Leishmaniasis

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Introduction

Classifications of Parasites		
Class	**Protozoa**	**Helminths**
Features	○ Unicellular ○ Single cell for all functions No sexual stage, replicate by binary fission	○ Multicellular ○ Specialized cells - They are like human, have systems: Respiratory, Reproductive. - As long as there is reproductive system so there will be sexual stage in their life cycle
Types	**1. Amoebae:** move by pseudopodia **2. Flagellates:** move by flagella - Intestinal flagella e,g Giardia & Entamoeba histolytica - Blood hemoflagellate e,g Trypanosoma - Tissue & visceral flagella e,g leishmania. **3. Ciliates:** move by cilia **4. Apicomplexa** (Sporozoa) tissue parasites	**1. Roundworms (Nematodes):** - Elongated, cylindrical, unsegmented **2. Flat worms** - **Trematodes:** leaf-like, unsegmented - **Cestodes:** tape-like,segmented ○ Mnemonic: trematodes = tree = leaf like Cestodes = cm = tape

Leishmaniasis

Leishmania is a genus of trypanosomatid protozoa, which causes vector-borne parasitic disease called leishmaniasis

It is spread by the bite of Sand flies of the genus Phlebotomus in the Old World, and of genus Lutzomyia in the New World

Leishmaniasis is the second-largest parasite killer in the world (after malaria) and is endemic in many parts of Africa, Asia and South America

Life Cycle of Leishmania

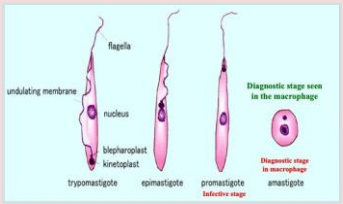
Leishmaniasis is transmitted by the bite of infected female sandflies (vector) ★★ -blood sucking-

→

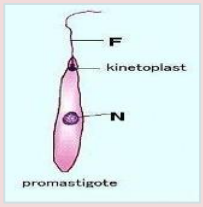
The sandflies inject the **infective stage (promastigotes)** ★ ,then the macrophages will engulf them and transfer them to ★ **amastigotes (the diagnostic stage)** within macrophages (1)

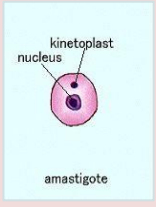
→

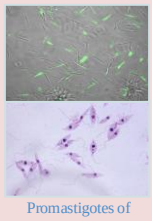
Leishmania parasite survive within the macrophages (amastigote stage) in the human body as intracellular parasites, cell mediated immunity determines the host response to infection & clinical manifestations of the disease.



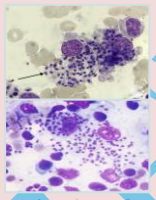
Different stages of Hemoflagellates



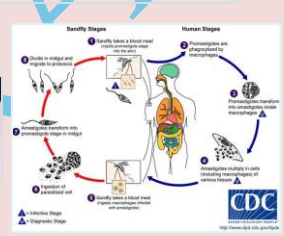




Promastigotes of Leishmania



Amastigotes of Leishmania



Leishmania Parasites & Diseases

◎ 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.

Disease	Species
Cutaneous leishmaniasis (**Oriental sore**)***	○ **Leishmania tropica*** ○ Leishmania aethiopica ★ ★ **Leishmania major*** (more in SA) ○ Leishmania Mexicana
Mucocutaneous leishmaniasis In the mouth & nose	◊ Leishmania Braziliensis in Brazil
Visceral leishmaniasis (**Kala azar**)***	◊ Leishmania donovani* ◊ Leishmania infantum* Found in SA ◊ Leishmania Chagasi

Treatment of leishmaniasis

Antiparasitic drugs, such as amphotericin B (Ambisome), treat this condition.
Your doctor may recommend other treatments based on the type of leishmaniasis you have.

Leishmania Parasites & Diseases

Disease	Cutaneous leishmaniasis	Mucocutaneous leishmaniasis
Overview	Cutaneous leishmaniasis 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.	A rare form of the disease, 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 & 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 & always requires treatment.
Clinical Types	★ *known as Oriental sore* classical self limited ulcer ◦ **Leishmania major:** *human* & Zoonotic cutaneous leishmaniasis (dogs, rodents): wet lesions with severe reaction. ★ Commonest in SA & more dangerous because it's spread by both human & animal so harder in prevention★ ◦ **Leishmania tropica:** Anthroponotic (human only) cutaneous leishmaniasis: Dry lesions with minimal ulceration.	L. Brasiliense's (In Brazil more not here)
Clinical presentation (3)	◦ This starts as a painless papule on exposed parts of the body (at the site of Sand fly bite), generally the face which enlarges. The lesion ulcerates after a few months producing an ulcer with an indurated margin. ◦ In some cases (**L.tropica**): the ulcer remains dry and heals readily **(dry-type-lesion)** ◦ In some other cases (**L.major**): the ulcer may spread with an inflammatory zone around , these known as **(wet-type-lesion) which heal slowly.**	◦ 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.
Diagnosis	◦ **The parasite can be isolated from the *edge (margin) of the *oriental sore ★ (ulcer)** ◦ Skin test: a diagnostic methods, known as Leishmanin test (Montenego Test) is useful. ★ Smear: gold standard Giemsa stain-microscopy for LD bodies (**Leishman-Donovan bodies**, amastigotes) in the ★ macrophages. ◦ Skin biopsy: microscopy for LD bodies or culture in NNN medium for finding promastigotes	 NNN medium
Treatment	◦ No treatment self-healing lesions ◦ Medical: Pentavalent antimony (Pentostam), Amphotericin B, Antifungal drugs, +/- Antibiotics for secondary bacterial infection. ◦ Surgical: Cryosurgery, Excision, Curettage	
	Cutaneous ulcers will often heal without treatment. However, treatment can speed healing, reduce scarring & ↓risk of further disease. Any skin ulcers that cause disfigurement may require plastic surgery.	These lesions don't heal naturally. They always require treatment. Liposomal amphotericin B and paromomycin can treat mucocutaneous leishmaniasis.

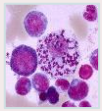



Pictures	  	  

Uncommon Types of Cutaneous leishmaniasis

Leishmaniasis recidiva (lupoid leishmaniasis)	Severe immunological reaction to leishmania antigen leading to persistent dry skin lesions, few parasites. 
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 ulcération, it needs numerous parasite. 

Visceral leishmaniasis (★Kala-azar)

Overview	Visceral leishmaniasis is sometimes known as systemic leishmaniasis or kala azar. It usually occurs 2-8 months after being bitten by a sand fly. It damages internal organs, such as your spleen & 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.
★ Clinical Types★	○ There are geographical variations. ○ **Leishmania infantum** mainly affect children ○ **Leishmania Donovani** mainly affects adults ○ Both are endemic in Saudi Arabia (important in Saudi Arabia and Middle East) ○ The incubation period is usually 2-8 / 4-10 months.
Symptoms 	○ Low grade fever, malaise, and sweating (early symptoms) ○ Splenomegaly, hepatomegaly, ★ hepatosplenomegaly ○ Weight loss ○ Anaemia ○ Epistaxis ○ Cough ○ Diarrhoea ○ Leucopenia ◎ In later stages, the fever becomes intermittent and they can have liver enlargement or spleen enlargement or Hepatosplenomegaly can be seen because of the hyperplasia of the lymphoid-macrophage system.  Fever 2 times a day due to kala-azar
Complication	Untreated disease can be fatal, after recovery it might produce a condition called post kala-azar dermal leishmaniasis (PKDL) 
★ Diagnosis★ (4)  ELISA test  DAT test  	**1. Parasitological diagnosis:** The specimen: ‣ ★ **Bone marrow aspirate** ‣ Splenic aspirate ‣ Lymph node ‣ Tissue biopsy The tests: ○ Microscopy (amastigotes) ○ Culture in NNN medium (Promastigotes) **2. Immunological Diagnosis:** ○ **Specific serologic tests: Direct Agglutination Test (DAT), ELISA, IFAT** ○ Skin test (leishmanin test): for survey of populations and follow-up after treatment

Treatment	◦ Recommended treatment varies in different endemic areas ◦ Visceral disease always requires treatment. Several medications are available. Commonly used medicines include Pentavalent antimony-sodium stibogluconate (Pentostam), amphotericin B, paromomycin, and miltefosine (Impavido). ◦ Side effect of the treatment : Anemia , Bleeding , Infections etc.

1. Found in kharaj, jazan & iraq and they came with ulcer in exposed area like hand & face

2. If there is ulcer in right hand, does this ulcer transmitted and infect other hand? NO cause it's amastigotes (non infectious)

3. ◎ The tests that used in the diagnosis of all the 3 types of leishmania are the SAME, the different is in the **site** of taking the sample
   - In cutaneous & mucocutaneous: from the edge of the ulcer
   - In visceral leishmaniasis from the bone marrow commonly

   ◎ imagine that NNN medium is the same as sandfly, so if biopsy was taken to culture in NNN medium, we will see promastigotes (normal life cycle of sandfly is to convert to promastigotes)

Summary

<table>
<tr><th colspan="5">Leishmania</th></tr>
<tr><td>Life cycle</td><td colspan="4">◦ Vector: Infected Female Sandflies
◦ Transmision: by the bite of infected female sandflies
◦ Infective stage: promastigotes
◦ Diagnostic stage: amastigotes within macrophage
◦ Life cycle story: infected female sandflies bites a person → inject promastigotes → macrophages engulf them → transfer them to amastigotes → survive in macrophages as intracellular parasites</td></tr>
<tr><td>Disease</td><td colspan="2">Cutaneous leishmaniasis (Oriental sore)</td><td>Mucocutaneous leishmaniasis</td><td>Visceral leishmaniasis (Kala azar)</td></tr>
<tr><td>Species</td><td>Leishmania major</td><td>Leishmania tropica</td><td>Leishmania Braziliensis</td><td>○ Leishmania donovani
○ Leishmania infantum</td></tr>
<tr><td>Overview</td><td>◦ Human & Zoonotic transmission (harder in prevention)
◦ Commonest in SA & more dangerous</td><td>Anthroponotic (human only)</td><td>-</td><td>◦ Leishmania infantum mainly affect children
◦ Leishmania Donovani mainly affects adults</td></tr>
<tr><td>Clinical presentation</td><td>◦ cause ulcer which is wet-type-lesion with severe reaction
◦ Heal slowly</td><td>◦ cause ulcer which is dry-type-lesion with minimal ulceration
◦ Heal readily</td><td>May cause destruction of nasal cartilage & facial bone</td><td>◦ fever, malaise, and sweating
◦ Splenomegaly, hepatomegaly, hepatosplenomegaly
◦ Weight loss & Anaemia</td></tr>
<tr><td>Diagnosis</td><td colspan="3">◦ The parasite can be isolated from the edge of the oriental sore
◦ Culture in NNN medium for finding promastigotes
◦ Gold standard Giemsa stain-microscopy for LD bodies (Leishman-Donovan bodies, amastigotes) in the macrophages.
◦ Skin test: leishmanin test (Montenego Test)</td><td>1. Parasitological diagnosis:
The specimen:
1. Bone marrow aspirate
2. Splenic aspirate
3. Lymph node
4. Tissue biopsy
The tests:
1. Microscopy (amastigotes)
2. Culture in NNN medium (Promastigotes)
2. Immunological Diagnosis:
1. Specific serologic tests: DAT, ELISA, IFAT
2. Skin test: leishmanin test (Montenego Test)</td></tr>
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1

Q: What is the symptom of visceral leishmaniasis?

A:

- fever, malaise, and sweating
- Splenomegaly, hepatomegaly, hepatosplenomegaly
- Weight loss
- Anaemia

2

Q: How to diagnose visceral leishmaniasis?

A:

1. Parasitological diagnosis:

- Microscopy for Bone marrow aspirate to look for macrophage containing amastigotes
- Culture in NNN medium to see promastigotes

2. Immunological Diagnosis:

- Serology (e.g. ELISA)