skin unlike the previous type . Actually the immune response is responsible for this dissemination as it is humoral immunity (ABs mediated immunity) which can't enter the cells (infected macrophages) and eradicate the parasite there, unlike the previous type which develops cell mediated immunity.

leishmania aethiopica could cause two types of leishmaniosis

- The third type is the **muco cutaneous leishmaniosis** , it usually present in America and caused by leishmania braziliensis . The story goes as a fly bites a person then he will get a lesion which will heal in one or three months but after many months or even a year or two he will get an activation of lesions at muco-cutaneous areas (the mouth, nose, ...) . This type is considered more serious as it develops chronic lesions which are vulnerable for bacterial superinfection and then bleeding and destruction of mucous areas, or by aspiration it could reach the lungs and cause pneumonia and death , so this type doesn't develop solid immunity like the cutaneous type and thats why there is reoccurrence of lesions .

Type 1-3 are related to the skin , Type 4 is related to viscera

- The last type is **visceral leishmaniosis** (or kala azar...means "black disease" because of the hyperpegmintation of the skin that is one of its symptoms). species that lives in cold environments like skin 34-35 C (L.tropica , L.aethiopica) cause cutaneous leishmaniosis. But other species like **L.denovani , L.chagasi , L.infantum** can live in cold tempreture and are **more resistant to cidal actions of the serum**, so they can live inside the macrophages in **viscera** (liver , spleen , bone marrow) and cause visceral leishmaniosis. so the disease is generalized (constitutional) . it goes like this , a fly bites then there is a small skin lesion (maybe not noticed) after several months the patient will become extremely sick having pyrexia(fever) , cachexia , loss of weight , enlargement of spleen and liver, and hyperpigmentation (black color) of the skin then death in 1 or 2 years if not treated.

✓ DIAGNOSIS

1. **Biopsy** from skin (types 1-3) or bone marrow (type 4)but not from spleen as it may cause bleeding
2. **serology** specially in kala azar