HEMATOPOIETIC & LYMPHATIC SYSTEM

SUBJECT : _____

LEC NO. : 3

DONE BY : Tabark Aldaboubi

وَقُل رَّبِّ زِدْنِي عِلْمًا

3- Leishmaniasis and Trypanosomiasis

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Objectives

- Describe the general characteristics, epidemiology, pathogenesis, clinical presentation and management of leishmania
- Describe the general characteristics, epidemiology, pathogenesis, clinical presentation and management of Trypanosomia

rare

(المجاثيرة العاضيات) Sporozoa

(مجاثيرة الدم) hemoflagelates

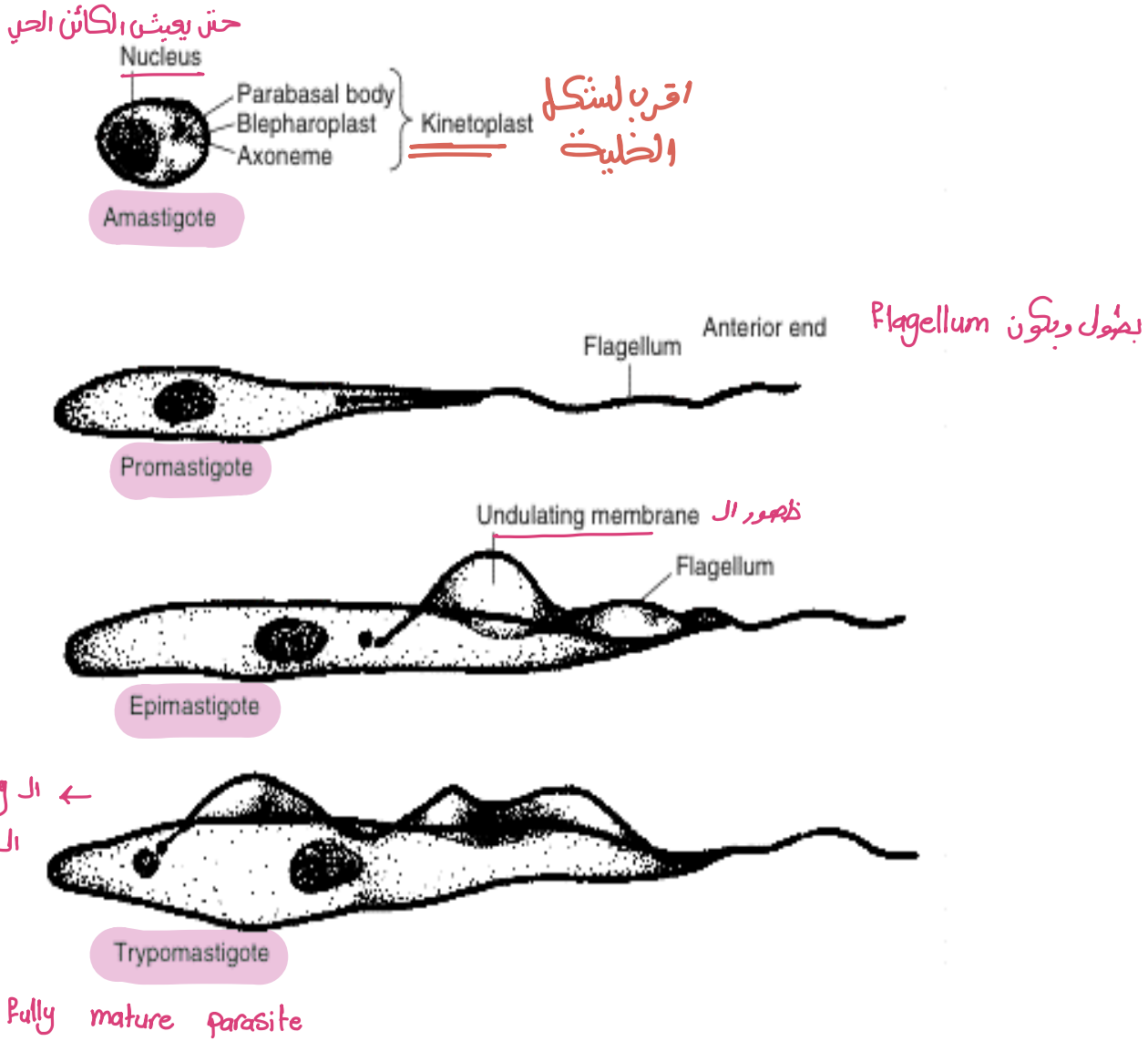
} طفيليات كبيرة Parasite

Introduction

- Two of the many genera of hemoflagellates are pathogenic to humans, Leishmania and Trypanosoma.
- They reside and reproduce within the gut of specific insect hosts. The life cycle is completed when a second insect ingests the infected mammalian blood
- During the course of their passage through insect and vertebrate hosts, flagellates undergo developmental change

Stages in the life cycle of the hemoflagellates

مراحل تطور الـ Parasite



Leishmania
(Kala Azar)

Species

في كثير strain فجمعوهم على حسب خصائصهم لـ ٣ مجموعات

- The many strains can be more simply placed in four major groups based on their serologic, biochemical, cultural, and behavioral characteristics
  - *Leishmania tropica* and *L. mexicana* produce a localized cutaneous lesion or ulcer, known popularly as oriental sore
  - *L. braziliensis* is the cause of American mucocutaneous leishmaniasis
  - *L. donovani* is the etiologic agent of kala azar

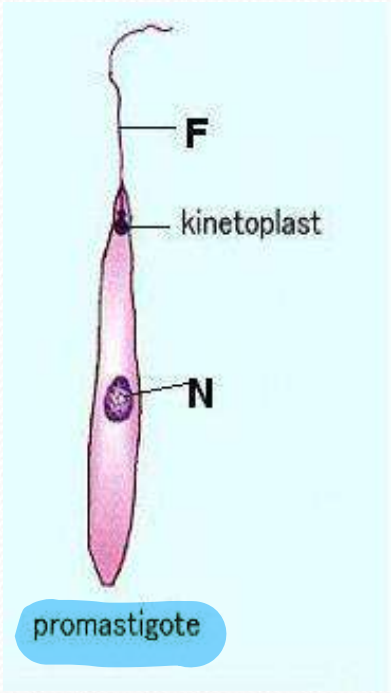
بتروح على الدم

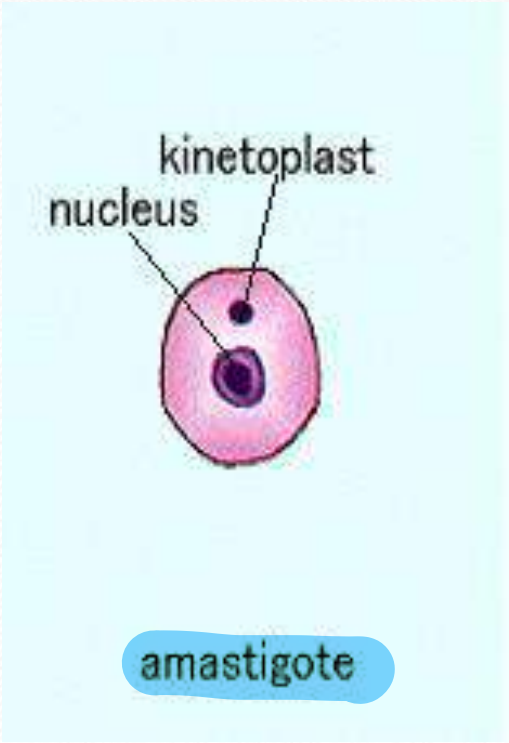
Morphology

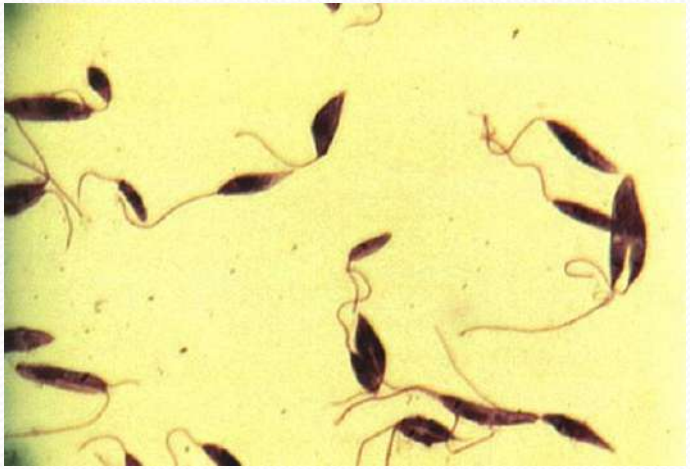
- Promasitogte
- Amastigote

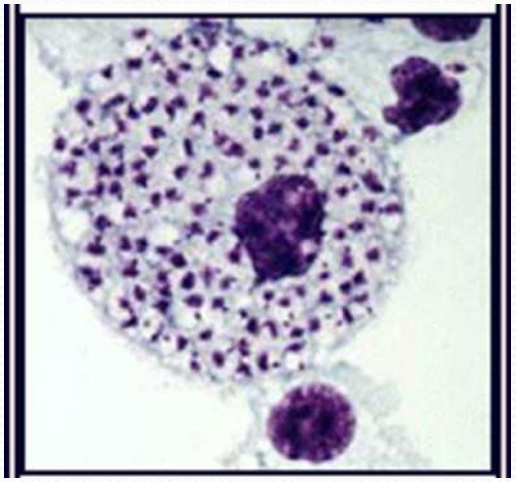
target cell هي ← macrophages

خطير لأنه يهاجم الـ WBC الي وظيفتها تقلل immunity









Epidemiology

- Endemic in 88 countries انتشاره واسع
- It is estimated that over 20 million people worldwide suffer from leishmaniasis and 1 to 2 million additional individuals acquire the infection annually.
- More than 90% of C.L. cases occur in; Iran, Algeria Afghanistan, Brazil, Peru, Saudi Arabia, and Syria (Cutanuos)
- More than 90% of V.L. Cases occur in 5 countries; Bangladesh, India , Nepal, Sudan, and Brazil
- Annual death due to V.L. is 59,000 cases

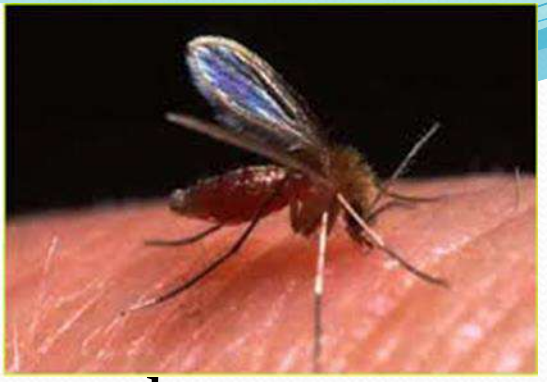
الارقام غير مطمئنة

المرض بينتقل على اعضاء ثانية وابضل على الجلد

rare ← انه ينتقل من شخص لاخر

Life Cycle

← عادة الناقل بكون حشرة



- Amastigotes ingested in the course of a meal assume the flagellated promastigote form, multiply within the gut, and eventually migrate to the buccal cavity of phlebotomine sandfly

Vector

بعوت Amastigot وبتحول لـ Pro جوا الـ gut وبتكاثر

- When the fly next feeds on a human or animal host, the buccal promastigotes are injected into the skin of the new host together with salivary peptides capable of inactivating host macrophages
- Amastogotes invade macrophage and divides until the infected cell ruptures
- The sandfly acquires the organisms during the blood meal

من تقريغ دفعة اول

2- When the fly next feeds on a human or animal host, the buccal promastigotes are injected into the skin of the new host together with salivary peptides capable of inactivating host macrophages.

هاي الذبانة نفسها راح تقرص شخص ثاني،، وبتنقل الطفيليات الي فيها بالإضافة الى شوي من لعابها الي بحتوي على مواد بتمنع تجلط الدم، ومواد بتعمل زي التخدير عشان ما نحس بألم القرصة، ومواد بتبطل عمل الmacrophages تبعت هاذ الشخص الي قرصته.

3- Amastigotes invade macrophages and divide until the infected cell ruptures.

لما تدخل هاي الطفيليات على دم الشخص المصاب بتتحول من promastigote إلى Amastigotes، وبتروح على الmacrophages وبتكاثر جواتها لحتى ما تفجر الخلية.

4- The sandfly acquires the organisms during the blood meal.

هون ممكن تيجي ذبانة ثانية مش مصابة ممكن تقرص هاذ الشخص المصاب وتوخذ هاي الطفيليات وتعمل دورة جديدة بكل الي حكيناه فوق.

ربط مع مايكرو الجينيرال 🤦‍♀️

Life cycle

ال hemoflagellat دورة حياتها بتكون معقدة
جزء بال human وجزء بالحشرة وال 2stages
بكملوا بعض يعني لازم انسان وحشرة اي
واحد فيهم بختفي بتوقف ال cycle

Definitive host: Man.

Habitat: Reticuloendothelial cells(REC)

↳ Liver, spleen,bone marrow lymph node

Vector: Female Sand fly.

Infective stage: Promastigote.

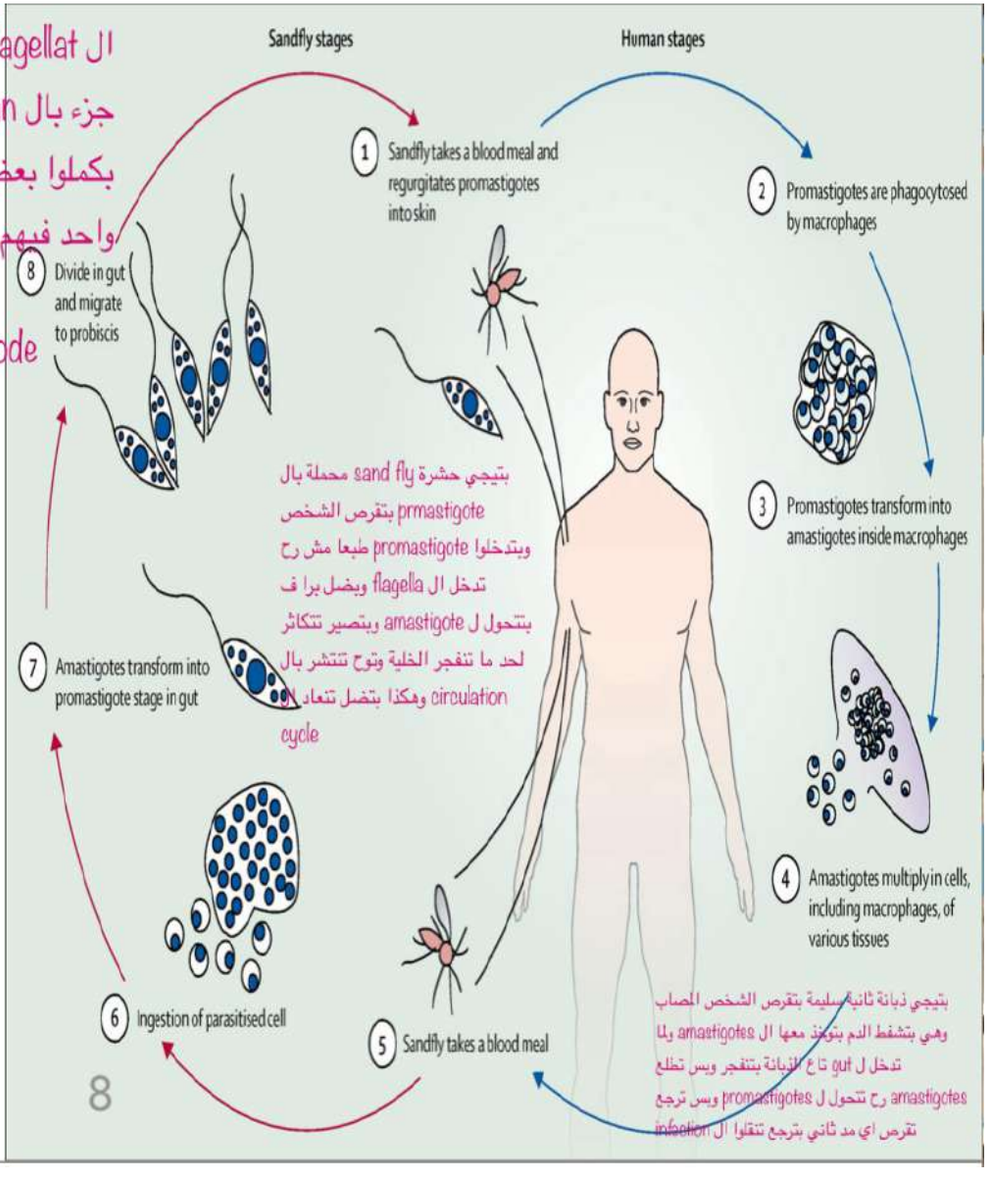
Mode of infection:

-Bite of an infected female sandfly.

-Vertically from mother to fetus.

-Blood transfusion.

Diagnostic stage: Amastigote.

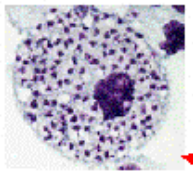


نفس الكلام اليفوق

THE LIFE CYCLE OF *LEISHMANIA* SPP.
(VARIOUS FORMS OF LEISHMANIASIS)

The vertebrate host is infected with promastigotes when bitten by the vector.

The promastigotes enter circulating macrophages and reproduce as asmastigotes.



The macrophage dies, the amastigotes are released, and they infect more circulating or fixed macrophages.

The amastigotes are released in the vector's gut, and the parasite reproduces as promastigotes.

The vector (a sand fly) ingests macrophages when it ingests blood.

The "type" of leishmaniasis (i.e., cutaneous, visceral, etc.) is determined by the primary location of the macrophages that are infected.

(Parasites and Parasitological Resources)

Pathogenesis

- After the host is bitten by an infected sandfly, the parasites disseminate in the bloodstream and are taken up by the macrophages of the spleen, liver, bone marrow, lymph nodes, skin, and small intestine
- Histiocytic proliferation in these organs produces enlargement with atrophy or replacement of the normal tissue

بس يفوت ال parasite ع ال macrophge بروح ع ال
spleen,liverbone marrow , lymph بكون جهاز المناعة مش
قادر يتعامل معه ف بتكون histiocytic proliferation الي ما

Disseminated Intravascular Leishmeniasis (Kala azar)

- Kala azar, which is caused by L. donovani, occurs in the tropical and subtropical areas of every continent except Australia
موجود بكل القارات ما عدا استراليا ويُعتقد بسبب انها معزولة وحاطة بالمياه من جميع الجهات
- In Africa, rodents serve as the primary reservoir. Human cases occur sporadically, and the disease is often acute and highly lethal. In Eurasia and Latin America, the domestic dog is the most common reservoir
الانسان مو هو ال host ممكن يكون الحيوانات هي الhost
كونه موجودة عند الحيوانات فرح تكون خطرة ومميتة اذا انصاب فيها الانسان
- Human disease is endemic, primarily involves children, and runs a subacute to chronic course
بالانسان
- In India, the human is the only known reservoir, and transmission is carried out by sandflies. The disease recurs in epidemic form at 20year intervals, when a new nonimmune children and young adults appears in the community
بصير chronic لأنه كثير منتشر وممكن المناعة تغلب ال parasite
- There appears to be a high incidence of visceral leishmaniasis in patients with HIV infection

**Human disease is endemic, primarily involves children, and runs a subacute to chronic course.

في المناطق الي بكون فيها الاصابات كثيرة للبشر زي الهند،، بكون عندهم مناعة منيحة تجاهه، وهاذ بفسر ليش معظم المصابين عندهم بكونو أطفال لأنهم لسا ما تعرضوا لهاي الطفيليات بحياتهم عشان يبنو ضدها مناعة، واذا هنول الأطفال رجعو انصابوا بالمستقبل بكون المرض عندهم أخف

واذا صابهم مرة ثالثة بكون أخف أكثر لحتى ما يبطل يصيبهم بالمرة أو يصير مرض مزمن (chronic).

**In India, the human is the only known reservoir, and transmission is carried out by sandflies. The disease recurs in epidemic form at 20 year intervals, when a new nonimmune children and young adults appears in the community.

الوضع بالهند لسا أسوء،، لأنه أصلا الطفيليات موجودة عند البشر مش القوارض،، يعني بتنتقل مباشرة من إنسان لأنسان،، وبالتالي المرض بكون منتشر أكثر بكثير،، فالأطفال هم الأكثر عرضة للإصابة وبتكون عليهم الأعراض كثير شديدة، اذا نجو من المرض ببنو مناعة جزئية تجاهه، واذا انصابو كمان مرة بكون المرض أخف زي ما حكينا فوق، وبعد عشرين سنة لما يكبرو هنول الأطفال بصير عندهم مناعة منيحة تجاه المرض،، ولما ييجي جيل جديد من الاطفال الغير مصابين بتبلش دورة جديدة للمرض وهكذا.

immunity of parasite :- slow development of immunity
multible exposure الحاجة الى

Manifestations

no symptom الـ Parasite بحاول يدخل بقضي عليه جهاز المناعة قدرش عليه بكون

- The majority of infections are asymptomatic
- Symptomatic disease most commonly manifests itself 3 to 12 months after acquisition of the parasite. It is often mild and self-limited ممكن تبدا اعراض بسيطة لكن برضو بيدا جهاز المناعة بسيطر عليه
- A minority of infected individuals develop the classic manifestations of kala azar → لما يدخل على الـ organ بسميه Typical

1. Fever, which is usually present, may be abrupt or gradual in onset. It persists for 2 to 8 weeks and then disappears, only to reappear at irregular intervals during the course of the disease. A double-quotidian pattern (two fever spikes in a single day) is a characteristic but uncommon finding باليوم الحرارة بتصعد العتحدد مرتين

اول ما يدخل للجسم بالمرحلة الـ Acute وجهان المناعة بيبذل اقصى جهده يقضي عليه بأوله الـ Cytokines برتفع وهاض برفع درجة الحرارة لما يوصل الـ organ والخلايا تاعت الـ macrophage بيعد عن المناعة وبتبلش الحرارة تخفف.

الـmacrophage بسبح ويوصل للـ Tissue حتى تحميها من الـ Parasite منها الـ intestine فالـmacrophage إلي حواليها وهي بيوصلها المرض بالتالي يوصل للـintestine

2. Diarrhea and malabsorption are frequent in Indian cases, resulting in progressive weight loss and weakness
3. Physical findings include enlarged lymph nodes and liver, massively enlarged spleen, and edema.
4. In light-skinned individuals, a grayish pigmentation of the face and hands is commonly seen, which gives the disease its name (kala azar, black disease)

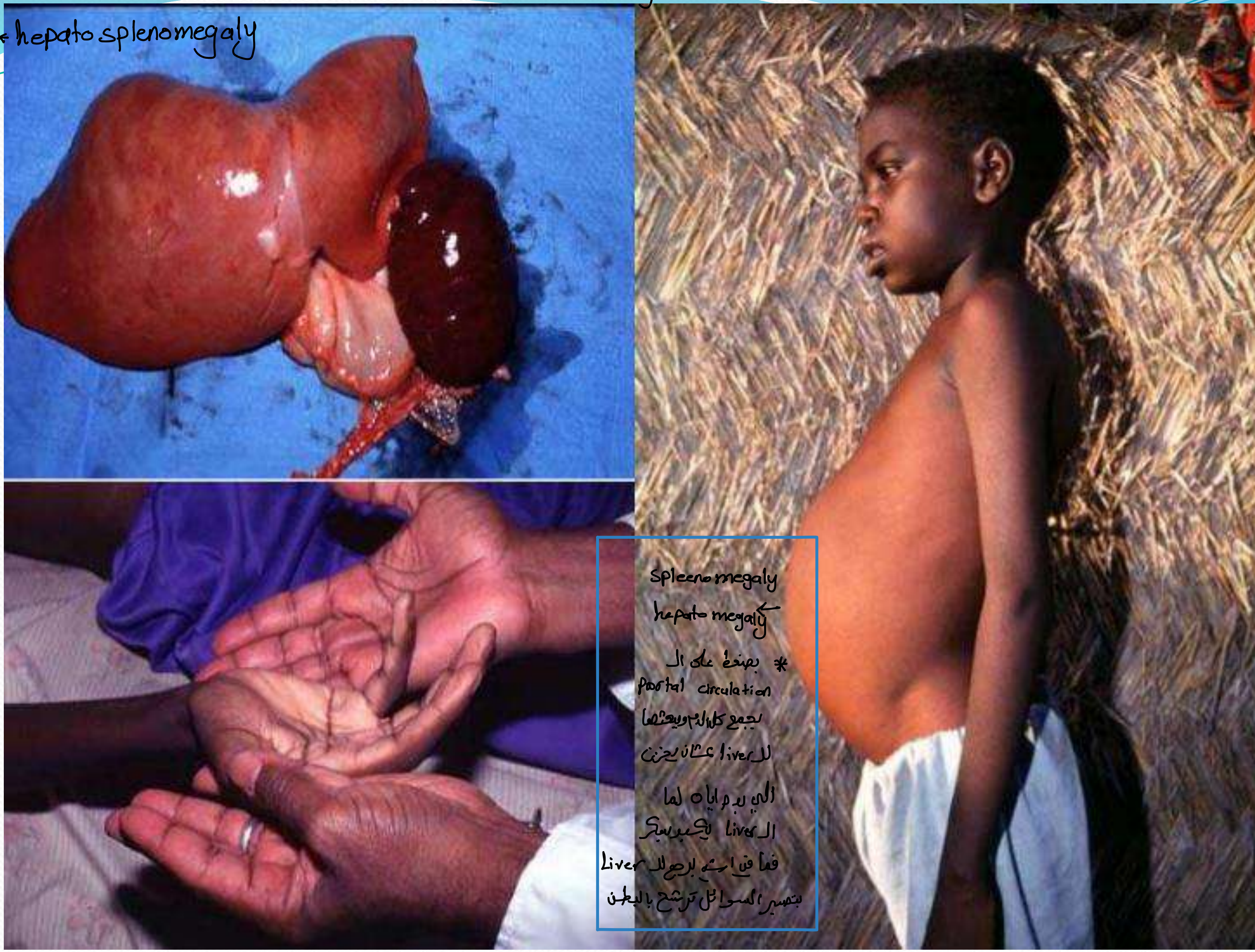
بنعس البلت الـ intestine وبجيبي تلف الـskin اللون الغامق

لأنو بروح على الـ bone marrow

5. Anemia are typical in advanced cases. Thrombocytopenia induces petechial formation and mucosal bleeding. The peripheral leukocyte count is usually low; agranulocytosis with secondary bacterial infections contributes to lethality.
6. Serum immunoglobulin G levels are enormously elevated but play no protective role. Circulating antigen-antibody complexes are present and are probably responsible for the glomerulonephritis seen so often in this disease

الـ spleen بكبر 20 لـ 40 مرة كل الـ Abdominal cavity بتكبر والـ spleen بتضغط باقي الـ organ

** hepato splenomegaly



Spleeno megaly
hepato megaly ←

* بضغط على الـ portal circulation
بجمع كل الدم ويبعثها للـ liver عشان يخزن
الي بدو اياه لما الـ Liver يصير بعمل سير
فما في اشي برجع للـ Liver
بتصير السوائل ترشح بالبطن

Cutaneous Leishmaniasis

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

دائرة حمرة فيها مسامات صغيرة

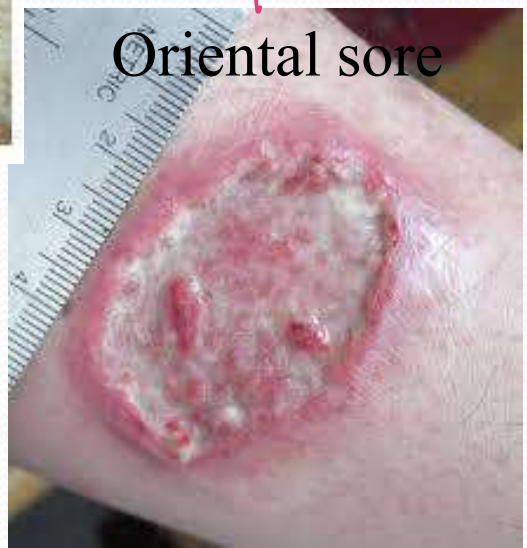
مبلش فيها damage

الوضع اسوء بلش يصير فيه ulcer ,total

damage to skin

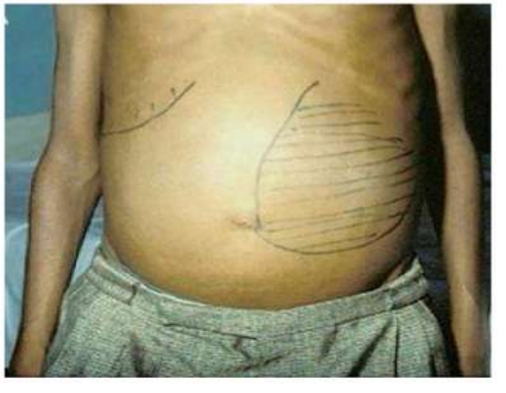
ليش ع الايد والوجه بنتشر اكثر لأنها هي اكثر اماكن بقرصها البعوض

Deep damage

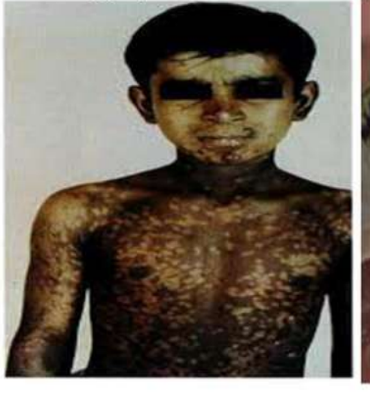


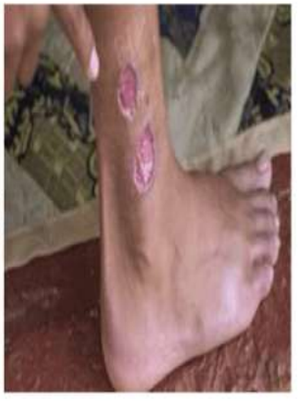
Leishmania → Leishmaniasis

Results from the invasion of RES by amastigotes which multiply enormously in the macrophages. This leads to a marked destruction and proliferation of reticuloendothelial tissue. It may be:



1) **Visceral leishmaniasis (kala-azar) (black fever):**
   - Persistent fever (Azar) and hyperpigmentation of skin (Kala).
   - Hepatomegaly, splenomegaly and generalized lymphadenopathy.
   - Pancytopenia (Anaemia, repeated infections, intestinal hemorrhage).





2) **Cutaneous leishmaniasis:**
   - Single or multiple papules that ulcerate.
   - The ulcers healed leaving scars or secondary infected.

3) **Mucocutaneous leishmaniasis:**- Rare, affect nasopharynx.

* blood smear

hepatomegaly ممكن اشوف organ من الـ organ بوخذ عينة *اذا وصل للـ

spleenomegaly

Diagnosis

- The diagnosis is made by demonstrating the presence of the organism in aspirates taken from the bone marrow, liver, spleen, or lymph nodes
- The specimens may be smeared, stained, and examined for the typical Leishman-Donovan bodies (amastigotes in mononuclear phagocytes) or cultured in artificial media and/ or experimental animals
- A rapid, direct, species-specific diagnosis by PCR and probes to kinetoplast DNA is used
- Results of the leishmanin skin test are negative during active disease but become positive after successful therapy

كل ما كانت بفترة مبكرة كل ما كان العلاج افضل

Treatment and Prevention

- The mortality in untreated cases of kala azar is 75 to 90%
- Treatment with pentavalent antimonial drugs lower this rate dramatically. Initial therapy, however, fails in up to 30% of African cases, and 15% of those that do respond eventually relapse
- Control measures are directed at the Phlebotomus vector, with the use of residual insecticides, and at the elimination of mammalian reservoirs by treating human cases and destroying infective dogs

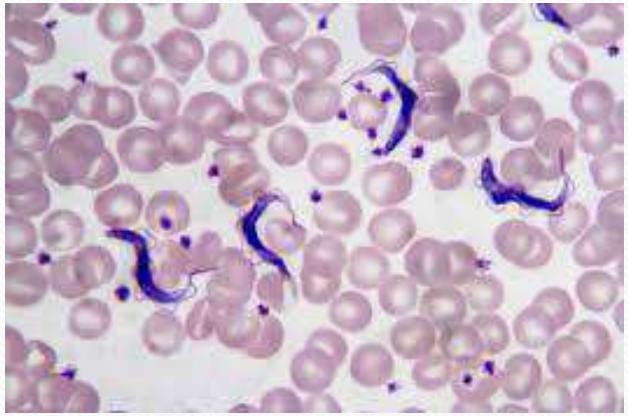
اللهُم إنّي أُحَاوِل
فَأَعِنّي.

African Trypanosoma (Sleeping sickness)

الاشياء المحددة هاي بس الحي حكاها الدكتور

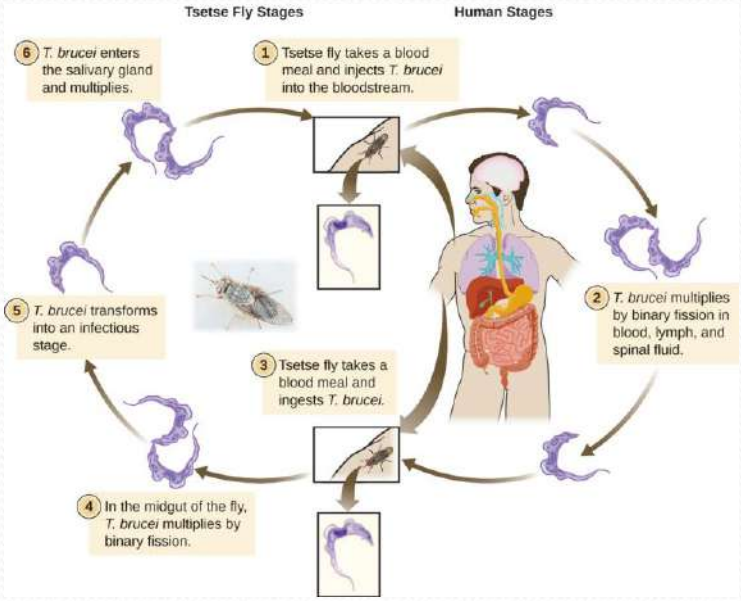
Parasitology

- The trypanosomes that produce these diseases are morphologically and serologically identical. Accordingly, they are considered varieties of a single species, *Trypanosoma brucei*
- The three subspecies, are *T. brucei gambiense, T. brucei rhodesiense,* and *T. brucei brucei*



Life Cycle

- On ingestion by the tsetse fly, and after a period of multiplication in the midgut, they migrate to the insect's salivary glands and assume the epimastigote form
- After a period of weeks they are transformed into trypomastigotes, rendering them infectious to mammals
- When the fly again takes a meal, the parasites are inoculated with the fly's saliva



فتتشر في افريقيا

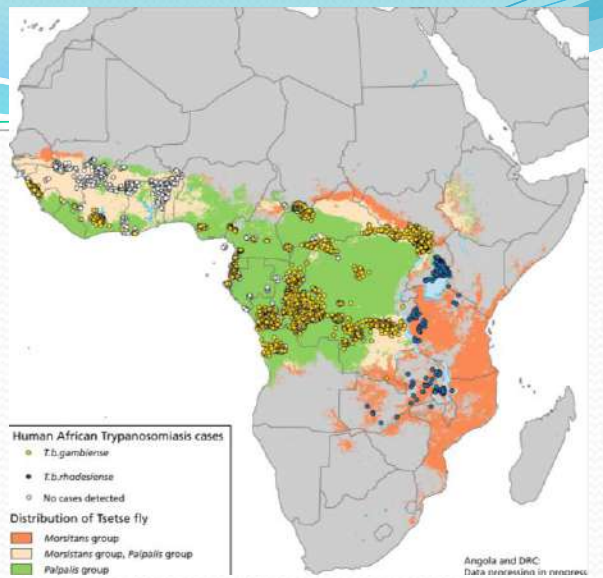
African trypanosomiasis (sleeping sickness)

مرض النوم ← يروح الـ Parasite على الـ brain بتضرب منطقة النوم وبصير بعاني المريض من النوم (نام ليوم يومين بعدين بصير شهور بدخل بعدها بـ coma).

- African trypanosomiasis is a highly lethal meningoencephalitis
- It occurs in two distinct clinical and epidemiologic forms:

1. West African or Gambian sleeping sickness 98%, found in 24 countries in west and central Africa
2. East African or Rhodesian sleeping sickness 2%, found in 13 countries eastern and southern Africa

Epidemiology

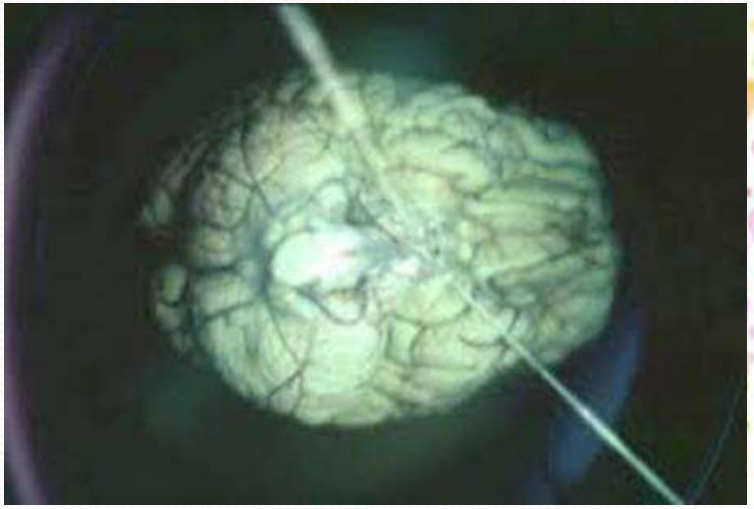


- Sleeping sickness is confined to the central area of Africa by that continent's two great deserts, the Sahara in the north and the Kalahari in the south.
- Sleeping sickness threatens millions of people in 36 countries in sub-Saharan Africa.
- In 1998, almost 40 000 cases were reported, but estimates were that 300 000 cases were undiagnosed
- The infection rate is affected by proximity to water but seldom exceeds 2 to 3% in nonepidemic situations.

Pathogenesis

- Multiplication of the trypomastigotes at the inoculation site produces a localized inflammatory lesion (chancre).
- Organisms spread through lymphatic channels to the bloodstream, inducing a proliferative enlargement of the lymph nodes.
- The subsequent parasitemia is typically low grade and recurrent.
- As host antibodies (predominantly IgM) are produced to the surface antigen they bind to the organism, leading to its destruction by lysis and opsonization.

- During the course of the parasitemia, trypanosomes localize in the small blood vessels of the heart and central nervous system
- This localization results in endothelial proliferation and a perivascular infiltration of plasma cells and lymphocytes. In the brain, hemorrhage and a demyelinating panencephalitis may follow



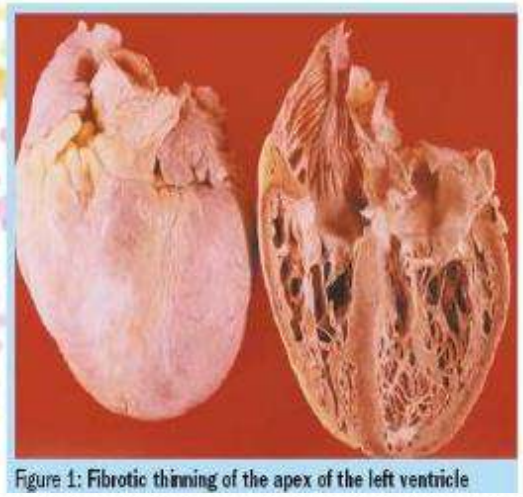
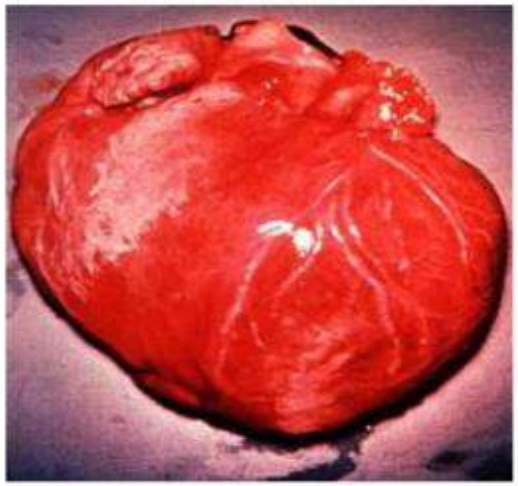


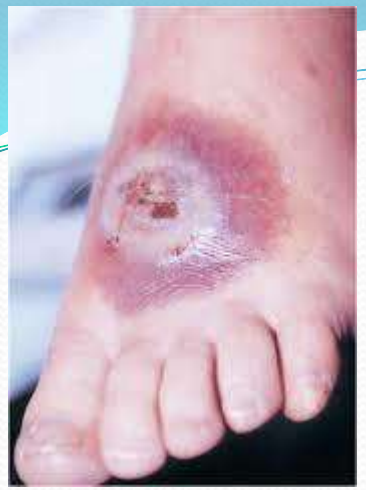
Figure 1: Fibrotic thinning of the apex of the left ventricle

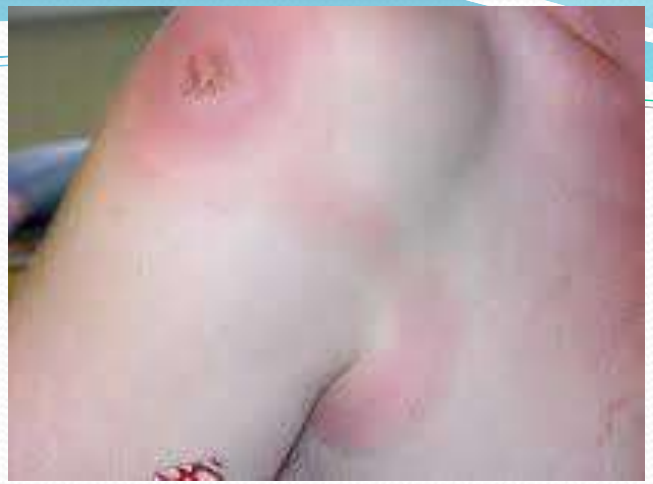


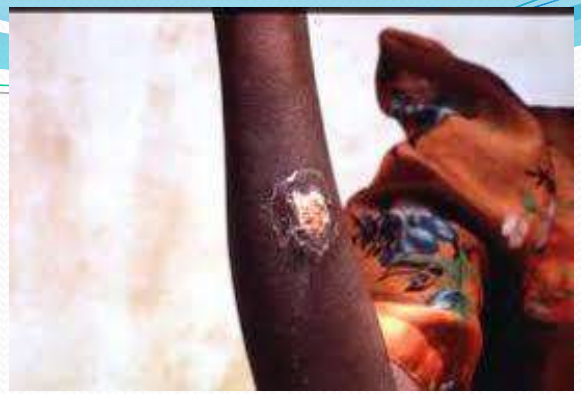
Manifestations

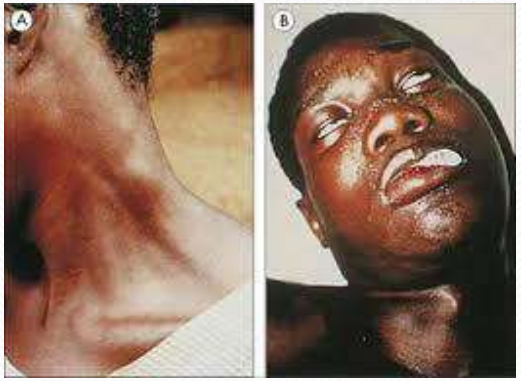
- The trypanosomal chancre appears 2 to 3 days after the bite of the tsetse fly as a raised, reddened nodule on one of the exposed surfaces of the body
- With the onset of parasitemia 2 to 3 weeks later, the patient develops recurrent bouts of fever, tender lymphadenopathy, skin rash, headache, and impaired mentation
- In the Rhodesian form of disease, myocarditis and CNS involvement begin within 3 to 6 weeks. Heart failure, convulsions, coma, and death follow in 6 to 9 months

- Gambian sleeping sickness progresses more slowly. Bouts of fever often persist for years before CNS manifestations gradually appear
- Spontaneous activity progressively diminishes, attention wavers, and the patient must be prodded to eat or talk
- Speech grows indistinct, tremors develop, sphincter control is lost, and seizures with transient bouts of paralysis occur.
- In the terminal stage, the patient develops a lethal intercurrent infection or lapses into a final coma








A
B

Diagnosis

- A definitive diagnosis is made by microscopically examining lymph node aspirates, blood, or cerebrospinal fluid for the presence of trypomastigotes
- Early in the disease, actively motile organisms can often be seen in a simple wet mount preparation smear
- If these tests prove negative, the blood can be centrifuged and the stained buffy coat examined
- Inoculation of rats or mice can also prove helpful in diagnosing the Rhodesian disease
- The patient may also be screened for elevated levels of IgM in the blood and spinal fluid or specific trypanosomal antibodies

Treatment and Prevention

- Lumbar puncture must always be performed before initiation of therapy. If the specimen reveals evidence of CNS involvement, agents that penetrate the blood-brain barrier must be included. Unfortunately, the most effective agent of this type is a highly toxic arsenical, melarsoprol (Mel B)
- If the CNS is not yet involved, less toxic agents, such as suramin, pentamidine, or eflornithine, can be used. In such cases, the cure rate is high and recovery complete
- Tsetse fly control measures, eradication of disease reservoirs, and attempts to develop effective vaccines have been tried with poor effect
- A degree of personal protection can be achieved with insect repellents and protective clothing