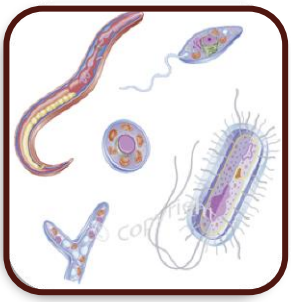


Parasitology

3rd Stage

Dr. Abdmohsin

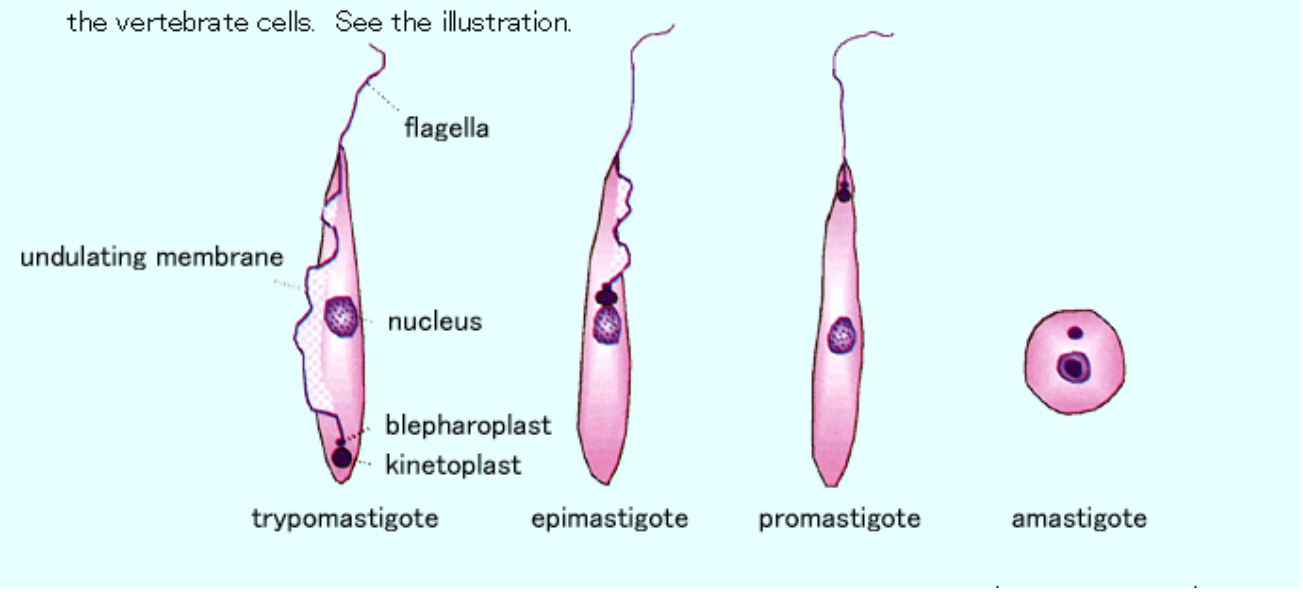
Blood and tissues flagellates (hemoflagellates)

Trypanosoma and *leishmania*

Characterized by:

A. Presence of four distinct phase (form) in the life cycle:

1. Amastigote (Leishman-Donovan bodies) (L.D bodies)
2. Promastigote
3. Epimastigote
4. Trypomastigote



B. Require insect biological vector for their transmission:

1. *Leishmania* spp.: *Phlebotomus* sandfly in old world and *Lutzomyia* sandfly in the new world .
2. African Trypanosomes: *Glossina* spp. (Tsetse)
3. American Trypanosomes : Triatomid bug (Kissing bug): *Triatoma* spp.

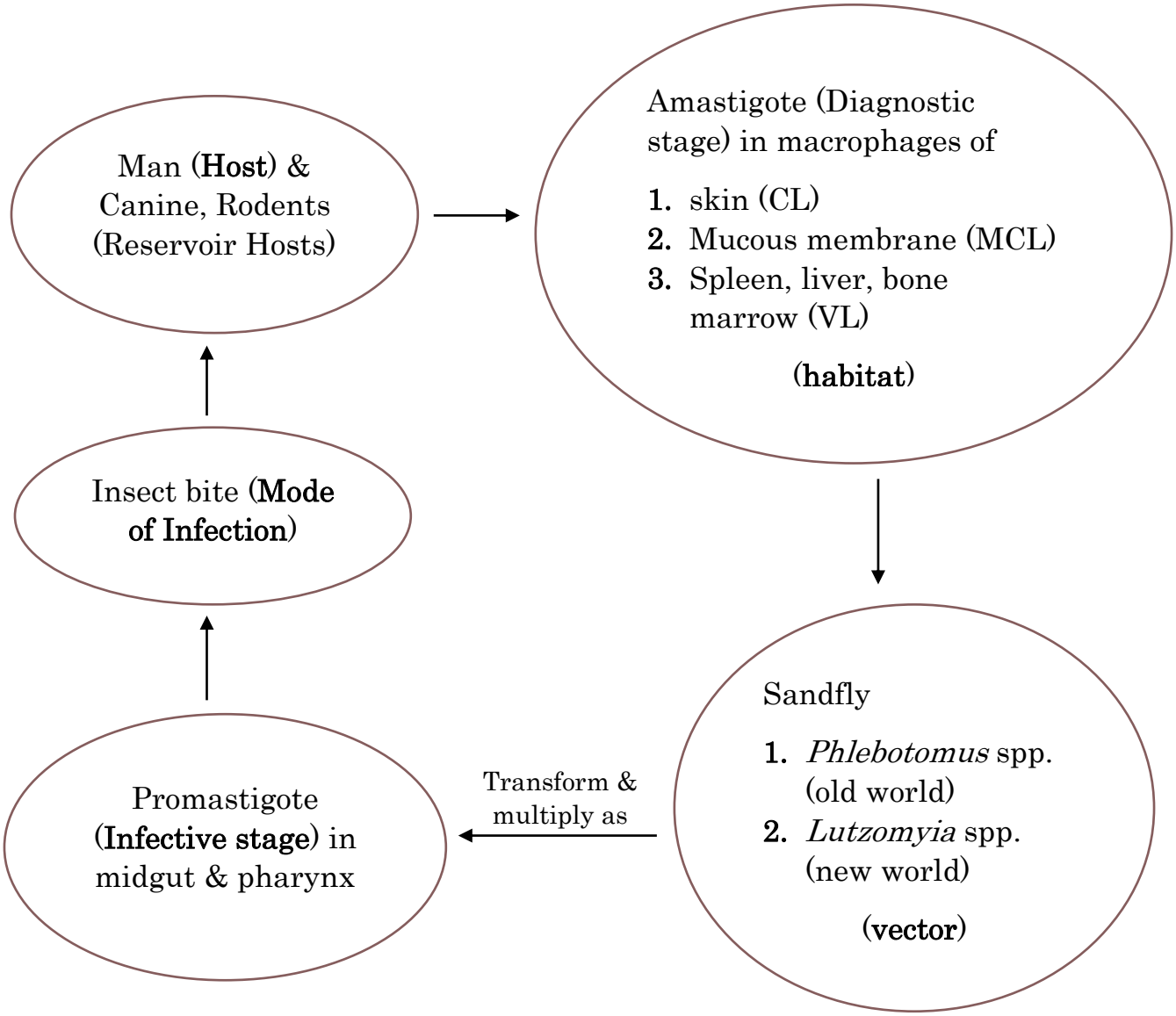
Leishmania (*L.*)

- Obligate intracellular parasites transmitted by the bite of infected sandfly.
- 14 spp. of *L.* responsible for wide spectrum of human diseases.
- Leishmaniasis usually zoonosis but few spp. are anthroponotic.

Life Cycle

L. has two distinct phase in the life cycle:

Amastigote in mammalian host and promastigote in sandflies vectors of culture



Life cycle of *Leishmania*

Note:

1. *L. tropica* & *L. donovani* are anthroponotic (man-man transmission)
2. No Reservoir hosts in the life cycle.
3. *L. infantum*: man is a dead end in the life cycle. The sandfly transmit the parasites from animal to man but cannot transmit the parasites from man to other man or animal.
4. Other spp. are zoonotic (man to man & man to animal & animal to animal)

Classification of Leishmaniasis

Amastigote of all *Leishmania* spp. morphologically identical so differentiation of the diseases and spp. based on the following:

A. Clinical ground:

1. Cutaneous Leishmaniasis (CL) or oriental sore, Baghdad boil
2. Mucocutaneous L. or Espundia
3. Visceral L. or kala azar

B. Geographic location:

1. Old world CL
2. New world CL.

C. Biochemical criteria e.g.:

1. Monoclonal antibodies
2. RNA & DNA techniques.
3. Isoenzyme patterns.
4. Serological tests.

Old world cutaneous leishmaniasis

- *L. tropica* complex
- *L. major* complex
- *L. aethiopica* complex

Pathogenesis & symptomatology: classical CL.

depend on

1. age
2. Spp.
3. previous exposure.
4. immune status of host.

- Incubation period l-2 weeks or as long as several months
- Pathogenesis is due to immune reaction to the parasite particularly cell mediated immunity (CMI).
- After introduction, the promastigote rapidly engulfed and change to amastigote in skin macrophage, multiply → the cell ruptures → amastigotes release → infect other cells, the process is repeated producing **firm painless papule** at insect Bite site. Papule may be intensely pruritic and slowly grow to 2 cm or more.
- Continuous multiplication of parasite and destruction of macrophages lead to destruction of papule along with necrosis of epidermis. The infection remain localized where a definite self-limiting Granulomatous tissue response develop (i.e. heal spontaneously). This is simple type of CL.
- IF macrophage and endothelial cells of blood vessels of epidermis infected, lead to tissue lysis, necrosis and ulcer formation, may be secondary bacterial & fungal infections.
- the ulcer has crater-like appearance with necrotic center and indurated margin. the ulcer heal spontaneously (several months) due to formation of Granulomatous tissue but leaves disfiguring scar.

NOTE: Host recovery depend on cellular immunity & give lifelong protection.

L. tropica	*L. major*
Produce chronic, dry type lesion (chronic CL., dry CL.)	Produce acute, wet type lesion (covered by serous exudates) (acute CL., wet CL.)
Papule ulcerate after longer period	Ulcerate rapidly
Produce single lesion	Produce multiple lesions
Little tissue reaction occur	More tissue reaction occur
Healing process may take place a year	Healing process take place within 6 months.
Found in urban areas (urban CL.)	In rural areas (Rural CL.)
Anthroponotic infection	Zoonotic infection
No reservoir host	Canine & rodents act as reservoir h.
Endemic infection	Sporadic infection

Diagnosis

1. Symptoms & signs (papule of slow progressive growth, ulcer of crater-like in appearance).
2. Recovery & identification of amastigote in Giemsa stained smear prepared from biopsy tissue, aspirates or skin scrapings from the margin or base of the ulcer or papule.
3. Identification of promastigote in culture media [culture of specimens (biopsy, aspirates, skin scrap)] in NNN medium or Schneider's Drosophila medium
4. Leishmanin skin test.

Epidemiology

- Transmission by direct contact or by sandfly vector.
- The vector is female *Phlebotomus* sandfly.
- *L. tropica* infection is endemic in urban area, anthroponotic (man to man transmission), no reservoir host.
- *L. major* infection is zoonotic, sporadic, in rural area, canine & rodents are the reservoir hosts.
- Both infections found in Mediterranean coastal area, south former USSR, Afghanistan.
- Infection give lifelong protection.

Control

1. Treatment.
2. Insect (sandfly) control:
    a. Insecticides
    b. Repellents
    c. Fine-mesh netting.
3. Reservoir host control:
    a. Killing of street dogs.
    b. Killing of rodents
4. Protect the lesion from insect bite.

Treatments

- ✓ Heal spontaneously → lifelong protection.
- ✓ Cryotherapy.
- ✓ Heat.
- ✓ Surgical.
- ✓ Chemotherapy:
    1. Antimonial compounds [sodium stibogluconate (pentostam) or meglumine antimoniate, intralesionally and/or parenterally].
    2. Amphotericin.
    3. Ketoconazole

L. aethiopica

Give rise to three types of lesions:

1. Classical CL.
2. Muco CL.
3. Diffuse CL.

DCL.

Thickening of skin in plaques, papules or multiple nodules usually in face or limbs. May resemble lepromatous leprosy. No mucosal involvement, no ulceration, not heal spontaneously, has tendency to relapse. Results from failure of cell-mediated immunity.

Leishmaniasis recidivans:

- Relapsing form CL.
- Is granulomatous non healing hyperactive dermal response occurring with *L. tropica* infection.
- Hypersensitive disease.
- Even though the primary lesion nearly heals, satellite lesions appear and slowly extend centrifugally.
- Scarring can be extensive.

New World Cutaneous Leishmaniasis

- ☒ *L. mexicana* complex
- ☒ *L. braziliensis* complex
- ☒ *L. guyanensis* complex.

Human infections are contracted primarily through forest dwelling or Forest-related activities in zoonotic areas.

Cause: Classical CL.; DCL.; MCL.

MCL.

- ♠ The primary lesions of MCL. are similar to other form of classical CL.
- ♠ Untreated primary lesions may develop into MCL.
- ♠ Metastatic spread to nasal or oral mucosa may occur in presence of active primary lesion or many years after the primary lesion has healed.
- ♠ Metastasis may be due to hematogenous spread of the parasites.
- ♠ There is progressive ulceration and erosion of soft tissue and cartilage.
- ♠ Ulceration can lead to loss of the lips, soft parts of the nose, & soft palate.

New world CL., is zoonotic, dog & rodents are reservoir hosts, the vector is *Lutzomyia* sandfly.

Visceral leishmaniasis

Kala azar, black fever

- ❖ Hindu name: blackening of the skin of forehead & hands.
- ❖ Parasitized mononuclear phagocytic cells (M.P.C.) throughout the body.
- ❖ *L. dononovani*, *L. infantum*, *L. chagasi*.

Pathogenesis:

Leishmania localized & multiply in (M.P.C.) of liver, spleen, bone marrow, lymph nodes, mucosa of intestine →

1. Hyperplasia of these cells → Hypertrophy of liver & spleen (hepatosplenomegaly)
2. Depression of hematopoiesis → reduction of RBC, neutrophil & platelet.
3. ↑ production of lymphocytes, monocytes & macrophages.
4. ↑ production of IgG & IgM (Hypergammaglobulinemia).
5. Suppression of cell mediated immunity lead to uncontrolled multiplication & dissemination of the parasites.
6. Suppression of delayed hypersensitivity reaction to skin test antigens (Leishmanin skin test is -ve).

Symptoms & Signs

- ☆ Majority asymptomatic or with minor symptoms.
- ☆ Incubation period 1-2 weeks → 2 years (usually 2-3 months).
- ☆ Classic signs & symptoms are:
    1. Fever for long duration (double or triple fever peak daily)
    2. Non tender hepatosplenomegaly
    3. Anemia → edema of face, trunk & face.
    4. Weight loss (wasting), anorexia, diarrhea, malabsorption.
    5. Neutropenia, lymphocytosis, monocytosis, .
    6. Thrombocytopenia → bleeding from gums, nares, lips.
    7. Lymphadenophy.
    8. Sometime acute abdominal pain.
- ☆ Untreated cases → Death.

Complication

1. Bacillary or amebic dysentery.
2. Septicemia.
3. Pneumonia.

Diagnosis:

1. Symptoms & signs (fever, hepatosplenomegaly, anemia.)
2. Finding of amastigote in Giemsa stained smear prepared from biopsy materials from bone marrow (usually), spleen, liver, lymph nodes.
3. Finding of promastigotes in culture media (culture of biopsy material In NNN medium or Schneider's Drosophila medium).
4. Serological tests [Direct agglutination test (DAT), IFAT].
5. Formol-gel test (1 ml serum + 1 drop of formalin = gel = +ve).

Treatment:

Chemotherapy as in CL.

Epidemiology:

L. donovani

- found in India, anthroponosis.
- Infect adult
- vector is *Phlebotomus* Sandfly.
- In Africa, zoonotic
- wild Canidae and rodents are reservoir hosts

L. infantum

- found in Africa, Europe, Mediterranean area, South West Asia.
- Infect primarily infant & children.
- Humans are accidental hosts and is not believed to be transmitted from man to man. Man is a dead end in the life cycle. Endemic in Iraq.
- Zoonotic, Canidae & rodents act as reservoir hosts.
- Vector is *Phlebotomus* sandflies.

L. chagasi

- ✓ Found in central & south America & primarily affects children.
- ✓ Zoonotic
- ✓ Canidae & Cats are the reservoir hosts.
- ✓ Vector is *Lutzomyia* sandflies.

NOTE: Clinically, it is difficult to differentiate between cutaneous lesion produced by CL and VL in dogs.

Post kala azar dermal Leishmaniasis:

A condition seen in India in some patients treated for VL.. The dermal lesion may be hypopigmented or appear as erythematous macules on any part of the body that may become nodular later.

Trypanosoma

African *Trypanosomes*:

1. *Trypanosoma gambiense*
2. *T. rhodesiense*

Cause African sleeping sickness (in Africa only).

Salivarian trypanosomes: The infective stage develops in salivary glands of the vector (anterior station development).

T. gambiense

Cause African chronic, anthroponotic sleeping sickness in central Africa

Pathogenesis & symptomatology

- ✓ Infective stage enter skin → multiply → local inflammatory reaction
- ✓ (chancre) in Europeans only → 1-2 weeks → subside.
- ✓ Parasites invade blood → parasitemia (no symptoms for months)
- ✓ Invade lymph nodes → **symptoms**:
    1. Febrile paroxysms → afebrile period → febrile paroxysms → .....
    2. Lymphadenopathy.
       Winterbottom's sign: Enlargement of posterior cervical lymph nodes
    3. Erythematous skin rash (during febrile periods).
    4. Kerandel's sign: Delayed sensation to pain.
    5. ↑ IgM due to periodic changes of surface coat Ag every 7-14 days to evade immune response → Immune dysfunction → Successive waves of parasitemia.
    6. If not treated years after infection → C.N.S. invasion → Mental changes (coma, emaciation, death).

T. rhodesiense

- cause acute east African sleeping sickness.
- Zoonotic.
- Rapid fulminating disease
- Progressive more rapid → death due to toxemia before C.N.S invasion
- High parasitemia, lymphadenopathy less pronounced, no winterbottom's sign, myocarditis more sever.

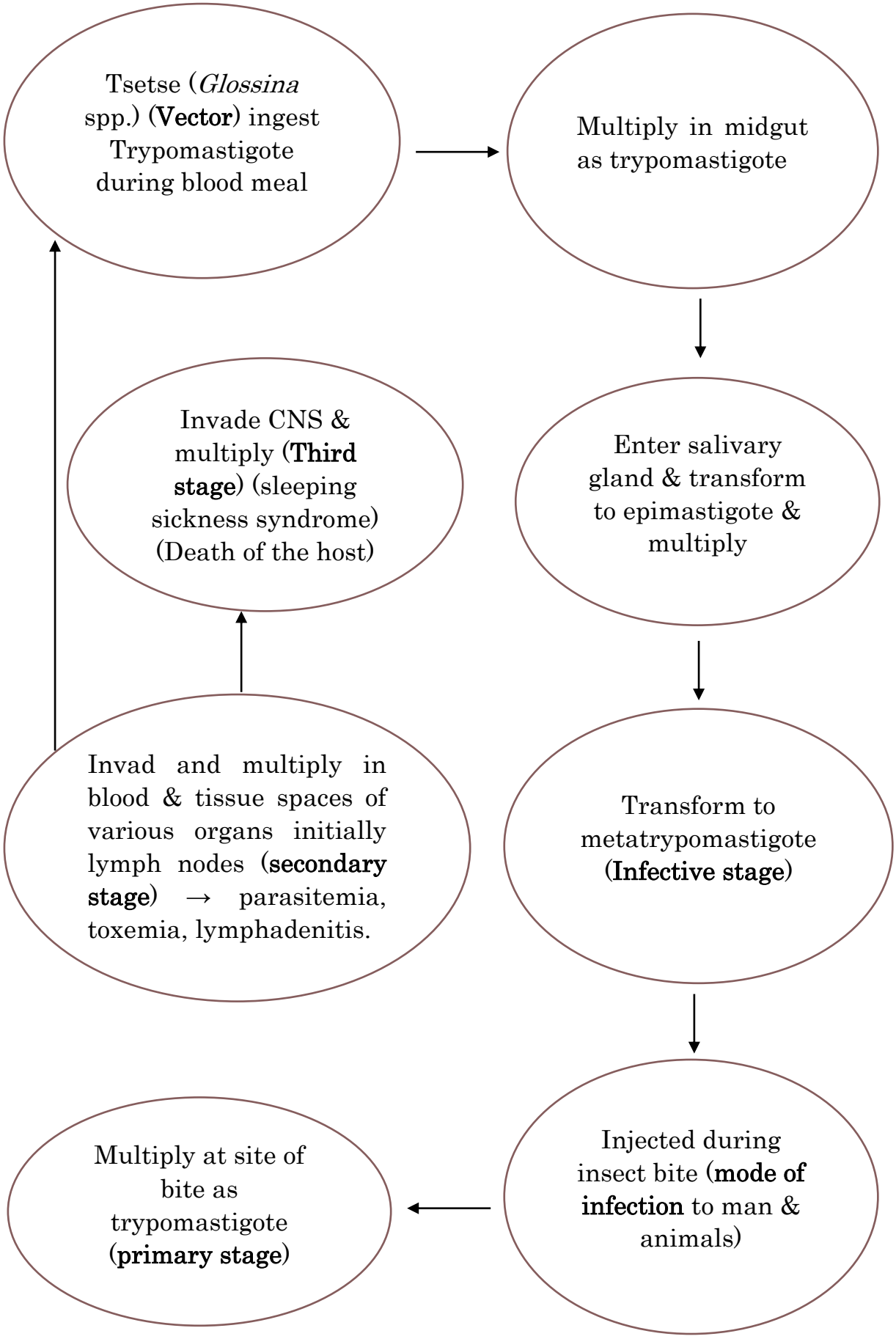
Diagnosis:

- ☒ Detection of trypomastigotes in wet and stained films of blood, lymph Node, C.N.S, skin.
- ☒ Serological test

Notes:

1. Man is the only host of *T. gainbiense*
2. Man & game animals are the host of *T. rhodesiense*.
3. Other methods of infections are:
    a. Congenital
    b. Blood transfusion.
    c. Mechanical by insect vectors.
4. Habitats are: Blood, lymph nodes, skin, CNS.

Life cycle of *T. Gambiense* and *T. Rhodesiense*



Trypanosoma cruzi

- ♠ Cause American trypanosomiasis or **Chagas disease**
- ♠ **Stercorarian trypanosomes**: The infective stage develops in hindgut of the vector & emerges from the intestine with feces (Posterior station development).
- ♠ **Chagoma**: Small granuloma in the skin caused by early multiplication of *T. cruzi*. It is erythematous subcutaneous nodule usually in face, painful, subside in 2-3 months.
- ♠ **Romana's sign**: Marked edema of one or both eyes, usually dry unilateral.
- ♠ The route of inoculation of infective stage is ocular mucosa.

Pathogenesis and symptomatology:

- ❖ At site of introduction (inoculation)
  - skin → Chagoma
  - Ocular mucosa → Romana's sign

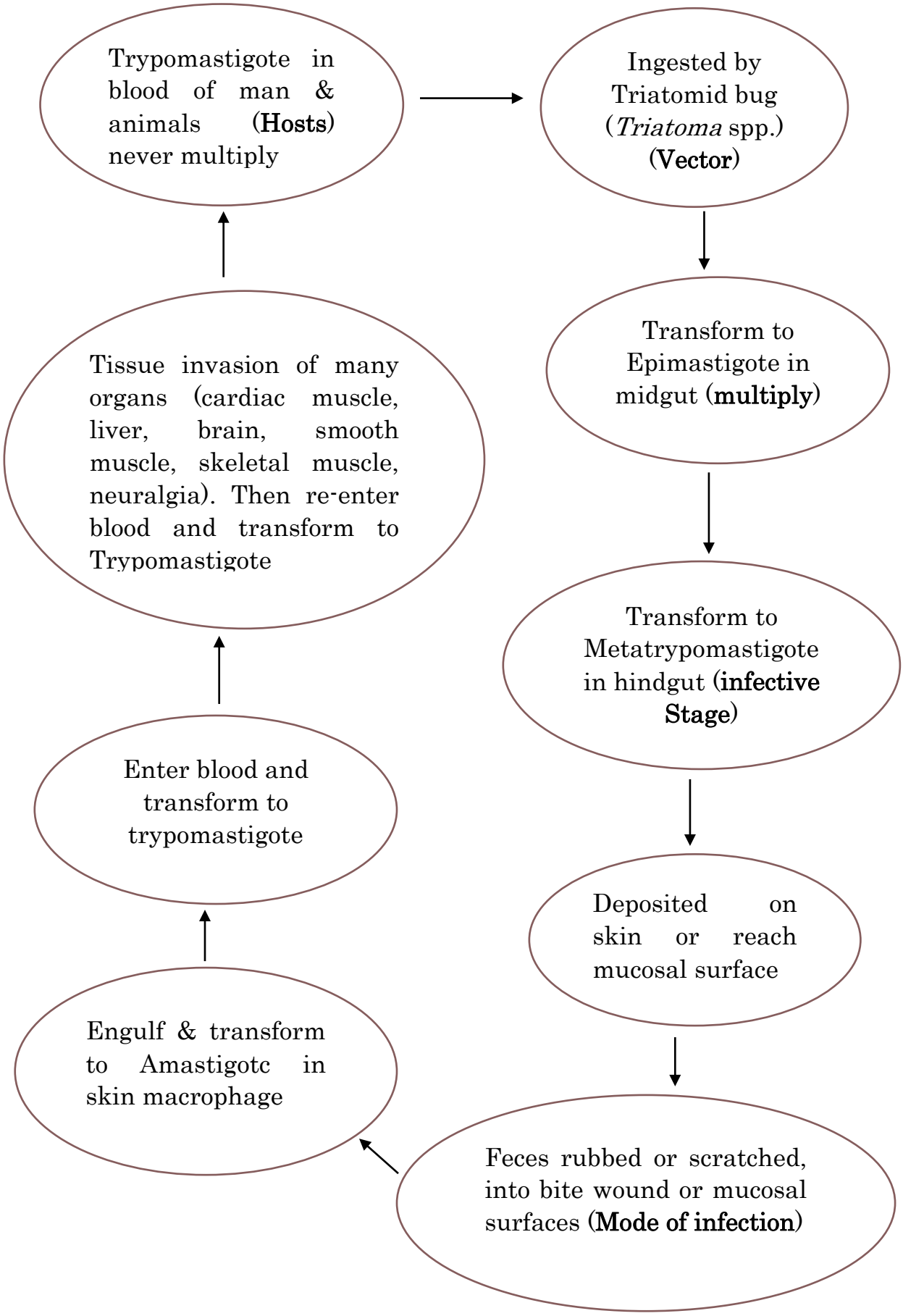
  ⇩
- ❖ Blood (no multiplication)

  ⇩
- ❖ Tissue organs

  Fever, hepatosplenomegaly, lymphadenopathy, subcutaneous edema of face, limb, rash, myocarditis, megaesophagus, cardiomyopathy (cardiomegaly), megacolon

Life cycle of *T. cruzi*

- ✓ Infective stage: Metatrypomastigote
- ✓ Diagnostic stage: Amastigote & trypomastigote
- ✓ Habitats: Blood (extracellular); Intracellular in macrophage of skin, liver, in Cardiac muscle cell, smooth & skeletal muscle & neuroglia.
- ✓ Mode of infection: By triatomid bug (*Triatoma* spp.), congenital, blood transfusion, ingestion of infected meat, ingestion of feces of infected bug.


Trypomastigote in blood of man & animals (Hosts) never multiply
Ingested by Triatomid bug (*Triatoma* spp.) (Vector)
Transform to Epimastigote in midgut (multiply)
Transform to Metatrypomastigote in hindgut (infective Stage)
Deposited on skin or reach mucosal surface
Feces rubbed or scratched, into bite wound or mucosal surfaces (Mode of infection)
Engulf & transform to Amastigotc in skin macrophage
Enter blood and transform to trypomastigote
Tissue invasion of many organs (cardiac muscle, liver, brain, smooth muscle, skeletal muscle, neuralgia). Then re-enter blood and transform to Trypomastigote

- **QI**: In the past, artificial infection with oriental sore may be induced in healthy individual, where (site) and why?
- **Q2**: In diagnosis of CL., specimens should be taken from the margin or the base of the lesion (papule or ulcer), why?
- **Q3**: Leishmanin skin (intradermal) test cannot be used in diagnosis of VL. Why?
- **Q4**: Although high production of Ig in VL., but has no role in recovery from the disease.
- **Q5**: Mention the specimen of choice for diagnosis of kala azar.
- **Q6**: Which organ is severely affected and invaded by large No. of amastigotes in VL.
- **Q7**: *L.donovani* is anthroponotic (man-vector-man transmission) but in *L. infantum* (endemic in Iraq), man is considered as a dead end point in the life cycle, why?
- **Q8**: Formol-gel test may be used in diagnosis of kala azar, but is not specific, why?
- **Q9**: *L. infantum* can be transmitted from animal to man but cannot be transmitted from man to man, why?
- **Q10**: Which of the following species of *Leishmania* considered as more serious in the old world and why ?
    - *L. tropica*
    - *L. major*
    - *L. aethiopica*.
- **Q11**: Mention three main symptoms and signs in patient suspected to has VL.
- **Q12**: African trypanosomiasis can easily be diagnosed by blood smear examination but in American trypanosomiasis is difficult, why?
- **Q13**: Chagas disease is more difficult to controlled than gambian trypanosomiasis, why?
- **Q14**: Immune dysfunction is usually occurs in African sleeping sickness, why?
- **Q15**: Successive waves of parasitemia usually occurred in African trypanosomiasis, why?
- **Q16**: African trypanosomiasis is commonly called sleeping sickness, why?
- **Q17**: Roman's sign sometime occurs in chagas disease, why?
- **Q18**: Mention the sign which considered as the first evidence of infection with *Trypanosoma gambiense.*
- **Q19**: Mention the vectors of the following diseases:
    1. Leishmaniasis in old world.
    2. Leishmaniasis in new world.
    3. Chagas disease.
    4. Sleeping sickness.

- **Q20**: African sleeping sickness and chagas disease are not recorded in Iraq, why?