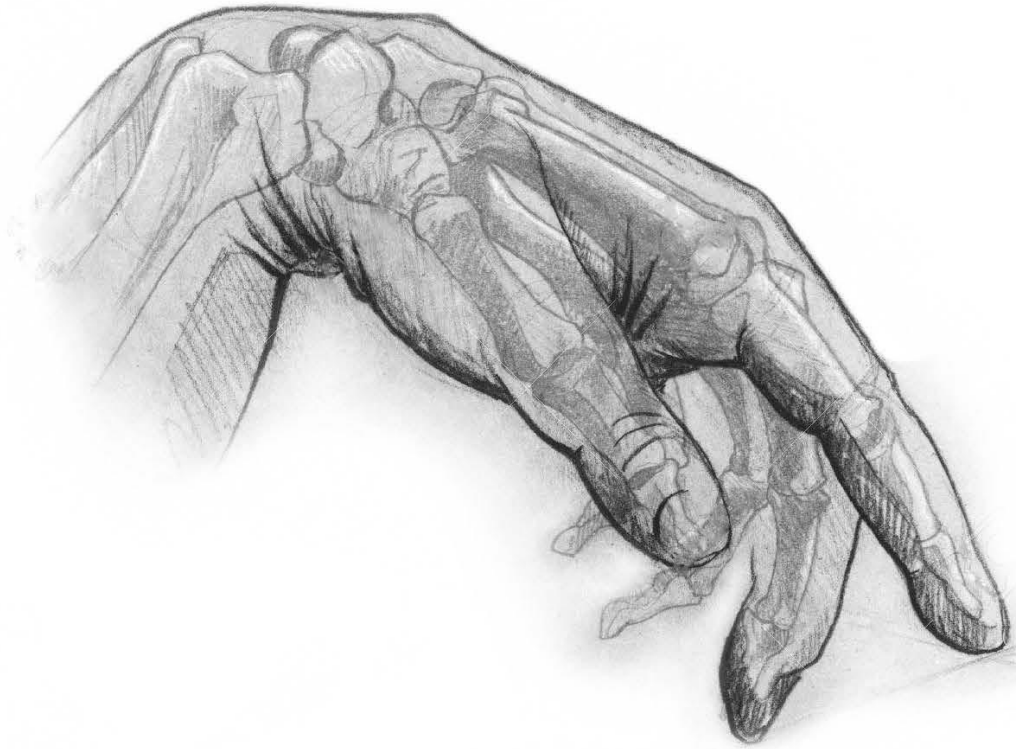


The **Musculoskeletal** System



Microbiology

☒ Sheet

☐ Slide

☐ Handout

Number:

Subject: Parasitology 2

Done By: Sally Al.sa'di

Doctor: Hassan Abu Raheeb

Date: 26/2/2016

Price:



LEISHMANIA / LEISHMANIASIS:

- The lesion in the above picture 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 well.



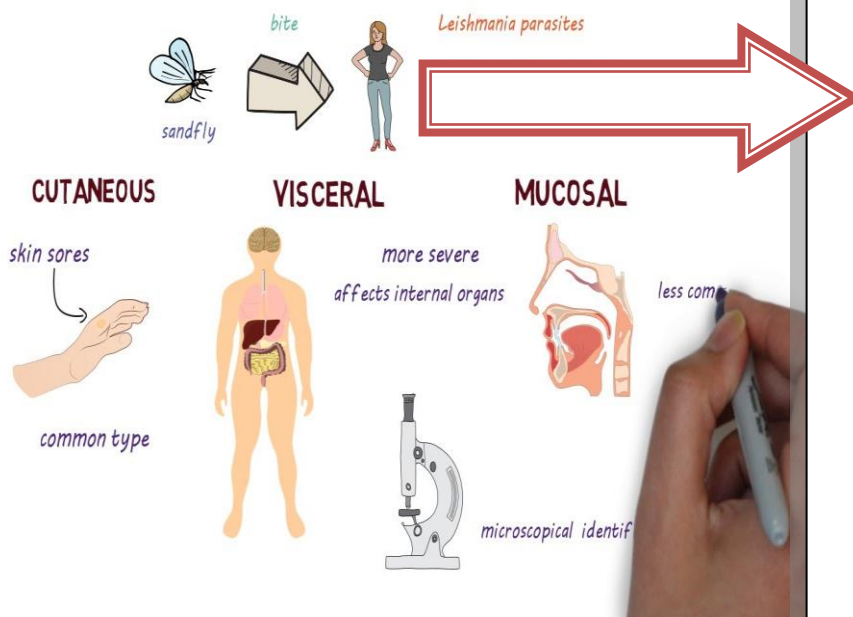
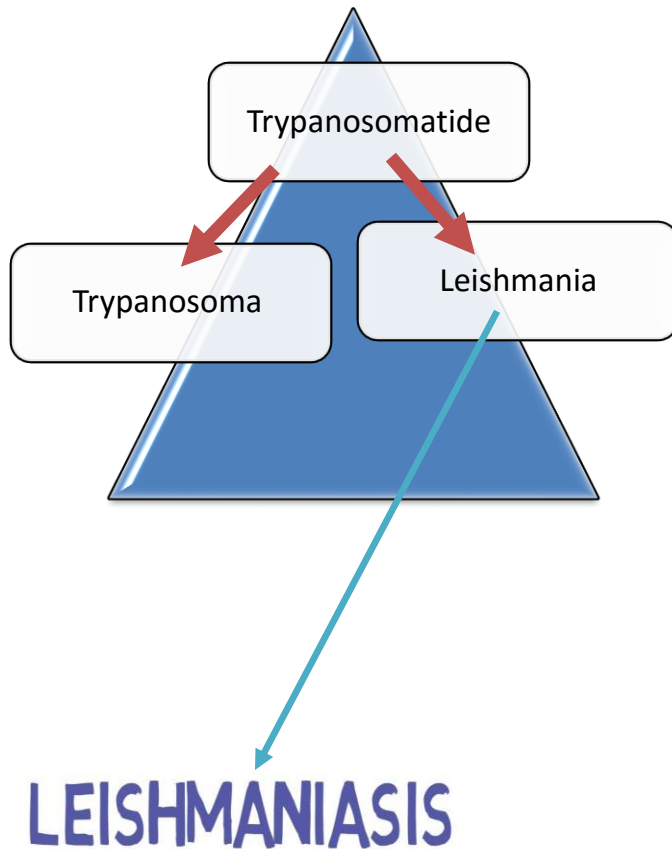
- The family itself is called **Trypanosomatidae** [in Greek names: **trypano**>>means borer: "a worm, insects..that bores into wood or other materials" / **soma**>> body]

Leishmaniasis is a parasitic infection caused by a trypanosomatid protozoan of the genus **Leishmania**

* The family of the trypanosomatidae contains only **2 genera** that parasitize humans:

-**Genus trypanosome** that may be found either in circulating blood or intracellularly.

-**Genus leishmania** are always intracellularly.



Quick view +Summary:

- There are three basic forms in which the disease presents: **cutaneous**, **mucocutaneous** and **visceral**, and many species of the genus are known to cause disease in humans.
- Blood-feeding sand fly **species** are known to transmit the disease. Different species cause different clinical forms of the disease in various parts of the world.
- The protozoan multiplies in the insect vector and is then inoculated into another mammalian recipient, possibly a human. There it is engulfed by macrophages but may survive and even replicate inside them.
- The **Cutaneous** form presents with skin ulcers, and the **Mucocutaneous** form with ulcers of the skin and also the mucous membranes of the mouth and nose. The **Visceral** form is more generalized, affecting internal organs.

Back to the Leishmania, there are a variety of species which can be grouped into two main categories,

		<p>Chagas Tarouco "Brazilian footballer"</p>	<p>1) New World:</p> <ul style="list-style-type: none"> A• Leishmania mexicana B• Leishmania braziliensis C• Leishmania utingensis D• Leishmania chagasi
<p>L.braziliensis -> ML</p>			<p>"Mnemonic: Chagas is a NEW Brazilian footballer played in Mexico in a unit+ genius "utigenis" way"</p>
			

2) Old World:

- A• Leishmania aethiopica
- B• Leishmania enrietti
- C• Leishmania major
- D• Leishmania infantum
- E• Leishmania tropica

Leishmania Parasites and Diseases

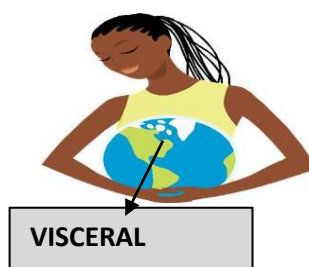
SPECIES	Disease
<i>Leishmania tropica</i> *	Cutaneous leishmaniasis CL
<i>Leishmania major</i> *	"Mnemonic: Major Tropic temperature in Mexico and Ethiopia is different so>> so the color of skin differs (CL) .
<i>Leishmania aethiopica</i>	
<i>Leishmania mexicana</i>	
<i>Leishmania braziliensis</i>	Mucocutaneous leishmaniasis ML
<i>Leishmania donovani</i> *	Visceral leishmaniasis VL
<i>Leishmania infantum</i> *	
<i>Leishmania chagasi</i>	

9

Mnemonic:

VL: the story goes thus:

Mum donor "L.DONOVANI" born infant "L.INFANTUM" and named him Chagas "L.CHAGASI"

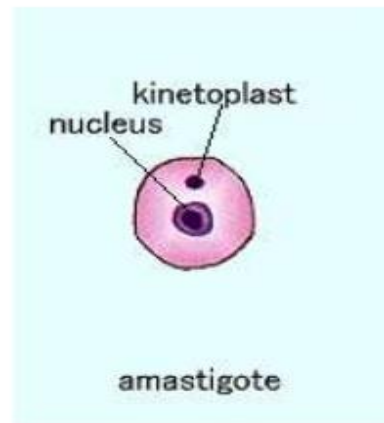
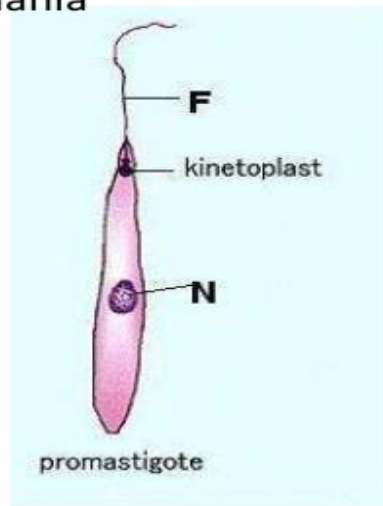


Leishmaniasis is Neglected Disease >>

Leishmaniasis is a globally important but neglected disease. For most people, infection results in a slow-to-heal skin ulcer.

MORPHOLOGY

Promastigote & Amastigote of Leishmania



<i>Digenetic Life Cycle</i>	
Promastigote	Amastigote
<ul style="list-style-type: none"> – Insect – Motile – Midgut 	<ul style="list-style-type: none"> – Mammalian stage – Non-motile – Intracellular

- ✓ This figure represents the Leishmania in its primary host (the right picture) and intermediate host (the left picture). So Leishmania is a **tissue dimorphic parasite** as it has two different structures in the primary and in the 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 right picture in the figure is actually an amastigote, this amastigote contains nucleus and a kinetoplast (which is made by DNA, RNA in the basal aspect of the flagellum).

- ✓ 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:

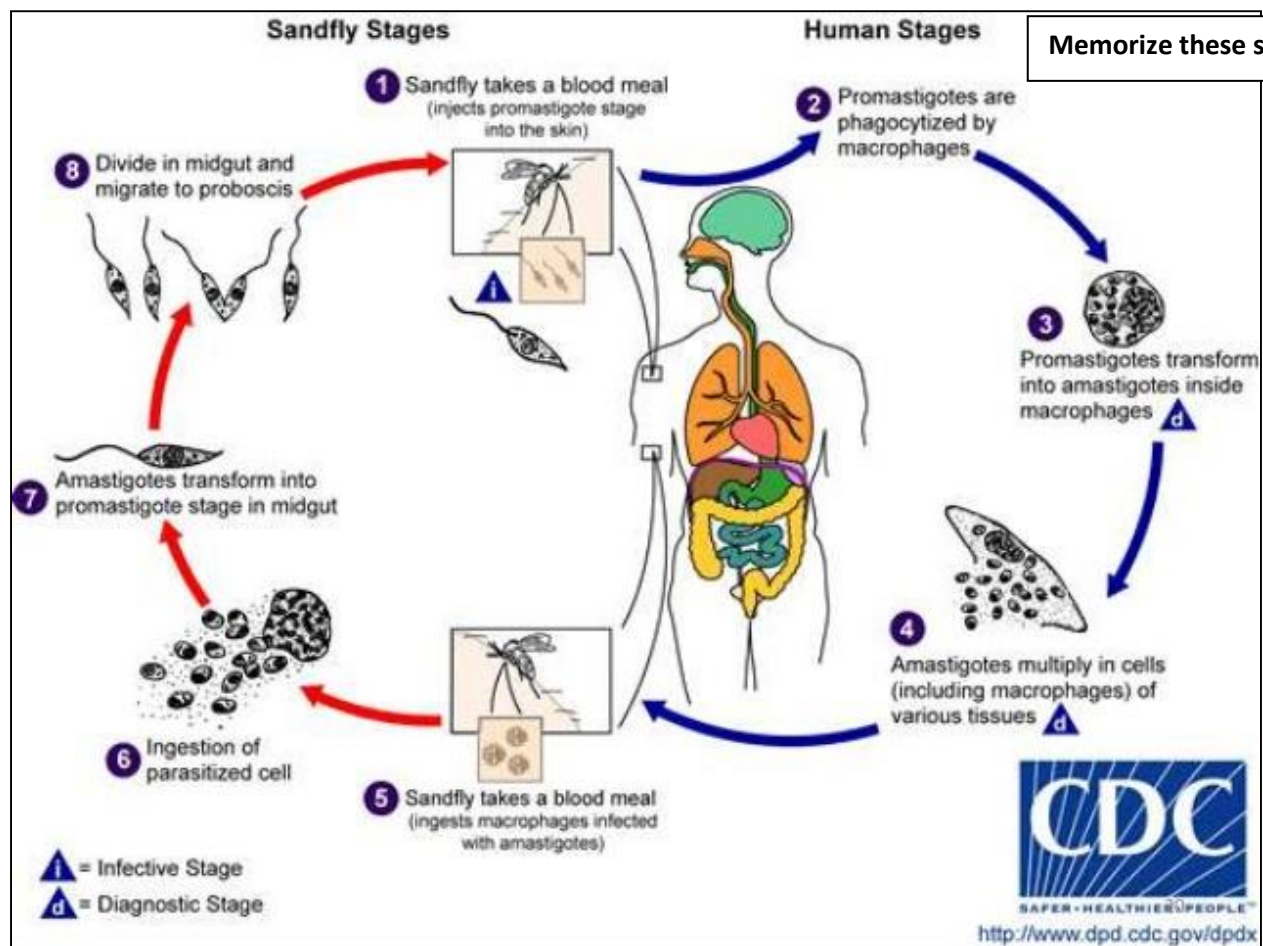
- o Hairy wings.
- o When it is not flying its wings project upward unlike the other kinds of flies which have horizontal (downward) wings when they land.

Life cycle

- o The organism is transmitted by the bite of several species of blood-feeding sand flies **which carries the promastigote** in it and can infect human or animals (usually vertebrates), that can naturally be transmitted to human later by Sand-flies.
- o These promastigotes in human body activate the complement system and facilitates the phagocytosis of them and gains access to mononuclear phagocytes/macrophages where it transform into **amastigote** and divides until the infected cell ruptures. (**They resist lysosomal enzymes** so that they can live intracellularly)

>>>They replicate so rapidly that they infect other macrophages and this will activate T-cells which come to the site of infection (bite), an accumulation will occur at the site of the lesion; this will result in swelling and induration and eventually transform into a granuloma and ulcers. After few months the ulcer will heal by **scarring**.

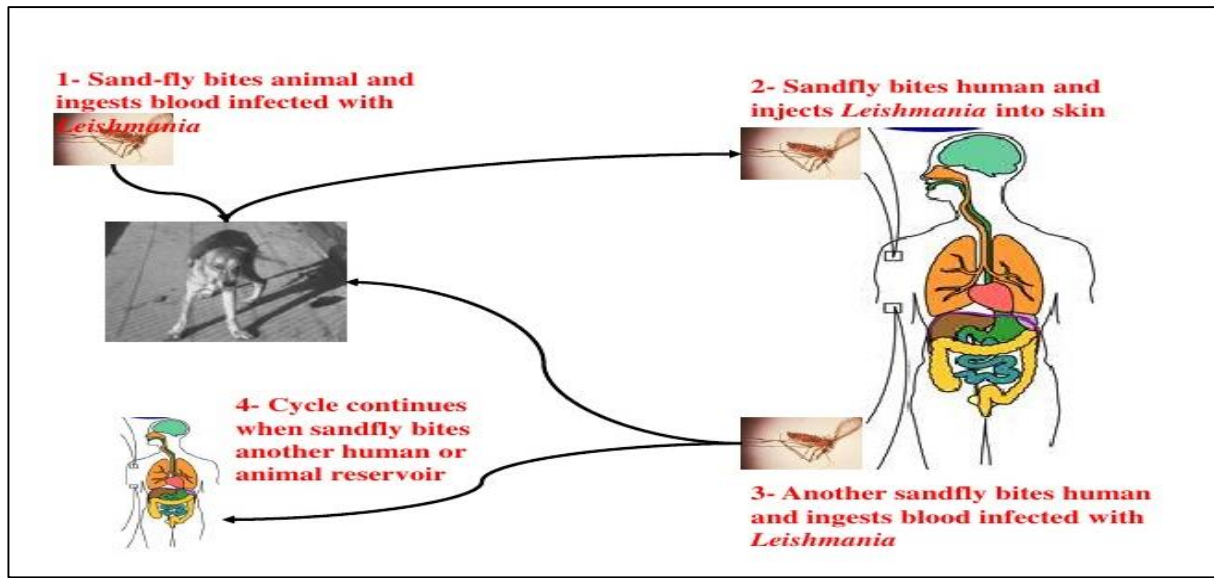
- o The released organisms infect other cells. The sand-fly acquires the organisms during the blood meal, the Amastigote transform into flagellate Promastigote and multiply in the gut. Dogs and rodents are common reservoirs



LEISHMANIA SPECIES

They are identical in their 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.

A- Cutaneous Leishmaniasis (CL):



*Lesions (ulcers) tend to occur on exposed parts which are easily bitten by sandflies, as most lesions are on exposed regions of the skin - for example, face, arms and legs.



- Is **the most common** form of leishmaniasis affecting humans.
- Is a **skin infection** caused by a parasite that is transmitted by **the bite of a sand fly**.
- This disease is considered to be a **Zoonosis** (an infectious disease that is naturally transmissible from vertebrate animals to humans), with the exception of *Leishmania tropica* — (an infectious disease that is naturally transmissible from humans to vertebrate animals).

Zoonosis from Greek: *zoon* "animal" and *nosos* "ailment").

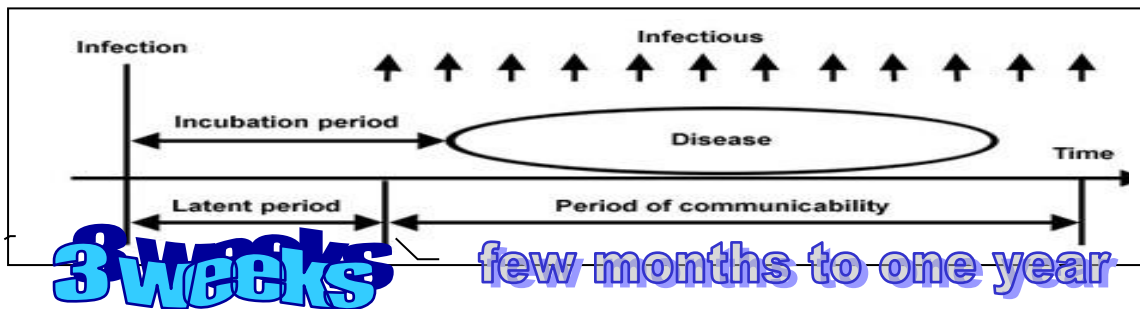
- ❖ Remember >>Reservoir: is an animal or groups of animals that can harbor the parasite.
- ❖ Keep in mind reservoir is not the intermediate host.

- **Cutaneous Leishmaniasis** is a skin infection

No involvement of nerves and there is no systemic invasion.

- CL presents in various forms, although most patients have limited cutaneous lesions that self-cure during **few months to one year**, leaving **scarred tissue**.

"Incubation period may reach up to **three weeks**"



- As we mentioned before CL is caused by *L.tropica*, *L.major*, *L. aethiopica* (Old World) and *L.mexicana* (New World), **is a solitary lesions**: a single lesion at the site of the bite, and this lesion begins to granulate to eventually be ulcerated, sometime it may be accompanied with **exudates** to form what is like a moist cutaneous leishmaniasis and other times, there is **a dry lesion** known as the dry cutaneous leishmaniasis.
- As a treatment; it will heal by itself leaving a disfiguring, depigmented scar at the sites of injury, this action is known as **the Baghdad boil (دمل بغداد) or Aleppo boil or Bombay Boil**, once it heals, the immunity **becomes solid** and you'll never get this disease again.



Diffuse CL:

- The normal immune response for CL is cell-mediated immune response. However, **Some patients with a poor immune response** will have humoral immune response (antibodies immune response), since Leishmania is intracellular, antibodies can't neutralize it and the disease prognosis will be worse and this is called Diffuse CL.
- There is a primary lesion which spreads to **involve multiple areas of the skin OVER THE BODY** "hence the name Diffuse CL" (not only one lesion as normal CL).
- It may look **similar to Leprosy (disambiguation)** but there is no involvement of nerves and there is no systemic invasion.

This figure is not included but just for clear explanation below.

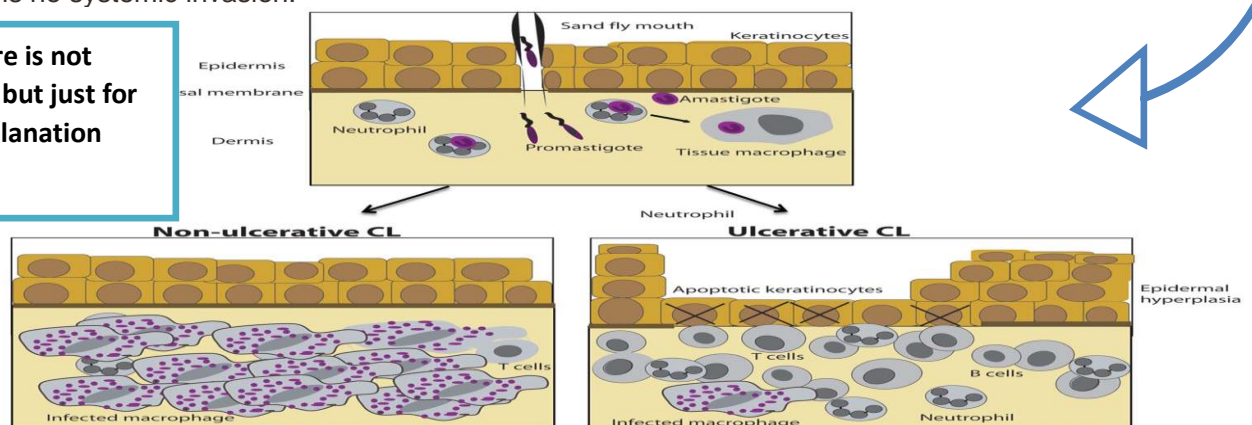


FIGURE 1. Histological hallmarks of diffuse and localized cutaneous leishmaniasis caused by *L. aethiopica*.

****Diffuse Cutaneous Leishmaniasis (DCL)** is associated with chronic inflammation and ulceration of the skin.

REMEMBER: ULCERATION is:

an **open sore** on an external or internal surface of the body, caused by a break in the skin or mucous membrane that fails to heal >>>allowing the diffusing of infected macrophages!!

Tissue macrophages serve as **host cells** and **immune activation** is necessary for **parasite clearance..** (The parasite is thought to be maintained inside the macrophages).

- The immune system was separated into two branches:

***Humoral immunity** "antibody-mediated immunity">> for which the protective function of immunization such as antibodies could be found in the humor (cell-free bodily fluid or serum)

and

****Cellular immunity**, for which the protective function of immunization was **associated with cells** that does not involve antibodies, but rather involves the activation of phagocytes, antigen-specific T-lymphocytes, and the release of various cytokines in response to an antigen.

Actually the immune response in **Diffuse CL** that is responsible for dissemination is **humoral immunity** (Antibodies mediated immunity) with lots of antibodies against Leishmania but very little T-cells and macrophages that are active against the disease (look to the picture above) that these antibodies will be **against leishmania** "intracellular parasite" **inside the cells** so antibodies can't enter the cells (infected macrophages) and eradicate the parasite there, unlike the previous type (Normal CL) which develops cell mediated immunity. SO: Diffuse CL is worse than CL.

- >> **Ulceration** has been proposed **to be a result of infiltration of activated immune cells into the skin**
- In a case of diffuse CL: in this cases the lesion tends to spread from the site of lesion to other places on the skin by macrophages themselves, which will form what is known as diffuse Cutaneous Leishmaniasis.

To remember the immune response you can watch this helpful animation:

http://highered.mheducation.com/sites/0072507470/student_view0/chapter22/animation_the_immune_response.html

Cell-mediated immune response:

<http://outreach.mcb.harvard.edu/animations/cellmediated.swf>

Diffuse CL is mostly associated with Leishmania aethiopica, in Ethiopia, Kenya, etc.

B- Muco-cutaneous Leishmaniasis (ML):

It usually presents in America and caused by **leishmania braziliensis**.

The story goes as a fly bites a person then he will get a lesion and induration and the patient will not pay attention to it, and it 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, ...) .



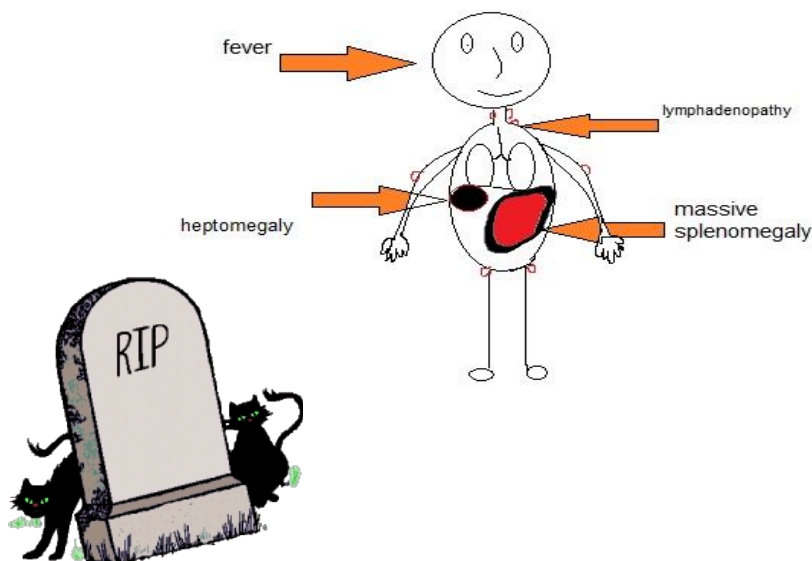
This type is considered more serious as it develops chronic lesions which are vulnerable for **bacterial superinfection** and then **bleeding and destruction of mucous areas**, or by **aspiration** it could reach the lungs and cause pneumonia and **death**, so this type doesn't develop solid immunity like the cutaneous type and that's why there is reoccurrence of lesions.

To sum up:

- MCL is usually acquired from New World species of sand fly.
- Initial infection gives a persistent cutaneous lesion that eventually heals.
- Several years later the oral and respiratory mucosa is involved, with inflammation and mutilation of the nose, mouth, oropharynx, and trachea.
- This leads to partial or total destruction of the mucous membranes of the nose, mouth and throat.
- Respiratory difficulties and malnutrition can cause death.

C- Visceral Leishmaniasis (VL):

- The last type is visceral leishmaniosis (or kala azar: serious visceral leishmaniasis, occurs several years after recovery from VL... kala azar means "black disease" because of the hyperpigmentation of the skin that is one of its symptoms).
- VL is fatal if left untreated.
- Species that lives in **cold environments** like skin 34-35 C (L.tropica, L.aethiopica) cause **cutaneous leishmaniosis**. But other species that cause VL like L.denovani , L.chagasi , L.infantum can survive core body's temperature " so it is a systemic disease", so they can live inside the macrophages in viscera (which are present in large numbers in: liver, spleen, bone marrow, lymph nodes) and cause visceral leishmaniosis >>so the disease is generalized (constitutional).
- Like ML, VL 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 enlargement in the spleen, the liver, lymph and bone marrow and the patient suddenly will feel ill, raise in body's temperature because of fever, anorexia (loss of appetite), weight loss and skin pigmentation; the skin turns out **black**, that's why it's called the black sickness (Kala Azar), then death in 1 or 2 years if not treated.



- Fever (PYREXIA).
- Weight loss.
- Hepatomegaly (can be marked).
- Splenomegaly (often enormous).
- Anaemia (can lead to death from haemorrhage or infection).
- Dark pigmentation of the skin is uncommon but the name kala azar is Hindi for black fever

DEATH IF NOT TREATED



Diagnosis of Leishmaniasis:

DIAGNOSIS

1) Direct detection

by:

-The skin lesion

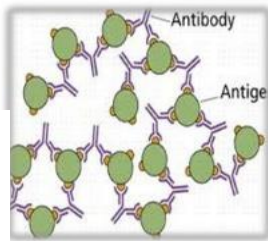
Or

-Microscopically



2) Serology especially in kala azar.

Serology is: identification of antibodies in the serum.



3) Biopsy from:

- Skin (types 1+2), looking for amastigotes in macrophages

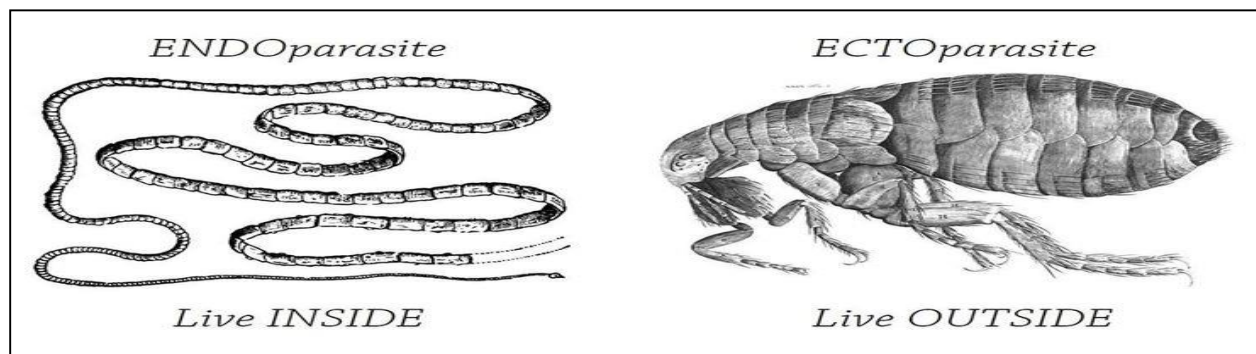
or

-Bone marrow (type3) but not from spleen or liver as it may causes bleeding.

Serology way always positive in all the varieties of this disease, however, it's most useful in **Visceral Leishmaniasis** because antibodies usually more, and also because you don't see the lesion because it's hidden.

ECTOPARASITES

So far we were talking about endoparasites, now we will talk about ectoparasites. **Endoparasites** are inside the body. **Ectoparasites** are the ones which live on the skin or outside environment.



1- Louse (plural: lice):



- The egg of a louse is called a **nit**.

They can be found stuck to the hair, and shine under fluorescent light which helps detect them.

A. Head Lice

- They are **confined** to the head, and are attracted to moist or damp areas; such as behind the ears and back of the head.
- Head lice **are not a hygienic issue**; they can easily be transmitted by close contact with an infected person. They do not transmit disease either.
- Are most commonly in school children, it has nothing to do with personal hygiene, and you can just take it from a child who carries it especially in winter months, girls more commonly than boys.
- Head lice are not responsible for transmission of a disease from one to another although they feed on patient's blood.

Symptoms: Results from allergic reaction to lice saliva: -Itchiness. - Scratching may lead to excoriation of the skin (abrasions; skin is worn off) which can be secondarily infected by bacteria.

B. Body Lice

- Are morphologically identical to head lice.
- They live on human bodies, but lay their eggs in the **seams of clothes**.



- They are a **hygienic issue**, commonly seen in people living in poor conditions; such as homeless people, jail inmates, and people living in war conditions.

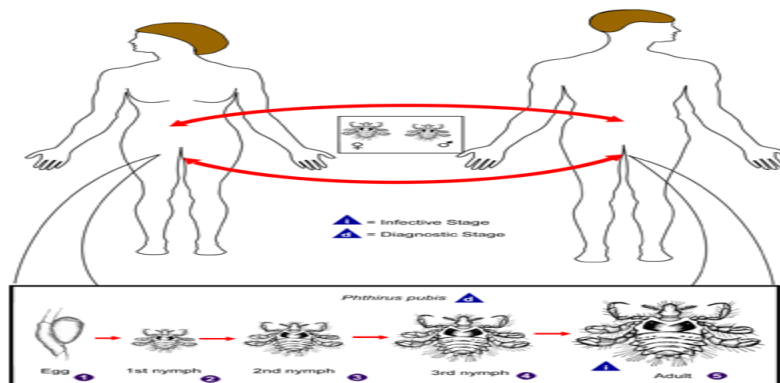
Washing of the body and clothes can easily prevent infection.

- Unlike Head lice, Body lice can be a vector for bacterial diseases; for example, ***Borrelia***, and ***Rickettsia typhi***.

Extra note:-*Borrelia*: A genus of parasitic irregularly coiled helical spirochetes, some species of which cause relapsing fever in humans.

***Rickettsia typhi*:** *Rickettsia* species are carried by many lice, and cause diseases in humans such as typhus.

C. Pubic Lice



- Commonly called “Crabs” because of their slightly similar appearances, they affect pubic hair, sometimes eyelashes and brows, and can be considered a **Sexually transmitted disease (STD)** in some cases.

- They are not vectors for other diseases. Their only consequences are **itchiness and excoriation of the skin**, and may develop secondary bacterial infection.

Note:

✚ The head and the body louse are similar in morphology between those three types:

The length ranges from 2 to 3 millimeters, **3 pairs of legs**,

each leg has a hook on the end of it so it can attaches to the clothes of the patients.

They also can interbreed between each other.

The Crab (pubic lice) is smaller and may range for about 1.2 millimeter, but again it also has 3 pairs of legs.

✚ Head Lice vs Dandruff :



Body louse



Body lice in seam of clothes



Lice eggs are called nits, could be white, clear or black, are located on the hair shaft near to the scalp, those nits can be confused with Dandruff.

But

- **Dandruff** are not attached to the hair "easily to get rid of them by rubbing your head" unlike the nits.

- **Nits** are fluoresce under UV light, so we can detect them unlike dandruff. Also, unlike dandruff, nits are attached to the stem of the hair.

2-Sarcoptes scabiei (Scabies)

What Is Scabies?

- Scabies is a skin infestation caused by a very tiny mite known as the **Sarcoptes scabiei**. These microscopic mites can live on your skin and for the first few weeks, no symptoms appear until their feces start to provoke allergies and cause itchiness all over the body.

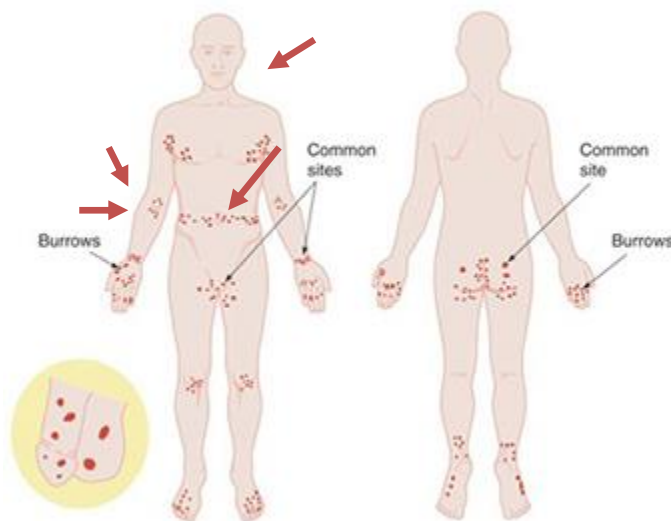
- They reproduce on the surface of your skin and then burrow into your skin, **producing tunnels** and lay eggs "as can be recognized as a black spot". You can recognize those tunnels unless the patient was scratching them, then you'll only see scratching marks, makes the patient allergic to feces of the mite and released chemicals causing the itching.

- As scabies live in skin, and feed on the keratin of the skin (**not on the blood**) causes a very itchy, scratch, pimple-like rash to form on the skin.

- Scabies **are not a hygienic issue**. But it can be transmitted (eg: in schools). Also it does not transmit disease but it may lead to excoriation of the skin which can be secondarily infected by bacteria

- The most vulnerable sites are the armpits, groin "inguinal region", wrists, and finger folds" طيات الأصابع", between fingers. **The face is usually not affected, except in babies.**

Common Sites for Scabies



Can easily be transmitted to Children.

- Can be considered an STD in certain cases + it's also considered as mechanical contact transmitted ectoparasite.

3-Bed bugs

- They nest in cracks in walls, wood, furniture, or anything similar. "They don't live on the body".
- They are not a hygienic issue.
- They feed on blood which will cause an allergic reaction due to their saliva, itching at the site of the bite happens. Their bites are similar to mosquito bites, only larger, and might cause skin rashes and allergic symptoms, they also bites in different places unlike mosquito bites.>>and bed bugs may lead to 2nd infection with bacteria.
- Do not transmit diseases, but are a nuisance because of their bad smell due to their stink glands.
- Acquisition is by close contact.
- Hard to eradicate and very successful to move from one place to another.



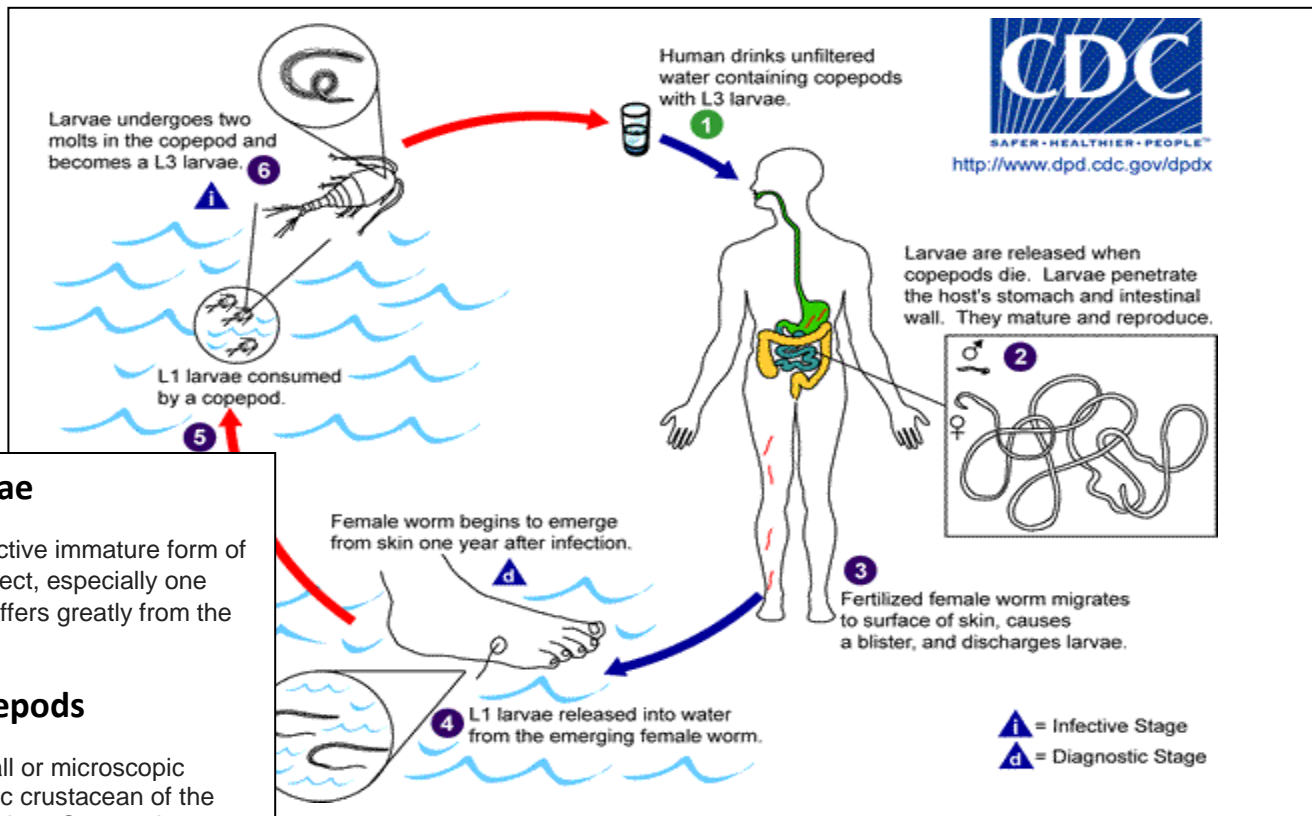
The end of Ectoparasites

Now I will back to continue sheet 1 with **Dracunculus medinensis (guinea worm)**

-It's a **worm of animals** but sometimes it could affect humans and it **lives in the subcutaneous tissue**. It's **very long between 50cm till 100cm in length**. It migrates itself in parts of the body where **there's contact with water** (e.g. the leg is infected and the anterior end of the worm is positioned in the soul of the foot, it ulcerate the skin there and release its larvae to the water)



Life cycle:-



Larvae

The active immature form of an insect, especially one that differs greatly from the adult.

Copepods

A small or microscopic aquatic crustacean of the large class Copepoda.

- 1) Human drinks water with copepod/cyclops (tiny creatures) containing larvae.
- 2) Larvae are released from copepod/cyclops in the small intestine
- 3) Larvae penetrate small intestine wall and enter the abdominal wall and enter subcutaneous tissue
- 4) Larvae then migrate to lower extremities and ulceration/blistering occurs
- 5) The head of the female adult then ruptures the blister and can be seen releasing larvae which are then ingested by copepods/cyclops in aqueous region.
- 6) In water the copepod/cyclops will eat the larvae and the larvae will develop in them (intermediate host).

** So when someone drinks the water, the cyclops will enter the GIT and the larvae will penetrate the wall of small intestine and migrate to the subcutaneous tissue where it will develop into the adult worm >>complete the cycle.

Diagnosis: local lesion with demonstration of worm or larvae.

Treatment: drugs and surgical methods (pulling the anterior end by using of forceps slowly so you won't detach it (the anterior end) from the rest of the worm which will lead to inflammatory reaction).

