Hemoflagellates: Leishmaniasis & Trypanosomiasis

Lecture 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

Color index:

- Important
- Doctors' note
- Extra
- Found in Girls' slides
- Found in Boys' slides

EDITING FILE

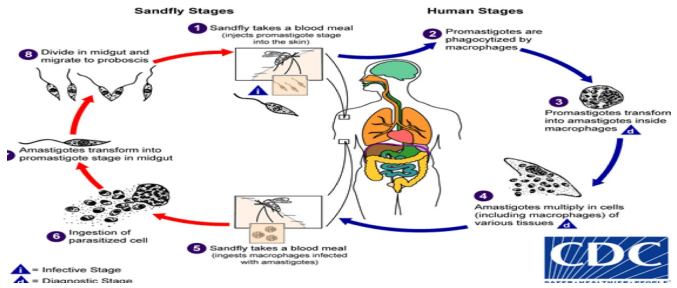
Leishmaniasis

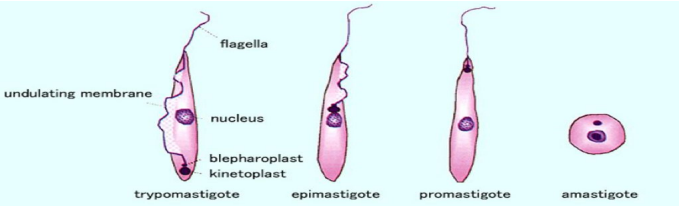
Introduction:

- 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]
- The disease can present in three main ways : **Cutaneous leishmaniasis, Mucocutaneous leishmaniasis and Visceral leishmaniasis**
- 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

- **Infective stage : promastigote**
- **Diagnostic stage : Amastigote[2]**

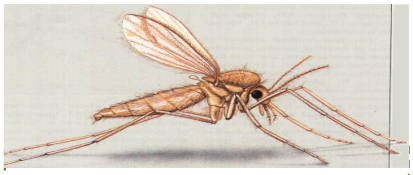




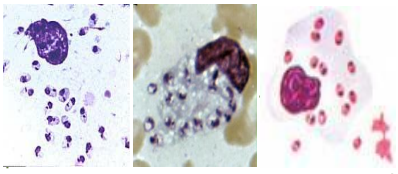
Leishmania species

Cutaneous Leishmaniasis	Mucocutaneous leishmaniasis	Visceral leishmaniasis
Leishmania tropica*	**Leishmania braziliensis**	**Leishmania donovani***
Leishmania major*		**Leishmania infantum***
Leishmania aethiopica		Leishmania chagasi
Leishmania mexicana		

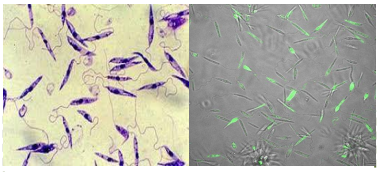
* Endemic in saudi arabia



Sandfly



Amastigotes of leishmania



Promastigotes of leishmania

1- Common in iraq and alkharj too.
2- found inside the macrophages

Leishmaniasis

1. 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.

Common Types of Cutaneous Leishmaniasis

Leishmania Major

- **Zoonotic** cutaneous leishmaniasis
- **Wet type lesions** with severe reaction
- the ulcer may spread with an inflammatory zone around ,which **heal slowly**

Leishmania Tropica

- **Anthroponotic (human to human)** cutaneous leishmaniasis
- **Dry type lesions** with minimal ulceration
- In some cases the ulcer remains dry and **heals readily**

- **Oriental sore (most common) classical self-limited ulcer**[1]
- 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

Uncommon Types of Cutaneous Leishmaniasis (Dr Mona told us to skip it)	
Diffuse cutaneous leishmaniasis (DCL)	**Leishmaniasis recidiva (lupoid leishmaniasis)**
• Caused by L. aethiopica • diffuse nodular non-ulcerating lesions • seen in a part of Africa • people with low immunity to Leishmania antigens • 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 

1- only cosmetic treatment may be needed.

Leishmaniasis

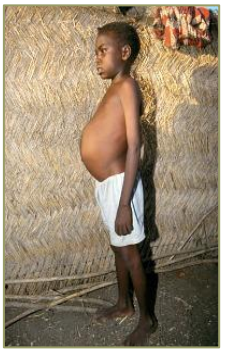
2. Mucocutaneous leishmaniasis

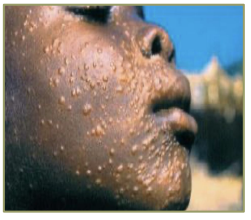
- A rare form of the disease is caused by the cutaneous form of the parasite and can occur several months after skin ulcers heal.
- With this type of leishmaniasis, the parasites spread to your nose, throat, and mouth. This can lead to partial or complete destruction of the mucous membranes in those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

- **starts as a pustular swelling in the mouth or on the nostrils**
- **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**

3. Visceral leishmaniasis

- Is the most serious form, and is potentially fatal if untreated, there are geographical variations.
- The diseases is called **kala-azar**
- **1) Leishmania infantum mainly affect children**
  2) Leishmania donovani mainly affects adult
- The incubation period is usually 4-10 months.
- The early symptoms are generally **low-grade fever, malaise, 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.
- **Untreated diseases can be fatal**
- After recovery it might produce a condition called post kala-azar dermal leishmaniasis (PKDL)



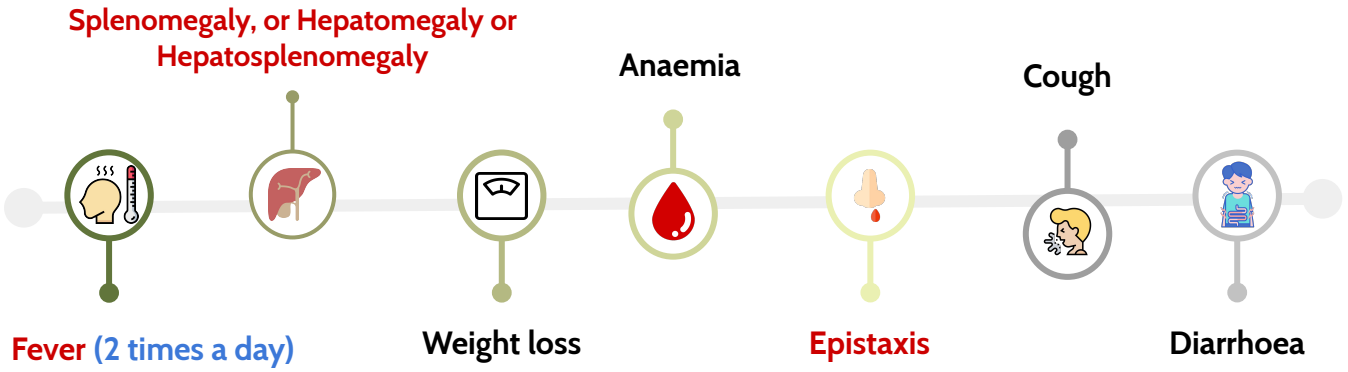


PKDL

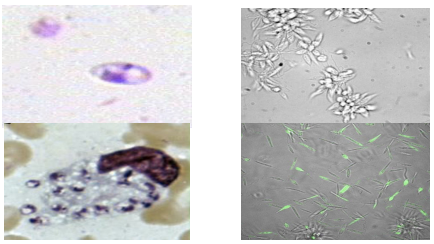
Leishmaniasis

3. Visceral leishmaniasis cont'

- **Clinical Presentation**



Lab diagnosis and treatment

Cutaneous & Mucocutaneous Leishmaniasis	
Diagnosis	**Treatment** (Dr mona told us to skip it)
- The parasite can be isolated from the **margin** of the ulcer. - A diagnostic skin test, known as **Leishmanin test (Montenego test)**, is useful - **Smear: Giemsa stain - microscopy for LD bodies (Leishman-Donovan bodies, amastigotes) in tissue macrophages** - Skin Biopsy: microscopy from **LD bodies** or culture in **NNN medium** for **promastigotes**. - **Polymerase chain reaction (PCR)** tests are available for the detection of Leishmania DNA 	- **No treatment** - self-healing lesions - **Medical:** - **Pentavalent antimony (Pentostam)** - Antifungal drugs - +/- Antibiotics for secondary bacterial infection. - **Surgical:** - Cryosurgery - Excision - Curettage - **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. - **Mucocutaneous Leishmaniasis:** These lesions don't heal naturally. They always require treatment. Liposomal amphotericin B and paramomycin can treat this.

Visceral Leishmaniasis con'

Diagnosis of visceral leishmaniasis	
Parasitological diagnosis	**Immunological diagnosis**
- **Bone marrow aspirate**, splenic aspirate, lymph node, liver biopsy[1] using: 1) microscopy (LD bodies) (amastigotes) 2) culture in NNN medium (promastigotes) - 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 .	- **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 are available for the detection of Leishmania DNA

Treatment (Dr mona told us to skip it)

Visceral disease always requires treatment. Recommended treatment varies in different endemic areas:

- Pentavalent antimony - sodium stibogluconate (Pentostam)
- Amphotericin B
- Paromomycin
- Miltefosin (Impavido)

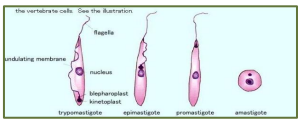
Treatment of Complications (Dr mona told us to skip it)

Anemia, Bleeding, Infections, etc.

1- bone marrow aspirate is the most common and number #1 in diagnosing visceral leishmaniasis, so if they asked you a question about the diagnosis and the answers were : bone marrow aspirate , splenic aspirate, lymph nodes, liver biopsy choose **bone marrow aspirate**

Trypanosomiasis

Introduction



- There are 4 stages of hemaflagellates : **Trypomastigote,** Epimastigote, Promastigote and **Amastigote**
- There are two types of trypanosomiasis[1] that affect humans 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 **Chaga's disease.**
- Caused by **Trypanosoma cruzi** parasites in **Latin America**
- transmitted by the **'kissing' bugs[2].**
- Chaga's disease in Central and South America

African Trypanosomiasis

What is African sleeping sickness?

- **African trypanosomiasis** is a parasitic disease **transmitted by the tsetse fly.**
- It gets its nickname **'sleeping sickness'** because symptoms can include a **disturbed sleep pattern**
- **Infection occurs through the bite of infected tsetse flies (intermediate host).**
- **Humans, domestic cattle and wild animals are the main reservoir host for Trypanosoma (definitive host).**
- T. gambiense causes a chronic illness.
- T. rhodesiense causes a more acute illness & more rapid in developing the disease.

1- unicellular parasitic flagellate protozoa, causing blood and tissue infections.
2-Triatominae(family: Reduviid) (kissing bug) bites and defecates around mouth or eyes; Fecal transmission into bite site.

African trypanosomiasis cont'

Transmission

Trypanosoma are transmitted from human to human through the bite of the tsetse fly which is only found in rural parts of Africa.

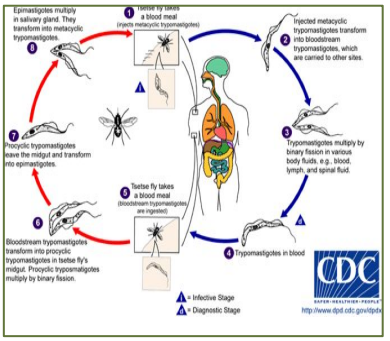
Transmitted from mother to child as the parasite can **cross** the placenta in the blood and infect the baby while it is still in the womb (uterus)

Contaminated needles can also contribute to the spread of trypanosomes, but this is rare.

Life cycle

The trypanosome parasite is first introduced into the mammalian host as **trypomastigotes (Infective stage & Diagnostic stage)** 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**[1].

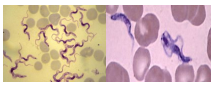


Pathology and clinical picture, Has 3 stages:

Skin stage	Systemic Haemato-lymphatic stage	Central nervous system (CNS) stage
A primary reaction occurs at the site of inoculation of trypomastigotes, **chancre** which resolve in 2-3 weeks. 	**intermittent fever**, headache & generalized lymphadenopathy mainly in the **cervical & sub-occipital region (Winterbottom' sign)**[2], anemia. 	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 a typical case, there is daytime sleeping, psychological changes, tremors, convulsions and finally coma. **without treatment, the disease is invariably fatal.**

Diagnosis

1. 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.**
2. **Serological** testing is also common as IF and ELIZA.



1- targeting the CNS.
2- lymph node enlargement due to the accumulation of the parasite.

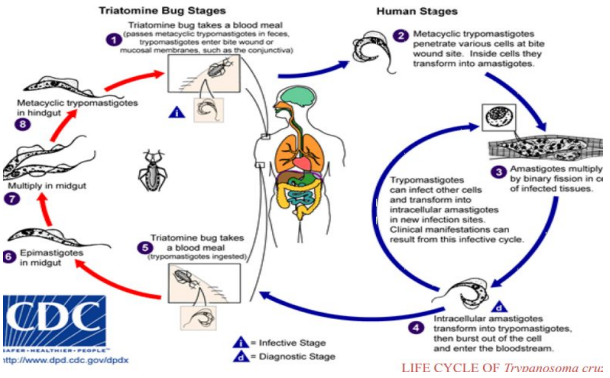
American Trypanosomiasis

General information

Chaga's disease : is a tropical parasitic disease caused by the **Trypanosoma cruzi**. It is spread mostly by insects known as **kissing bugs (Reduviid (Triatomine) bug)**. **The human disease occurs in two stages: an acute stage and chronic stage**

Life cycle

- 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)**

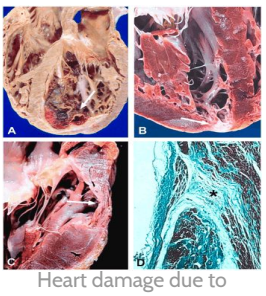
→ after that parasites (trypomastigote) enter the blood stream and find there way, mainly on the **face near the eyelids**, it produces a swelling of the eye and temporal region with conjunctivitis **(Romanas sign)**

→ 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 tissue it become in form of (Amastigote).

Romana's sign

T. cruzi causes cutaneous stage (chagoma)



Heart damage due to American trypanosomiasis

kissing bug

American Trypanosomiasis

Clinical features

Acute phase

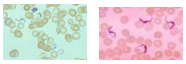
- T.cruzi causes Acute illness in children, which is followed by chronic manifestations later in life.
- In the early stage, symptoms are typically either not present or mild, and may include **fever, swollen lymph nodes,** headaches, or local swelling at the site of the bite **(chagoma).**
- The most 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.

Chronic phase

- 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.
- T. cruzi causes a chronic illness with progressive **myocardial damage leading to cardiac arrhythmias and cardiac dilatation.**
- Gastrointestinal involvement leading to **megaesophagus and megacolon.**
- 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.

Diagnosis

Microscopical examination of Giemsa – stained blood film, we will find C- shaped trypomastigotes



Serology: IFAT (immunofluorescence antibody test)

Xenodiagnosis: feeding bugs on a suspected cases.

PCR: used to detect Trypomastigotes

Treatment (NOT IMP)

American

- Benznidazole
- Nitrofurazone

African

- For early infection
  - Pentamidine
  - Suramin
- for late infection
  - eflornithine (Difluoromethylornithine-DFMO)

Dr.Mona's Notes (Trypanosomiasis)

➔ African trypanosomiasis

- **Disease:** Sleeping sickness
- **Caused by:** Trypanosoma brucei
- **Transmission:** by the tsetse fly
- **Infective stage:** trypomastigotes
- The trypomastigote enters through the skin and multiply in the blood, lymph or spinal fluid.

1. **Primary reaction: chancre** which resolve in 2-3 weeks.
2. **Systemic Haemato-lymphatic stage:** intermittent fever, **Winterbottom sign**
3. **CNS stage:** change in behavior, confusion, and disturbance of sleep

- **Diagnosis:**
  - Microscopically: trypomastigote in peripheral blood and CSF stained by GIEMSA
  -

➔ American trypanosomiasis

- **Disease:** Chagas disease
- Caused by: Trypanosoma cruzi
- **Transmission:** by the kissing bug
- **Infective Stage:** trypomastigotes

1. The trypomastigotes first cause **chagoma**
2. **Acute Chagas disease** → Enters the bloodstream to the face, producing **Romana's sign**
3. **Chronic illness** → MAINLY Cardiomyopathy and cardiomegaly, Also to the GIT causing megacolon

- **Trypomastigotes → in the blood**
- **Amastigote → in the tissue (seen in autopsy)**
- **Diagnosis:**
  - Microscopically: trypomastigote in the blood stained by GIEMSA
  - Serology: Immunofluorescence

➔ Doctor's Questions:

Q1: A patient came from latin America with inflammation, and enlarged eyelid. What is the most likely diagnosis? American trypanosomiasis (chagas disease)

Q2: A patient is having sleep disturbance, change in behaviors, & convulsions.

1. **What is the most likely diagnosis ?** African trypanosomiasis (sleeping sickness)
2. **How it is transmitted ?** by the tsetse fly
3. **How to diagnose it ?** trypomastigote in peripheral blood and CSF stained by GIEMSA

Q3: What is the causative organism of sleeping sickness ? Trypanosoma brucei

Q4: What is the causative organism of chagas disease ? Trypanosoma cruzi

Dr.Mona's Notes (Leishmaniasis)

- **Transmission:** by the sandfly
- **Infective stage:** promastigote
- **Diagnostic stage:** amastigote (phagocytized by macrophages where they transform)

➔ Cutaneous leishmaniasis (keyword: skin)

- Leishmania Major → zoonotic → wet lesions with severe reaction
- Leishmania Tropica → human → dry lesions with minimal ulceration
- It starts as a painless papule and it's self limited ulcer.

➔ Mucocutaneous leishmaniasis (keyword: mucus & cartilage)

- **Caused by:** Leishmania braziliensis
- **Diagnosis**: parasite can be isolated from the margin of the ulcer
  - Giemsa stain - microscopy for **amastigotes**
  - Culture in NNN medium for **promastigotes**

➔ Visceral leishmaniasis (keyword: bone marrow)

- **Disease:** kala-azar
- **Caused by:**
  - Leishmania donovani → affect adults
  - Leishmania infantum → affect children
- **Symptoms:** intermittent fever, and hepatosplenomegaly
- **Diagnosis:**
  - Microscopy
  - Culture in NNN medium
- **Samples:**
  - **Bone marrow aspirate**
  - Splenic aspirate
  - Lymph node
  - Tissue (liver) biopsy

➔ Doctor's Questions:

Q1: What is the most common sample obtained to diagnose Visceral leishmaniasis ?

Bone marrow aspirate

Q2: Which of the following samples is used to diagnose Visceral leishmaniasis ?

A. Nasal aspirate
B. Splenic aspirate
C. Margin biopsy

Quiz:

MCQ:

Q1:A, Q2:D, Q3:C, Q4:C , Q5:D

Q1: 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

Q2: Which ONE of the following transmits leishmaniasis?
A- Tsetse fly
B- Kissing bug
C- Cockroaches
D- Sandflies

Q3: Which ONE of the following medias are used for diagnosing leishmaniasis?
A- L-J media
B- Blood agars
C- NNN media
D- LD media

Q4: Which ONE of the following organisms causes mucocutaneous Leishmaniasis
A- Leishmania Tropica
B- Leishmania Donovani
C- Leishmania braziliensis
D- Leishmania Infantum

Q5: Which ONE of the following is the swelling of the eyelids Caused by american trypanosomiasis?
A- chagoma
B- Winterbottom' sign
C- Chancre
D- Romanas sign

SAQ:

Case: this 23-year-old girl who resides in Central africa has had recurrent fevers for the last 6 weeks, accompanied by persistent diarrhea and weight loss. a physical examination reveals her to be alert, but with significant generalized weakness, widespread lymphadenopathy, hepatomegaly, and massive splenomegaly.

Q1; What is your diagnosis
Visceral leishmaniasis

Q2; What is most likely causative organism
Leishmania donovani

Q3; How is this disease transmitted
By sandfly

Q4; If the patient was 2 years old, what is the most likely organsim?
Leishmania infantum

Q5; How would you diagnose this patient?
Microscopy on giemsa stain (silver stain) and culture on NNN media of bone marrow aspirate

Quiz:

MCQ:

Q1:C, Q2:C, Q3:B, Q4:A , Q5:D

Q1 : which one of the following describes the parasite in the bloodstream ?
A- Trypanosoma cruzi
B-Amastigotes
C-Trypomastigotes
D-Trypanosoma brucei

Q2 : Chagas disease is caused by :
A-kissing bug
B-Trypanosoma brucei
C-Trypanosoma cruzi
D-Tsetse fly

Q3 : which of the following cause acute trypanosomiasis?
A-T. Gambiense
B-T. Rhodesiense
C-T. Cruzi
D- none of the above

Q4 : what is the intermediate host of African trypanosomiasis "sleeping sickness"?
A-Tsetse fly
B-kissing bug
C-Human
D-Sand fly

Q5: a 76 year old Argentinian man was diagnosed with Chaga's disease. unforunately , he died. Upon performing an autopsy, which one of the following would be seen in his heart ?
A- C- shaped trypomastigote of T. cruzi
B- C- shaped trypomastigote of T. Brucei
C- Amastigote of T.Brucei
D- Amastigote of T. cruzi

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 your diagnosis
African trypanosomiasis

Q2: What is the most likely pathogen?
T. Brucei

Q3: How is this disease transmitted
By Tsetse fly

Q4: The swelling on his neck s also known as
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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