

Hemoflagellates: Trypanosomiasis and Leishmaniasis



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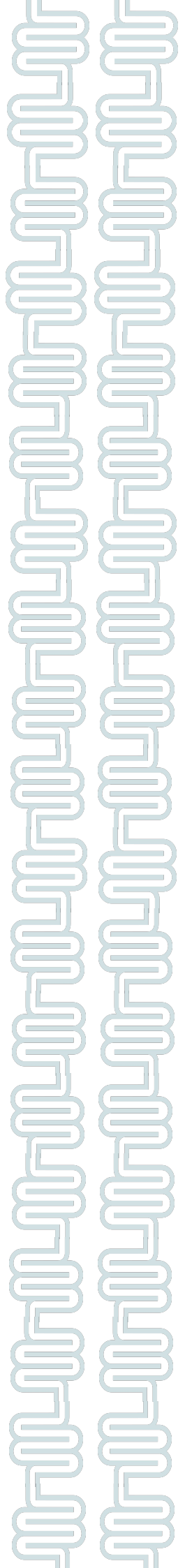
Objectives:

1. Leishmaniasis

- Know different stages of Leishmania parasites
- Describe life cycle of Leishmania parasites
- Discuss what diseases caused by Leishmania parasites and what is endemic in Saudi Arabia
- Geographical distribution of Leishmania in the world either cutaneous or visceral
- Leishmaniasis
- Know what are the vectors of Leishmania
- Discuss clinical types of Leishmaniasis
- Know uncommon types of the diseases
- How Leishmaniasis is diagnosed in the labs
- What is the best treatment for Leishmaniasis

2. trypanosomiasis

- Know stages of Hemoflagellates
- Know geographical distribution of African sleeping sickness
- Describe life cycle of African trypanosomiasis
- Discuss pathology and diagnosis of African sleeping sickness
- Describe life cycle of American trypanosomiasis.
- Know signs and symptoms and how to diagnose American trypanosomiasis
- discuss the treatment of trypanosomiasis.
- Summarize major filarial infections of Humans.
- Describe life cycle of Onchocerca volvulus.
- Know pathology, diagnosis and treatment of onchocerciasis.
- Discuss pathology caused by lymphatic filariasis
- Describe life cycle of Wuchereria bancrofti.
- Know about diagnosis and treatment of lymphatic filariasis.
- Describe life cycle of Loa loa and how it diagnosed and treated



Leishmaniasis

Introduction

Males slides

Leishmaniasis is a parasitic disease caused by the *Leishmania* parasite.

This parasite typically lives in infected sand flies.

You can contract leishmaniasis from a bite of an infected **sand fly**.

The sand flies that carry the parasite typically reside in tropical and subtropical environments.

Have occurred in areas of Asia, East Africa, and South America.⁽¹⁾

Leishmaniasis comes in three forms: cutaneous, visceral, and mucocutaneous. Different species of the *Leishmania* parasite are associated with each form.

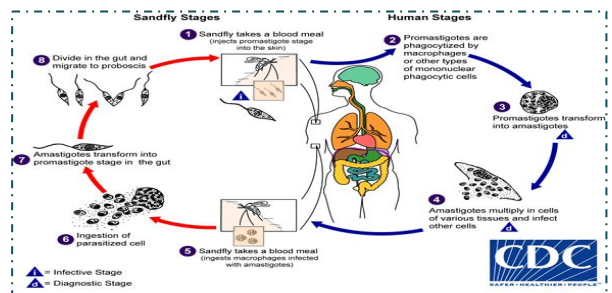
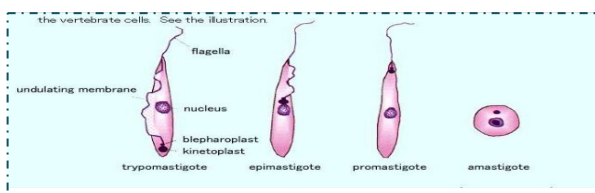
Experts believe that there are about 20 *Leishmania* species that can transmit the disease to humans.

Life cycle

Females slides, but pictures were found in both

- Leishmaniasis is transmitted by the bite of female **sandflies (vector)**.
- The sandflies inject the **★ infective stage (promastigotes)**, then the macrophages will engulf them and transfer them to **★ amastigotes⁽²⁾(the diagnostic stage)**.
- Leishmania* parasite **survive within the macrophages** (amastigote stage) in the human body as intracellular parasites, cell mediated immunity determines the host response to infection and clinical manifestations of the disease.

Different stages of Hemoflagellate protozoa⁽³⁾



1. Also can be seen in Saudi Arabia
2. Unlike American Trypanosomiasis, where Amastigote is seen only on Autopsy.
3. Promastigote: As you can see in the pic the Flagella begun from the end of the mastigote. So, this is what "pro" means here.

Leishmaniasis

Leishmania Parasites and Diseases

There are three 3 main form of Leishmaniasis each caused by a different species :

Disease	Species
Cutaneous leishmaniasis <small>External layer of skin</small>	<i>Leishmania tropica</i> * <i>Leishmania major</i> * <i>Leishmania aethiopica</i> (in ethiopia) <i>Leishmania mexicana</i> (in mexico)
Mucocutaneous leishmaniasis <small>Skin that has mucus (nose,mouth)</small>	<i>Leishmania braziliensis</i> (in brazil)
Visceral leishmaniasis <small>Internal</small>	<i>Leishmania donovani</i> * <i>Leishmania infantum</i> * <i>Leishmania chagasi</i>

Cutaneous leishmaniasis

Dr's Q: What types cause cutaneous leishmania?
Leishmania major & *Leishmania tropica*

causes ulcers on your skin. It's the most common form of leishmaniasis.

Treatment may not always be necessary depending on the person, but it can speed healing and prevent complications.

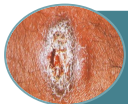
Clinical types of **cutaneous** leishmaniasis known as (Oriental sore)

Leishmania major: (Wet-type-lesion)

Human and Zoonotic cutaneous leishmaniasis (dogs,rodents) :
 wet lesions with **severe** reaction.
More difficult to control

Leishmania tropica: (Dry-type-lesion)

Anthroponotic (human only) cutaneous leishmaniasis:
 Dry lesions with **minimal** ulceration.

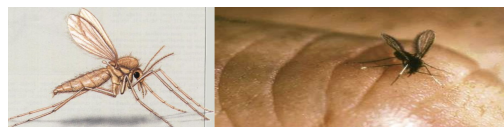


Oriental sore ⁽¹⁾

(most common) is classical self-limited ulcer.

Sand flies

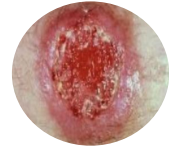
vector of transmission, via the bite of infected blood –sucking



1. this sign is seen in most iraqi people (means they had leishmania before)

Cutaneous Leishmaniasis (The common type)

- This starts as a **painless papule** on exposed parts of the body , at the site of Sand fly bite, generally the **face⁽¹⁾**, which enlarges ,The lesion ulcerates after a few months with an indurated margin (well demarcated/clear edges).
- In some cases the ulcer remains dry and heals readily (**dry-type-lesion**) especially in **L.tropica** .
- In some other cases the ulcer may spread with an inflammatory zone around , these known as (**wet-type-lesion**) which heal slowly **L.major**.

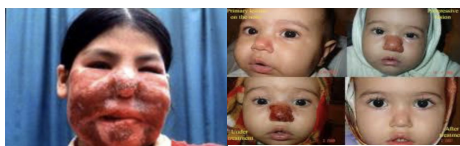


Uncommon types of cutaneous Leishmaniasis

Dr mona:
Not important,
just for your knowledge

Diffuse cutaneous leishmaniasis (DCL):

- Caused by *L. aethiopica*.
- diffuse nodular Non-ulcerating lesions, seen in a part of Africa, people with low immunity to *Leishmania* antigens.
- Diffuse cutaneous (**DCL**) , and consists of nodules and a thickening of the skin, generally without any ulceration , it needs numerous parasite.



Leishmaniasis recidiva (lupoid leishmaniasis):

- Severe immunological reaction to *leishmania* antigen leading to persistent dry skin lesions , few parasites.



1. Most commonly affect the face, but other areas could be affected as well

Leishmaniasis

Mucocutaneous leishmaniasis

Caused by **Leishmania braziliensis** (in brazil)

A rare form of the disease, mucocutaneous leishmaniasis is caused by the cutaneous form of the parasite and can occur several months after skin ulcers heal. With this type of leishmaniasis, the parasites spread to your nose, throat, and mouth. This can lead to partial or complete destruction of the mucous membranes in those areas. Although mucocutaneous leishmaniasis is usually considered a subset of cutaneous leishmaniasis, it's more serious. It doesn't heal on its own and always requires treatment.

The lesion starts as a pustular swelling in the mouth or on the nostrils.

The lesion May become ulcerative after many months and then extend into the nasopharyngeal mucous membrane.

Secondary bacterial infection is very common with destruction of the nasal cartilage and the facial bone



Visceral leishmaniasis (In india called: Kala-azar) Leishmania donovani || Leishmania infantum

There are geographical variations . The disease is called kala-azar. Visceral leishmaniasis is sometimes known as systemic leishmaniasis or kala azar. It usually occurs two to eight months after being bitten by a sand fly. It damages internal organs, such as your spleen and liver. It also affects your bone marrow, as well as your immune system through damage to these organs. The condition is almost always fatal if it's not treated

Leishmania infantum mainly affect children (infantum=infant)

Leishmania donovani mainly affects adults

The incubation period is usually(2-8) (4-10) months

Symptoms are generally : fever , anemia , malaise , hepatomegaly ,weight loss with splenomegaly, leukopenia and sweating Epistaxis ,Cough ,Diarrhoea

The early symptoms are generally low grade fever with malaise and sweating. In later stages, the fever becomes intermittent and their can be liver enlargement or spleen enlargement or Hepatosplenomegaly can be seen because of **the hyperplasia of the lymphoid-macrophage system**

Both are endemic in Saudi Arabia (in jazan and southern regions)

Untreated disease can be fatal After recovery it might produce a condition called post kala-azar dermal leishmaniasis (PKDL) **Not imp**



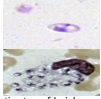
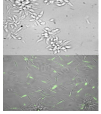


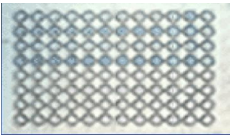

Hepatosplenomegaly in visceral leishmaniasis.

Differential parasitological diagnosis for hepatosplenomegaly is visceral leishmania **AND** schistosoma mansoni



PKDL

Diagnosis and Treatment

Cutaneous & Mucocutaneous Leishmaniasis	<p>Diagnosis</p> <p>Diagnostic stage: ★Amastigotes★</p>	<ul style="list-style-type: none"> - The parasite can be isolated from the margin of the ulcer. - A diagnostic skin test, known as Leishmanin test (Montenegro test), is useful - Smear: Giemsa stain - microscopy for LD bodies (Leishman-Donovan bodies, amastigotes) in tissue macrophages - Skin Biopsy : <ol style="list-style-type: none"> 1. Microscopy in Giemsa stain show LD bodies ⁽¹⁾ (amastigote) in macrophages 2. Culture in NNN ⁽²⁾ medium for promastigotes. Dr: بليز احفظوه 	 <p>Amastigotes of Leishmania</p>  <p>Promastigotes of Leishmania</p>
	<p>Treatment</p> <p>Dr mona: We will NOT ask u about it</p>	<p>No treatment- self-healing lesions</p> <p>Medical:</p> <ul style="list-style-type: none"> - Pentavalent antimony (Pentostam), Amphotericin B - Antifungal drugs - +/- Antibiotics for secondary bacterial infection. <p>Surgical:</p> <ul style="list-style-type: none"> - Cryosurgery - Excision - Curettage <p>Antiparasitic drugs, such as amphotericin B (Ambisome), treat this condition. Your doctor may recommend other treatments based on the type of leishmaniasis you have.</p> <p>Cutaneous Leishmaniasis: cutaneous ulcers often heal without treatment. However, treatment can speed healing, reduce scarring, and decrease risk of further disease. Any skin ulcers that cause disfigurement may require plastic surgery</p> <p>Mucocutaneous Leishmaniasis: These lesions don't heal naturally. They always require treatment. Liposomal amphotericin B and paromomycin can treat this.</p>	
Visceral Leishmaniasis	<p>Diagnosis</p>	<p>1) Parasitological diagnosis</p> <p>Bone marrow aspirate (GOLD STANDARD), splenic aspirate, lymph node, tissue biopsy using:</p> <ol style="list-style-type: none"> 1- Microscopy in Giemsa stain (LD bodies) (amastigotes) 2- Culture in NNN medium (promastigotes). 	 <p>Bone marrow amastigotes</p>  <p>Bone marrow aspiration</p>
		<p>2) Immunological diagnosis</p> <ul style="list-style-type: none"> - Specific serologic tests: Direct Agglutination Test (DAT), ELISA, IFAT - Skin test (leishmanin test) for survey of populations and follow-up after treatment. 	
	<p>DAT test</p> 	<p>ELISA test</p> 	
<p>Treatment</p> <p>Dr mona: We will NOT ask u about it</p>	<p>Visceral disease always requires treatment. Several medications are available. Commonly used medicines include :</p> <p>Recommended treatment varies in different endemic areas:</p> <ul style="list-style-type: none"> - Pentavalent antimony - sodium stibogluconate (Pentostam) - Amphotericin B - Paromomycin - Miltefosin (Impavido) 		
<p>Side effect the treatment</p>	<p>Anemia, Bleeding, Infections, etc.</p>		

1. macrophages with many amastigotes inside
2. This media mimics the appearance of a sand fly with amastigotes inside converting it to promastigote.



Dr's Q for OSPE

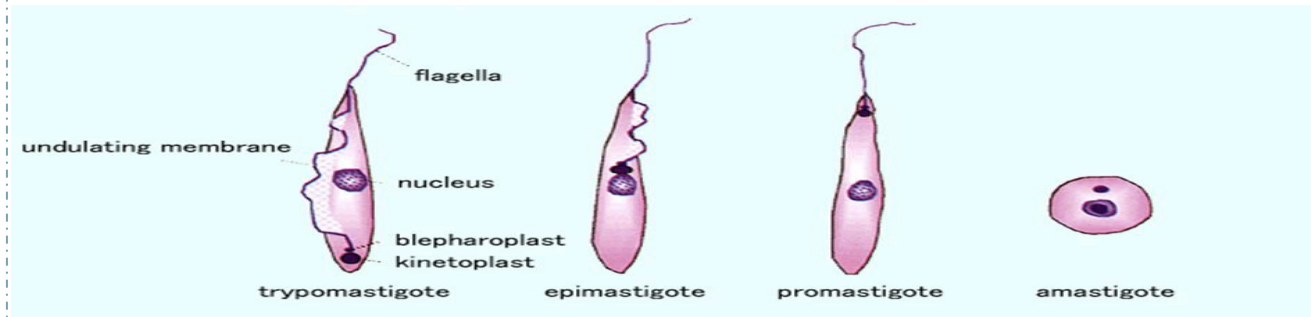
A patient living in Al Kharj (or Baghdad) with ulcer in his face. Microscopy for skin biopsy is shown in the pic (pic: macrophage with many amastigotes inside = LD bodies)

Diagnosis? Diagnostic stage? Etc..

Trypanosomiasis

Introduction

There are 4 stages of hemoflagellates ⁽¹⁾
Trypomastigote, Epimastigote, Promastigote and **Amastigote** ⁽²⁾



There are two types of trypanosomiasis that affect humans
 They are divided based on their geographical location:


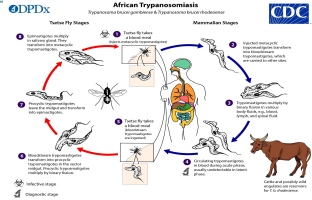




African trypanosomiasis

- Known as **African sleeping sickness**.
- Caused by **Trypanosoma brucei** parasites in **Africa**
- Transmitted by the **tsetse fly (intermediate host)**.
- Trypanosoma brucei **rhodesiense**: East Africa, wild and domestic animal reservoirs
- Trypanosoma brucei **gambiense**: West and Central Africa, mainly human infection
- Development of the disease is more rapid in Trypanosoma brucei rhodesiense

American trypanosomiasis

- Known as **Chagas disease**
- Chagas disease in Central and South America
- Is a tropical parasitic disease caused by **Trypanosoma cruzi** parasites in **Latin America**
- transmitted by the **'kissing' bugs** (bug NOT fly)
- The human disease occurs in two stages : acute and chronic stages

1. Notice the differences in the length of the flagella in each one.
 2. Note that amastigote has no tail or extension to the outside.

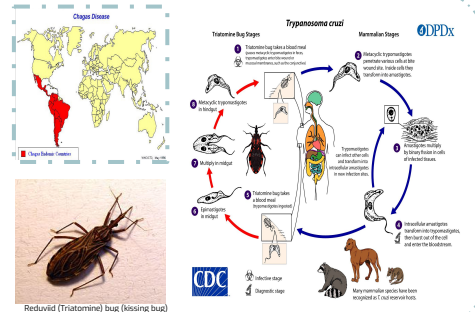
African sleeping sickness	
definition	<ul style="list-style-type: none"> A parasitic disease transmitted by the tsetse fly. It gets its nickname 'sleeping sickness' because symptoms can include a disturbed sleep pattern.
Pathogen	<ul style="list-style-type: none"> T. gambiense causes a chronic illness. T. rhodesiense causes a more acute illness.
Host & Reservoir	<ul style="list-style-type: none"> Infection occurs through the bite of infected tsetse flies (intermediate host), vector of the trypanosoma Humans, domestic cattle and wild animals are the main reservoir host for Trypanosoma (definitive host).  <p>Tsetse fly intermediate host</p>
Transmission	<ul style="list-style-type: none"> Has 3 ways of transmission <ol style="list-style-type: none"> from human to human through the bite of the tsetse fly which is only found in rural parts of Africa. (mainly) from mother to child through placenta in the blood and infect the baby while it is still in the womb (vertical transmission) Contaminated needles (very rare)
life cycle	<ul style="list-style-type: none"> Trypanosome parasite is first introduced into the mammalian host as trypomastigotes when a tsetse fly takes a blood meal and secretes parasite-filled saliva into the host's skin. Once in the bloodstream the trypomastigotes multiply in the blood, lymph or spinal fluid. To the Brain. 
Diagnosis	<ul style="list-style-type: none"> Diagnosis relies on recognition of the trypomastigote in peripheral blood & CSF, during fever, sternal bone marrow, lymph node aspirates and CSF. Motile organisms may be visible in the buffy coat (between plasma & blood cells) Serological testing is also common as IF and ELISA.  <p>Trypomastigotes in the blood stream</p>
Treatment Dr mona: We will NOT ask u about it	<ul style="list-style-type: none"> For early infection Pentamidine & Suramin. for late infection Eflornithine (Difluoromethylornithine-DFMO)
Pathology and clinical picture, Has 3 stages:	
Skin stage	<p>A primary reaction occurs at the site of inoculation of trypomastigotes, chancres (التهاب صغير نفس اللي يجي بعد التطعيم) which resolve in 2-3 weeks.</p>  <p>Chancre skin stage</p>
Systemic Haemato-lymphatic stage	<p>intermittent fever, headache & generalized lymphadenopathy mainly in the cervical & sub-occipital region ('Winterbottom' sign)⁽¹⁾ anemia</p>  <p>Winterbottom's stage</p>
(CNS) stage	<p>This stage begins when the trypanosome parasites cross from the blood- brain barrier into the spinal fluid, infecting the CNS including the brain, result in change in behavior, confusion, poor coordination difficulties with speech and disturbance of sleep (sleeping during day and insomnia at night.) & (Meningoencephalitis) In typical case, there is daytime sleeping, psychological changes, tremors, convulsions and finally coma. Without treatment, the disease is invariably fatal.</p>  <p>CSF lumbar puncture for diagnosis</p>

1. When Americans took Africans in the boats As slaves they dump every person into the ocean if he has the "Winterbottom' sign" because they are infected.

Life cycle

Dr Mona: when you see **BUG** in the mcqs, remember American trypanosoma as it is the only bug-transmitted disease that we studied so far.

- **C-shape Trypomastigotes**
- **Trypomastigotes in blood**
- **Amastigotes in the muscle (tissue)**
- **Infective & Diagnostic stages: Trypomastigotes**



Pathogenesis

The parasites produce focal lymphangitis and oedema at the site of parasites entry (**chagoma**)

After that parasites (trypomastigote) enter the blood stream and find their way, mainly on the **face near the eyelids**, it produces a swelling of the eye and temporal region with conjunctivitis (**Romana's sign**)

And also find their way mainly the **cardiac muscles** cells. The most constant feature of the cardiac disease is **cardiomyopathy**, in severe cases can lead to partial or complete heart block which may lead to cardiac failure.

NOTE: Parasite when free in blood stream in form (**trypomastigote**), but in the cardiac tissue it become in form of (**Amastigote**)⁽¹⁾ at autopsy.

Symptoms

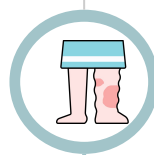
In the early stage, symptoms are typically either not present or mild, and may include



Fever



Swollen lymph nodes



local swelling at the site of the bite (**chagoma**)



Headache

1. (without any flagella) it can only be seen in heart tissue after death autopsy, so it is not considered to be diagnostic

Presentation & Complications

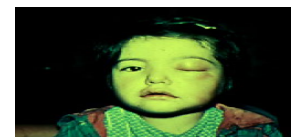
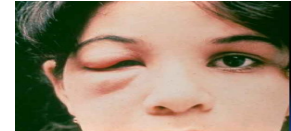
Presentation

T. cruzi causes cutaneous stage (chagoma)



Ocular lesion (Romana' sign)

The most recognized marker of acute Chagas disease is called Romaña's sign, which includes swelling of the eyelids on the side of the face near the bite wound or where the bug feces were deposited or accidentally rubbed into the eye.



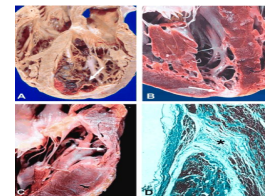
Complications

T. cruzi causes a chronic illness with progressive myocardial damage leading to cardiac arrhythmias and cardiac dilatation, and gastrointestinal involvement leading to mega-oesophagus and **megacolon**.

T. cruzi causes acute illness in children, which is followed by chronic manifestations later in life. intracellular **amastigotes** destroy the intramural neurons of the **autonomic nervous system** in the intestine and heart, leading to megaintestine and heart **aneurysms**. If left untreated, Chagas disease can be fatal, in most cases due to heart muscle damage.

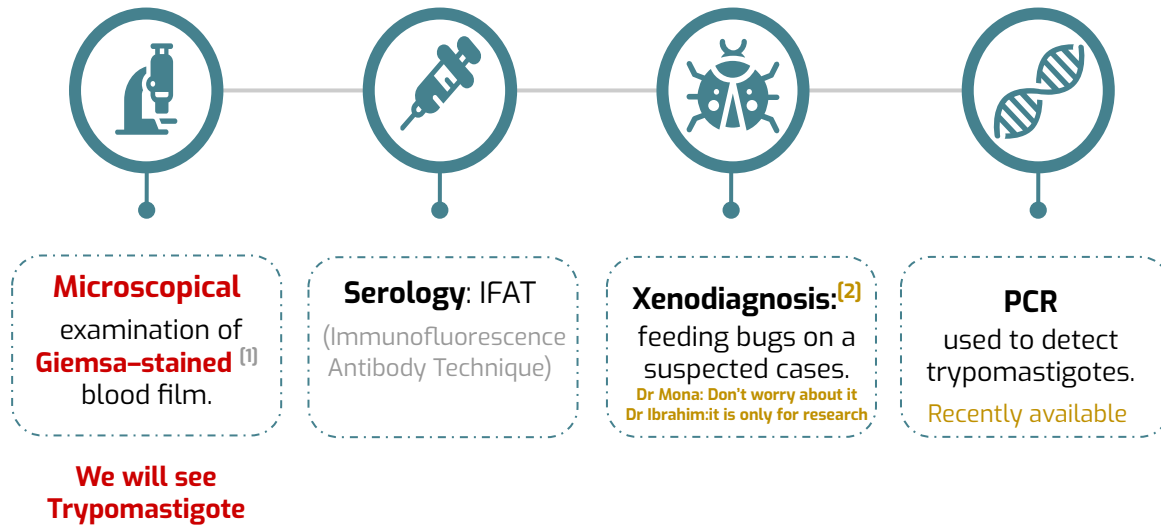
Heart damage due to American trypanosomiasis

About two-thirds of people with chronic symptoms have cardiac damage, including **dilated cardiomyopathy**, which causes heart rhythm abnormalities and may result in sudden death.



American trypanosomiasis

Diagnosis



Treatment of trypanosomiasis

Dr Mona: treatment is not important



American trypanosomiasis (Chaga's disease)

- Benznidazole
- NITROFURAZONE .



1. Giemsa stain is a classic blood film stain for peripheral blood smears and bone marrow specimens.
2. Experimental method: they bring clean bugs (not infected), and they let it bite the trypanosoma suspected person. later on, they examine the bug's stomach looking for trypomastigote.

Leishmaniasis:-

- **Cutaneous leishmaniasis:**
 - Sandfly takes a blood meal from someone and introduces the promastigotes.
 - The promastigotes will be phagocytosed by macrophage.
 - Inside the macrophage, promastigotes will develop into amastigote.
 - When macrophage is full of amastigotes, it will burst/be lysed and amastigotes will be released.
 - The released amastigotes will go infect other macrophages.
- **Diagnosis of cutaneous leishmaniasis (skin biopsy from margin of the ulcer)**
 - **Microscopy** in Giemsa stain shows LD bodies (amastigote inside macrophages)
 - **Culture** in NNN medium for promastigotes.
- **Visceral leishmaniasis:**
 - Sandfly takes a blood meal from someone and introduces the promastigotes.
 - The promastigotes will be then be phagocytosed by macrophage.
 - However, unlike cutaneous leishmania, visceral leishmania parasites do not stay in macrophages.
 - Instead, they circulate in the system and finally go to the liver/spleen/lymph nodes.
 - Manifestation of visceral leishmaniasis include anemia, fever, and hepatosplenomegaly.
 - Differential parasitological diagnosis for hepatosplenomegaly is visceral leishmania AND schistosoma mansoni.
- **Diagnosis of visceral leishmaniasis (Gold: Bone marrow aspirate)**
 - **Parasitological diagnosis:** (same as cutaneous)
 - Microscopy in Giemsa stain shows (amastigote)
 - Culture in NNN medium for promastigotes.
 - **Immunological diagnosis:**
 - Serological tests
 - Skin test (leishmanin test)
- **Dr's Qs:**
 - What is the vector of leishmania? Sandfly
 - What is the infective stage of leishmania? Promastigotes
 - What is the diagnostic stage of leishmania? Amastigotes
 - What types cause cutaneous leishmania? Leishmania major (wet-type-lesion) & Leishmania tropica(dry-type-lesion)

Trypanosomiasis:-

- Both African and American trypanosomiasis are caused by the same parasite (but the two diseases are totally different depending on the geographical area).
- **African trypanosomiasis:**
 - Mainly transmitted by the bite of **tsetse fly**, and it may also be transmitted by vertical transmission (pregnant women to baby through placenta).
 - The intermediate host and vector of African trypanosoma is tsetse fly.
 - When tsetse fly bites someone, it absorbs blood. In the same time, it injects saliva into the blood introducing trypomastigotes to the human.
 - This trypomastigotes will multiply in the bloodstream and finally go to the brain (favorite site).
- There are **three** stages of **African trypanosoma's pathology (African sleeping sickness):**
 - First (skin), there will be a **chancre** on the site of inoculation of trypomastigotes.
 - Second (**systemic**), there will be fever, general symptoms, and **winterbottom' sign** will develop.
 - Lastly (CNS), when the trypanosome reaches the CSF, it will cause **CNS manifestations** and **disrupted sleep patterns** (it can lead to death if it was left untreated).
 - When the infection reaches the third stage when CNS manifestations start to show, lumbar puncture has to be done.
- There are **three** stages of **American trypanosoma's pathology (Chagas disease):**
 - First, when **Triatomine bug (kissing bug)** takes a blood meal from someone, it passes some feces that will penetrate the cells and cause **Chagoma** (local lymphangitis & odema).
 - Second, it will enter bloodstream and go to its favorite site (**eyelids**) causing **Romana's sign** to appear.
 - Lastly, it will go to systemic circulation and find its way to cardiac muscle (it can cause **cardiomyopathy**, complete heart block, and it can also affect the colon).
 - When the parasite is in the blood, it will be in the form of Trypomastigote (diagnostic). However, by the time it reaches the heart tissue it becomes Amastigote (Not diagnostic)..
 - Since the Amastigote form can only be seen in the heart tissue itself, it can only be used it for confirmation after death (autopsy) but not for diagnosis when the patient is alive.
- Diagnosis of Trypanosomiasis is mainly done by microscopical examination of blood using Giemsa-stain. In the smear, we will see Trypomastigote (diagnostic).

Leishmaniasis:-

- When the sandfly firstly encounter someone with leishmaniasis (first source of infection), it will either take the parasite as Amastigote, or it will take the whole macrophage filled with Amastigotes inside. Later on, the Amastigote will grow to be promastigote and infect other people.
- **Dr's Qs:**
 - Leishmaniasis donovani causes? Visceral leishmaniasis/Kala azar.
 - If a smear was taken from human the expected stage will be? Amastigote.

Trypanosomiasis:-

- The African Trypomastigote is "S" shaped parasite, and it is not found inside the RBC's. (can be found between the cells in the blood).
- The American Trypomastigote is "C" shaped parasite.

Quiz

MCQ

Q1: Leishmaniasis is transmitted by the bite of:

- A- Anopheles
- B- Sandfly
- C- Kissing bug
- D- Tsetse fly

Q2: oriental sore is a clinical presentation to which one of the following?

- A- Cutaneous Leishmaniasis
- B- Mucocutaneous leishmaniasis
- C-Visceral leishmaniasi
- D- None of the above

Q3: the treatment of cutaneous & muco-cutaneous leishmaniasis can be :

- A- self limiting
- B- With medication
- C- Surgical
- D- All of them

Q4: which of the following could cause dilated cardiomyopathy?

- A- african sleeping sickness
- B- visceral leishmaniasis
- C- chaga's disease
- D- cutaneous leishmaniasis

Q5: African Trypanosomiasis is caused by a microscopic parasites of the species called :

- A- Trypanosoma glossina
- B- Trypanosoma Brucei
- C- Trypanosoma cruzi
- D- Trypanosoma plasmodia.

Q6: A 16-year-old boy was brought to a district hospital by his parents complaining of fever, dizziness, sleeping mainly during the day, and constipation The blood film demonstrated the presence of trypanosomes but no malaria parasites. What's the most likely diagnosis in this case ?

- A- American trypanosomiasis
- B- African trypanosomiasis
- C- Leishmaniasis
- D- Malaria

Answers: Q1:B | Q2:A | Q3:D | Q4:C | Q5:|B Q6:B

SAQ

CASE:A 64 year old American businessman presented to the clinic with fever, headache with a swelling in his neck. Upon taking history, he mentioned that he went to africa a month ago for a business trip, he also said that he had a painless purple nodule in his left forearm for a couple of weeks. He also said that the that his fever come and goes. His CBC showed anemia.

Q1: What is the most likely diagnosis?

A:African trypanosomiasis

Q2: What is the most likely causative agent?

A: T. Brucei

Q3: How is this disease transmitted?

A: By Tsetse fly

Q4: The swelling on his neck s also known as?

A:Winterbottom's sign

Q5: what is the next expected complication if he wasn't treated?

CNS involvement that will result in change in behaviour, confusion, poor coordination, difficulties with speech and sleep disturbances

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