Microbiology
437

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MED437
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LEISHMANIASIS

PARASITIC INFECTION OF GIT

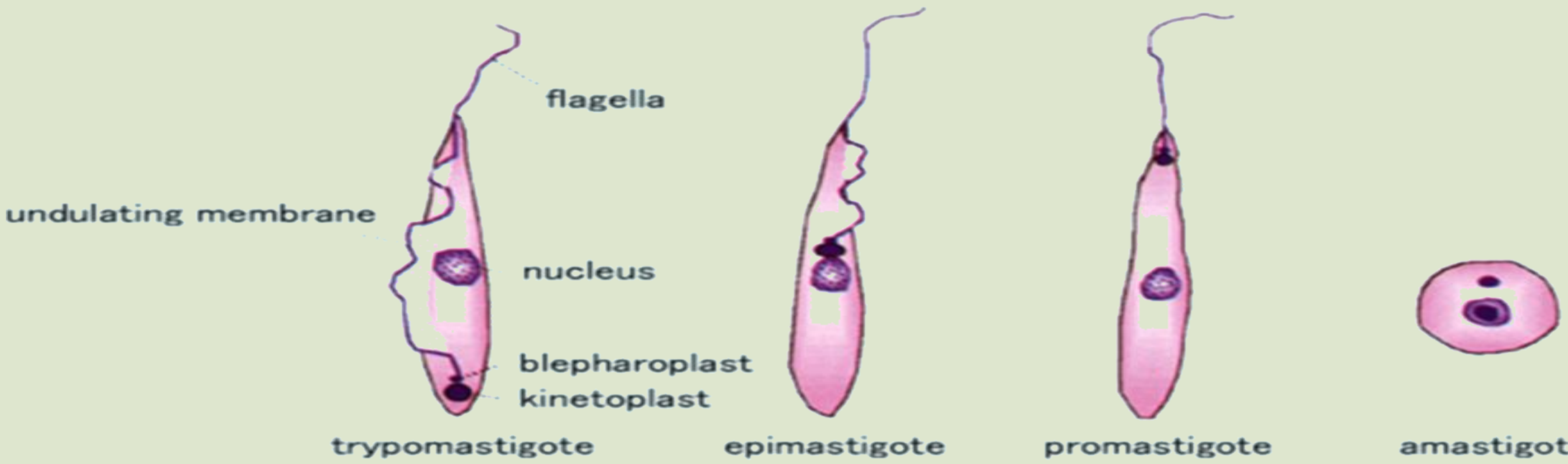
Leishmaniasis

- Leishmaniasis is a disease caused by parasites name Leishmania, it is spread by the bite of certain type of sandflies.
- The disease can present in three main ways :
  1. Cutaneous
  2. Mucocutaneous
  3. Visceral (Kala-azar) most serious form of the disease can be fatal if not treated.

Leishmania Parasites and Diseases

Species	Disease
Leishmania tropica (endemic in SA) Leishmania major (endemic in SA) Leishmania aethiopica Leishmania mexicana	Cutaneous leishmaniasis
Leishmania braziliensis	Mucocutaneous leishmaniasis
Leishmania donovani (endemic in SA) Leishmania infantum (endemic in SA) Leishmania chagasi	Visceral leishmaniasis

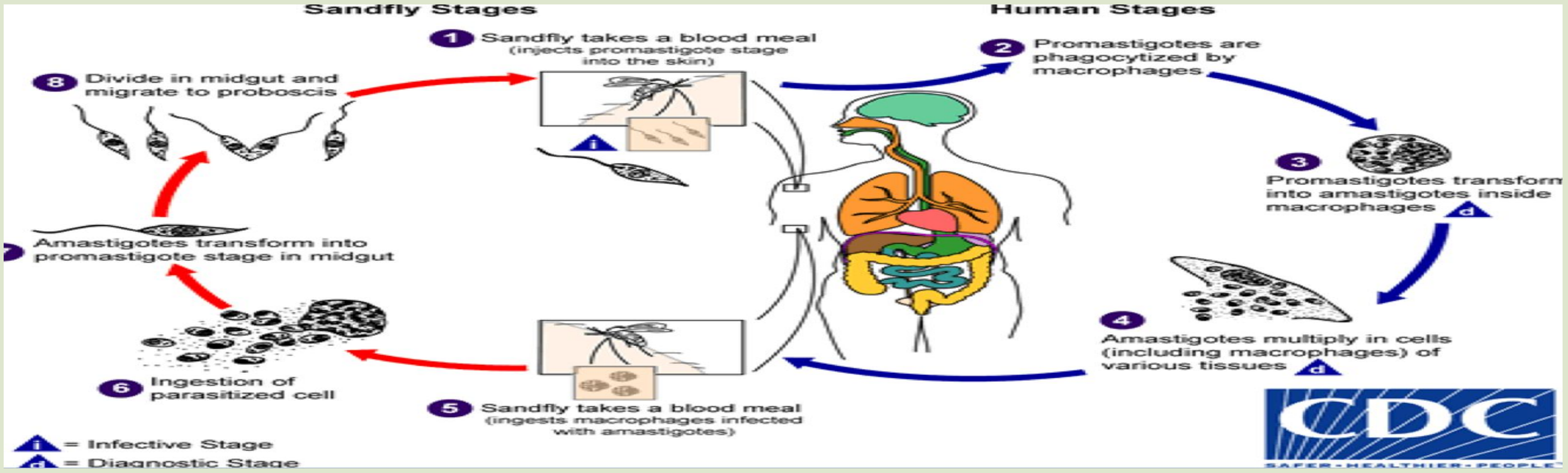
Different stages of Hemoflagellates



1. Trypomastigote is when the flagella extend from the beginning till the end of the parasite
2. Epimastigote is when the flagella extend from the middle till the end of the parasite
3. Promastigote is when the flagella extend from the end of the parasite
4. Amastigote is found in the tissue




The Life Cycle of Leishmania



Common Types of Cutaneous Leishmaniasis

Leishmania major	Leishmania tropica
Zoonotic cutaneous leishmaniasis: wet lesions with severe reaction 	(human to human) cutaneous leishmaniasis: Dry lesions with minimal ulceration • Oriental sore (most common) classical self-limited ulcer 

★ This starts as a painless papule on exposed parts of the body, generally the face.
★ The lesion ulcerates after a few months producing an ulcer with an indurated margin.

1. Dry-type-lesion → In some cases the ulcer remains dry and heals readily (Leishmania Tropica; Oriental sore)
2. Wet-type-lesion → In some other cases the ulcer may spread with an inflammatory zone around. These known to heal slowly (Leishmania major)

Uncommon Types of Cutaneous Leishmaniasis

Diffuse cutaneous leishmaniasis (DCL)	Leishmaniasis recidiva (lupoid leishmaniasis)
- Caused by L. aethiopica(اثيوبيا), diffuse nodular non-ulcerating lesions, seen in a part of Africa, people with low immunity to Leishmania antigens.  - Diffuse cutaneous (DCL), consists of nodules and a thickening of the skin, generally without any ulceration, it needs numerous parasite.	Severe immunological reaction to leishmania antigen leading to persistent dry skin lesion & few parasites. 




Mucocutaneous leishmaniasis

Leishmania braziliensis

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 naso- pharyngeal mucous membrane.
Secondary infection is very common with destruction of the nasal cartilage and the facial bone.

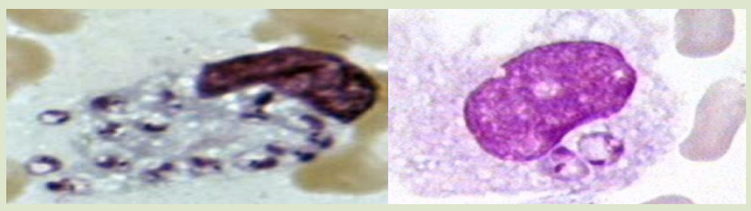
Cutaneous & Mucocutaneous Leishmaniasis

Diagnosis

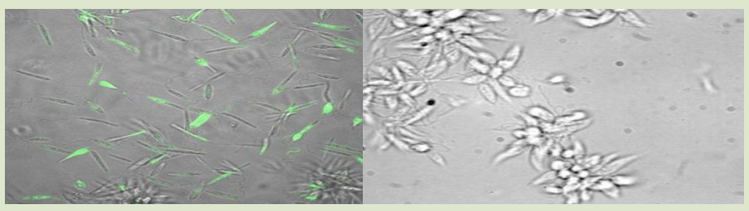
The parasite can be isolated from the margin of the ulcer.

- ★ Smear: Giemsa stain – microscopy for Leishman-Donovan (LD) bodies (amastigotes) in tissue macrophages.
- ★ Biopsy: microscopy for LD bodies or culture in NNN medium for promastigotes. (Noura, Nouf, & Nada medium)
- ★ polymerase chain reaction (PCR) tests are available for the detection of Leishmania DNA

Amastigotes of Leishmania



Promastigotes of Leishmania



Treatment

- ★ No treatment – self-healing lesions
- ★ Medical:
  - ○ Pentavalent antimony (Pentostam)
  - ○ Amphotericin B
  - ○ Antifungal drugs
  - ○ +/- Antibiotics for secondary bacterial infection.
- ★ Surgical:
  - ○ Cryosurgery
  - ○ Excision
  - ○ Curettage

Visceral Leishmaniasis

- ★ It the most serious form, and is potentially fatal if untreated, There are geographical variations.
- ★ The diseases is called kala-azar.

1. Leishmania infantum mainly affects children
2. Leishmania donovani mainly affects adults

- ★ The incubation period is usually 4-10 months.
- ★ The early symptoms are generally low grade fever with malaise and sweating and anemia.
- ★ In later stages, the fever becomes intermittent and then liver enlargement, spleen enlargement or hepatosplenomegaly because of the hyperplasia of the lymphoid–macrophage system and bone marrow.

Clinical Presentation:

- ★ Fever, weight loss & anemia
- ★ Splenomegaly, hepatomegaly & hepatosplenomegaly
- ★ Epistaxis, cough & diarrhoea

Untreated disease can be fatal.
After recovery it might produce a condition called post kala-azar dermal leishmaniasis (PKDL)

Diagnosis

Parasitological Diagnosis

- ★ Bone marrow aspirate, splenic aspirate, lymph node, & liver biopsy using microscopy & culture on NNN medium
- ★ Leishmaniasis is diagnosed in the hematology laboratory by: direct visualization of the amastigotes (Leishman-Donovan bodies).
- ★ Buffy-coat preparations of peripheral blood or aspirates from marrow, spleen, lymph nodes, or skin lesions should be spread on a slide to make a thin smear and stained with Leishman or Giemsa stain.
- ★ Amastigotes are seen within blood macrophage and spleen monocytes or, less commonly, in circulating neutrophils.

Immunological Diagnosis

- ★ Specific serologic tests: Direct Agglutination Test (DAT), ELISA, IFAT
- ★ Skin test (leishmanin test) for survey of populations and follow-up after treatment.
- ★ **Polymerase chain reaction (PCR) tests**
  - ○ Available for the detection of Leishmania DNA

Treatment

Varies in different endemic areas:

- ★ Amphotericin B
- ★ Pentavalent antimony- sodium stibogluconate (Pentostam)

Treatment of Complications

Anemia, bleeding, infection etc.




Doctor's Notes

- Leishmania is a protozoa and its a hemoflagellate (goes to the blood)
- **Life Cycle of Leishmania**
  - After getting a bite from the sandfly → introduce promastigote to the body → macrophages immediately eat it → in the macrophage it turns into amastigotes so it can replicate and protects itself → the amastigote undergo multiple binary fission & rupture the macrophage → then it reaches the blood circulation and become promastigote again → another uninfected sandfly come to bite the same infected person → become infected by ingesting the promastigote from the blood
- **Diagnostic stage:**
  - In serum → promastigote
  - In macrophages or tissue → amastigote
- **Infective stage** → promastigote
- **Vector** → sandfly
- **Diagnosis of cutaneous and mucocutaneous:**
  - First we swap the ulcerated area and we will find amastigotes using Giemsa stain
  - Second we take a biopsy of the tissue containing the macrophages and amastigote (CSF or bone marrow) and culture it in NNN medium where the amastigote where it will become promastigotes (here find promastigote)
- We have 3 types of the disease

1. Cutaneous → go to the skin
   a. Common Types: (these are found in Saudi Arabia)
      i. Leishmania major → zoonotic so its control is hard, severe & wet lesion
      ii. Leishmania tropica → only hyman to human so it could be controlled, dry lesion
         1. Make an ulcer called oriental sore
         2. Most common site is the face bc it's mostly the location of the bite
   b. Uncommon/ Atypical Types: (not in Saudi Arabia but could be found RARE)
      i. Diffuse cutaneous leishmaniasis (DCL) → caused by Leishmania Aethiopica
      ii. Leishmaniasis recidiva (lupoid leishmaniasis)
2. Mucocutaneous → skin and cartilage
   a. Leishmania braziliensis (found in brazil)
3. Visceral (kala-azar) → organs (found in Saudi Arabia)

- very severe bc it it affects liver, spleen, bone marrow, & lymph nodes
  a. Leishmania infantum → mainly kids
  b. Leishmania donovani → mainly adults




Summary

Leishmaniasis						
Transmitted by	Sandflies	**Infective stage**	Promastigotes	**Diagnostic stage**	●Amastigotes: inside macrophages of the tissue or serum ●Promastigotes: in serum	
Cause (Disease)	**Cutaneous leishmaniasis**			**Mucocutaneous leishmaniasis**	**Visceral leishmaniasis**	
Caused by	Leishmania tropica	Leishmania tropica	Leishmania aethiopica	Leishmania braziliensis	Leishmania donovani	Leishmania infantum
	●Zoonotic ● Wet and severe lesions ●Heals slowly	●Human only ●Dry lesions with Oriental sore ●Heals readily	Diffuse cutaneous leishmaniasis: diffuse nodular non-ulcerating lesions	1-lesion starts as a pustular swelling in the mouth or on the nostrils. 2-may become ulcerative 3- extend into the naso- pharyngeal mucous membrane.	●Serious ●The diseases is called **kala-azar** ❖ Early symptoms: fever with malaise, sweating and anemia. ❖ Later stages: intermittent feverand hepatosplenomegally because of the hyperplasia of the lymphoid –macrophage system and bone marrow.	
Complication	-	-	-	-	After recovery it might produce a condition called post kala-azar dermal leishmaniasis	
Diagnosis	❖ parasite can be isolated from the margin of the ulcer: ● Smear: Giemsa stain for LD bodies (amastigotes) in tissue macrophages. ● Biopsy: microscopy for LD bodies or culture in NNN medium for promastigotes. ●PCR				❖ parasite can be isolated from: Bone marrow and Splenic aspirate Lymph node - Liver biopsy. 1-Parasitological: Microscopy - culture in NNN medium 2-Immunological: Direct Agglutination Test (DAT), ELISA, IFAT - Skin test (leishmanin test) ●PCR	
Treatment	Pentavalent antimony (Pentostam) Surgical: Cryosurgery – Excision - Curettage				- Pentavalent antimony- sodium stibogluconate (Pentostam) - Amphotericin B	




MCQs:

1- Which of the following cause oriental sore?
A- Leishmania tropica.
B- Leishmania major.
C- Leishmania donovani.
D- Leishmania aethiopica.

2- If someone has been infected with Leishmania major, what will you see under the microscope?
A- Trypomastigotes.
B- Leishman donovan bodies.
C- Promastigotes.
D- Epimastigote.

3- Which of the following parasites cause destruction of nasal cartilage?
A- Leishmania donovani.
B- Leishmania infantum.
C- Leishmania tropica.
D- Leishmania braziliensis.

4- If you perform a blood test for a patient how have Kala-azar disease, what will you find?
A- Macrophages with promastigotes.
B- Amastigote in the serum.
C- Promastigotes in the serum.
D- LD bodies in the serum.

5-Which of the following pathogen we can use skin test to follow-up with the patient?
A- Leishmania donovani.
B- Leishmania braziliensis.
C- Leishmania tropica.
D- Leishmania major.

6- Which of the following is vector of leishmania?
A- Human.
B- kissing bug.
C- tsetse fly.
D- Sandfly.

SAQ:

1-A 4-C
2-B 5-A
3-D 6-D

- A patient came to the ER with enlarged abdomen, on history he mentioned fever that comes and go. On examination the spleen was palpable. Under the microscope you saw LD bodies.

1-What is your diagnosis?

Kala-azar disease

2- What is the most likely parasite?

Leishmania infantum or Leishmania donovani

2- The specimen is more likely to be taken from?

Bone marrow and Splenic aspirate - Lymph node and Liver biopsy.

3- What further test would you order ?

culture in NNN medium
Direct Agglutination Test (DAT), ELISA, IFAT - Skin test (leishmanin test) - PCR

4- Treatment?

Pentavalent antimony- sodium stibogluconate (Pentostam)
Amphotericin




THANK YOU!

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