Leishmaniasis Etiology

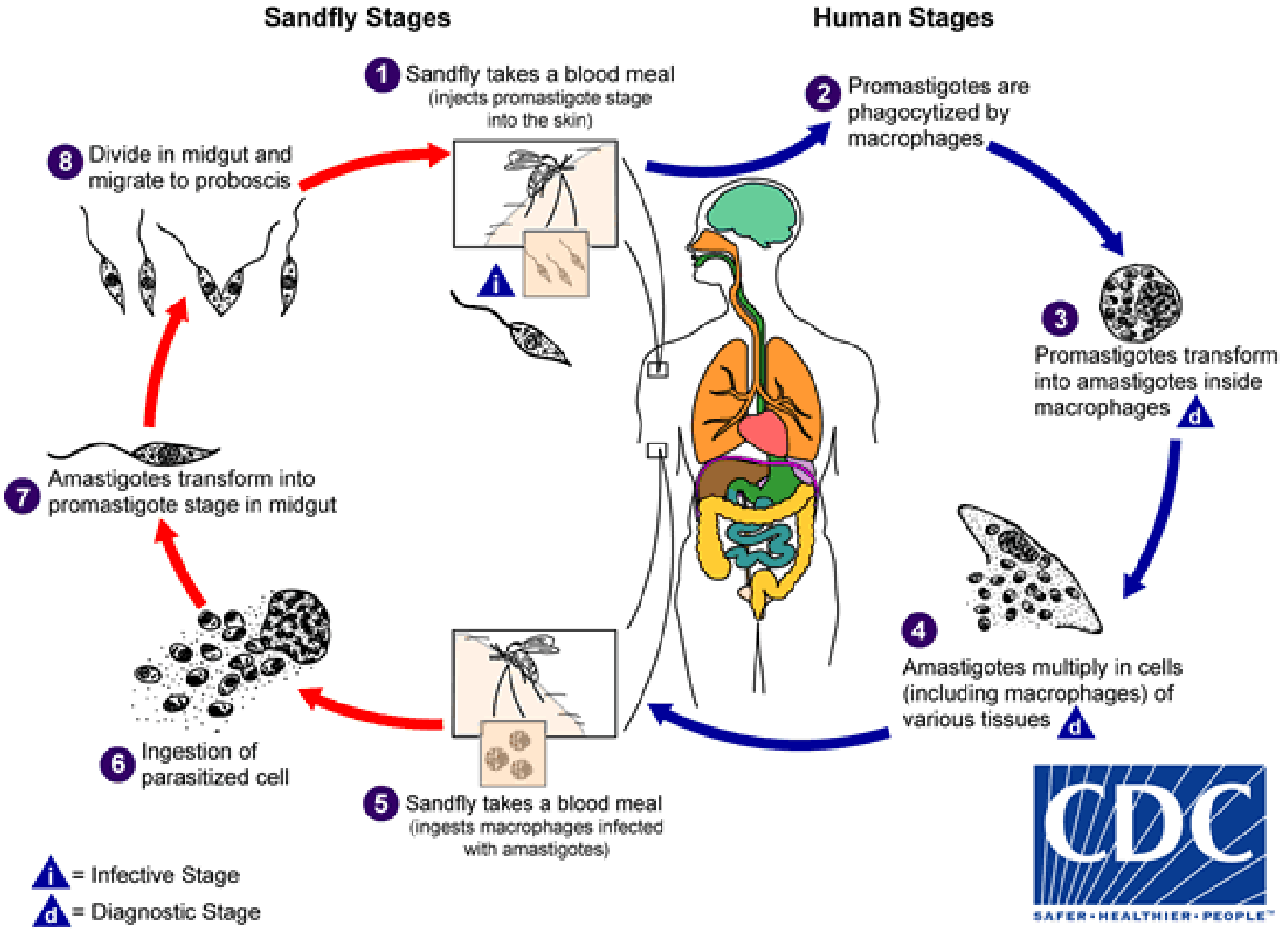
- **O. Kinetoplastida, Fam. Trypanosomatidae**
- **Dimorphic with 2 main stages:**

Intracellular amastigote	Flagellate promastigote
Round 2 – 6 µm Φ	Long, slender 15 - 30 µm long
Nucleus , kinetoplast, internal flagellum	Central nucleus, kinetoplast , long anterior flagellum
In mononuclear phagocytic system of the mammal host	In intestinal tract of the insect vector (or in culture)

- **Classification revised, based on observable similarities (phenetics) & evolution history**
- **Isoenzyme electrophoresis is the reference technique for classification**

Sandfly, Diptera, Sub-fam Phlebotominae

Leishmaniasis Life cycle



CDC
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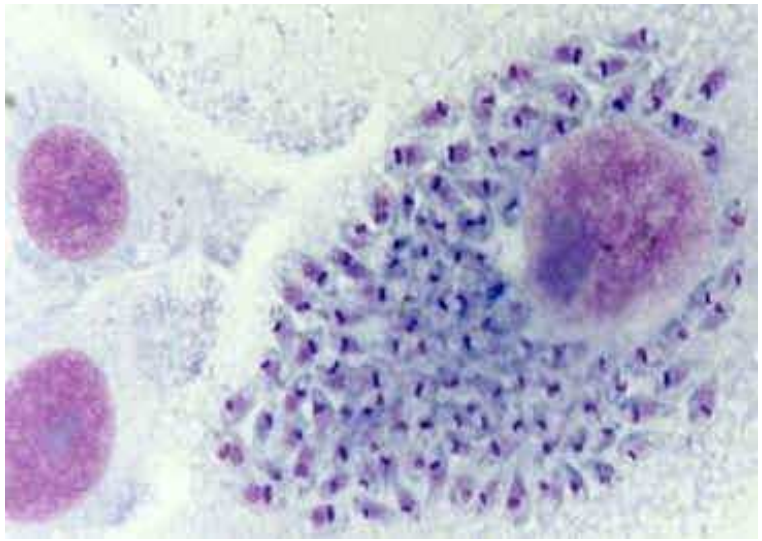
http://www.dpd.cdc.gov/dpdx

Promastigotes and amastigotes of *L. donovani*



amastigotes in macrophage

Leishmaniasis Geographical distribution

- **Worldwide. Distribution of disease related to the distribution of the sand fly. 12 M cases**

VL	CL
• 47 counties (also in East-Africa) • *L. donovani* (anthroponotic) is found in China, India, East-Africa • *L. infantum* (zoonotic) is found in China, Brazil, India • 90% of cases are in India, Bangladesh, Nepal, Sudan, Brazil	• Majority of Old World CL is due *to L. major* (zoonotic*)* & *L. tropica* in Near and Middle East (Afganistan to Syria) • *L. major* if also found in West, North, East Africa and Central Asia • *L. tropica* (anthroponotic) is also found in North Africa • *L. aethiopica* is found in Ethiopia and Kenya • In the New World, *L. braziliensis* has a wide distribution then *L. mexicana* or *L. panamensis* more restricted.

Leishmaniasis Clinical features VL

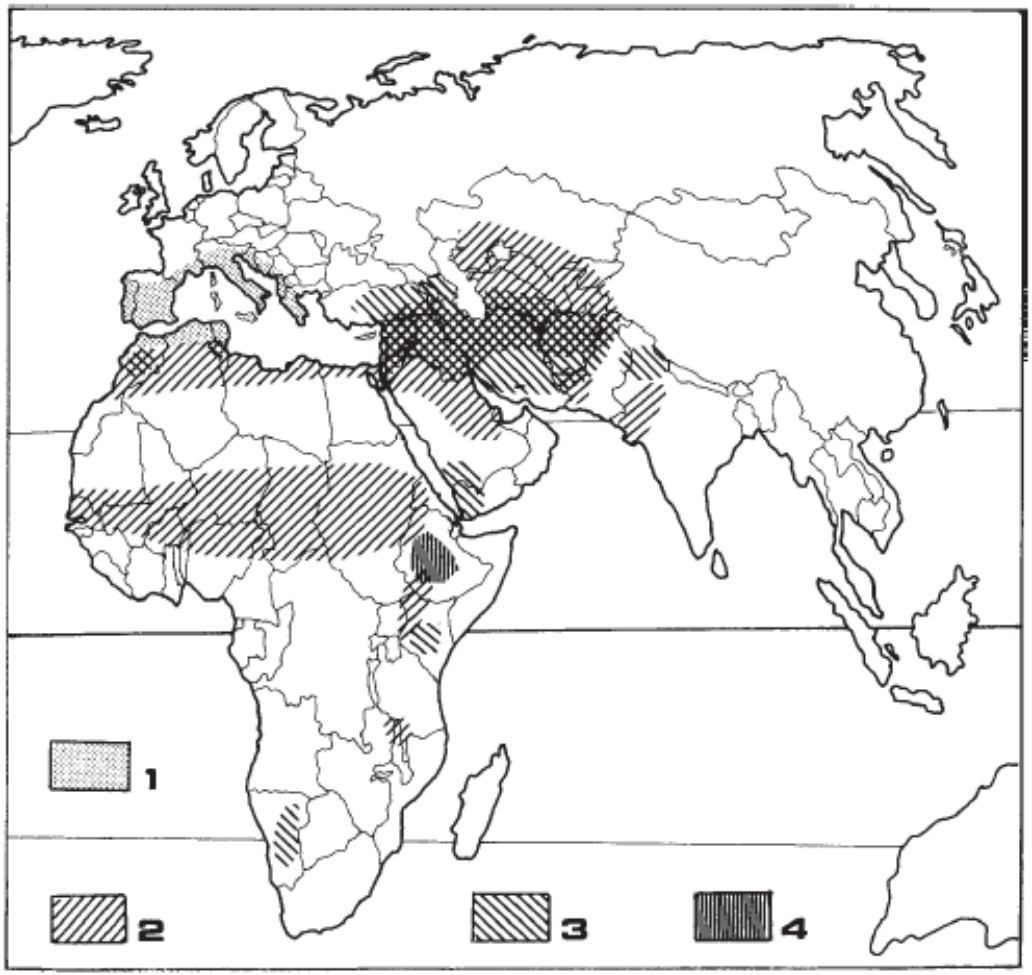
VL (*L. donovani, L. infantum; L. archibaldi* in E-Afr)

- **Incubation period: 2-6 m (10d to 10y!)**
- **Onset: sudden (T°c ↗, fever for days) or gradual (irregular fever)**

Then:

- **Protuberant abdomen**
- **Muscle wasting of limbs**
- **Anaemia, fever, weight loss, splenomegaly, hepato megaly, adenopathy**
- **In India, grayish skin due to anaemia ⟶ kala-azar**
- **Diarrhoea often reported (ulcerations of digestive mucosa)**
- **Pulmonary involvement possible (dry cough)**
- **Epistaxis (nose bleed mostly, sometimes gums)**

Distribution of Leishmania sp. in the Old World



Geographical distribution of Old World CL. 1, *L. infantum* CL; 2, Zoonotic CL caused by *L. major*; 3, *L. tropica* CL; 4, *L. aethiopica*

Leishmaniasis Clinical features VL

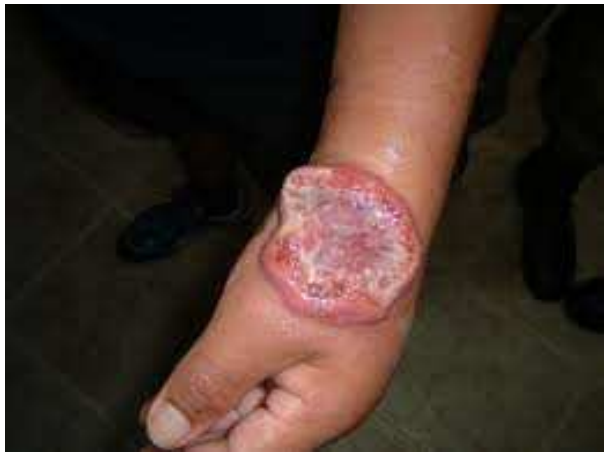
Then worsening with amplification of all symptoms

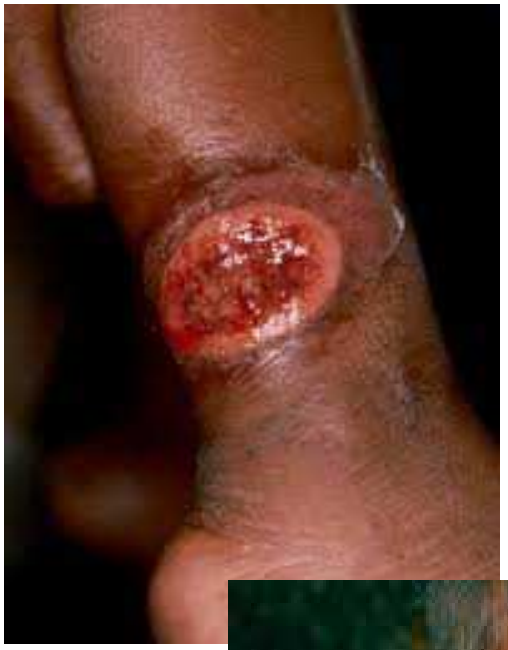
- Ascites are late signs of bad prognosis
- Sometimes oedema/pleural effusion
- Renal involvement may occur (albuminuria)

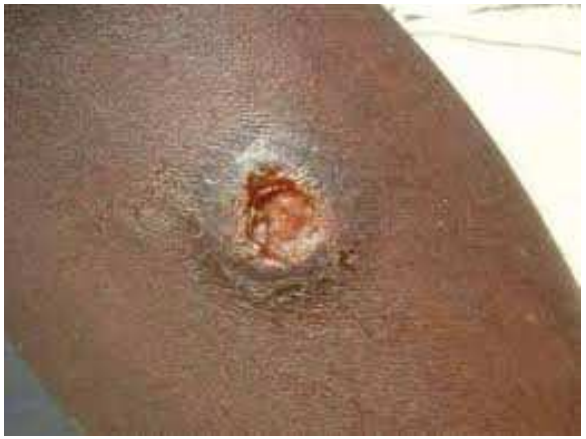
Biological parameters: alterations

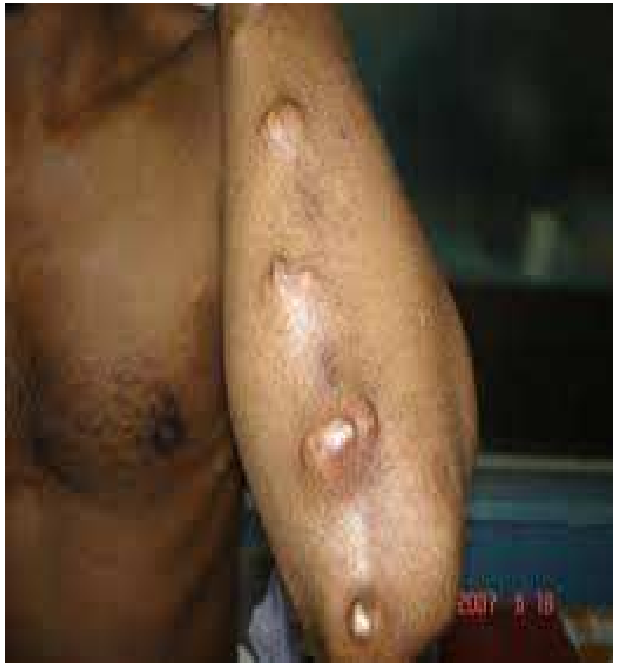
Haematology	Plasmatic proteins
•Anaemia (normochromic/normocytic) is intense (Hb levels 7-10g/dL) •Leucopenia (1-3000/mm^3) •Severe thrombopenia (≤ 4000/mm^3) •Pancytopenia is communly associated with VL	•Inflammation syndrome with raised erythrocytes sedimentation rate and increase of C reactive protein •Low albumin levels •Hypergammaglobulinaemia (over production of IgG mostly)

Cutaneous leishmaniasis



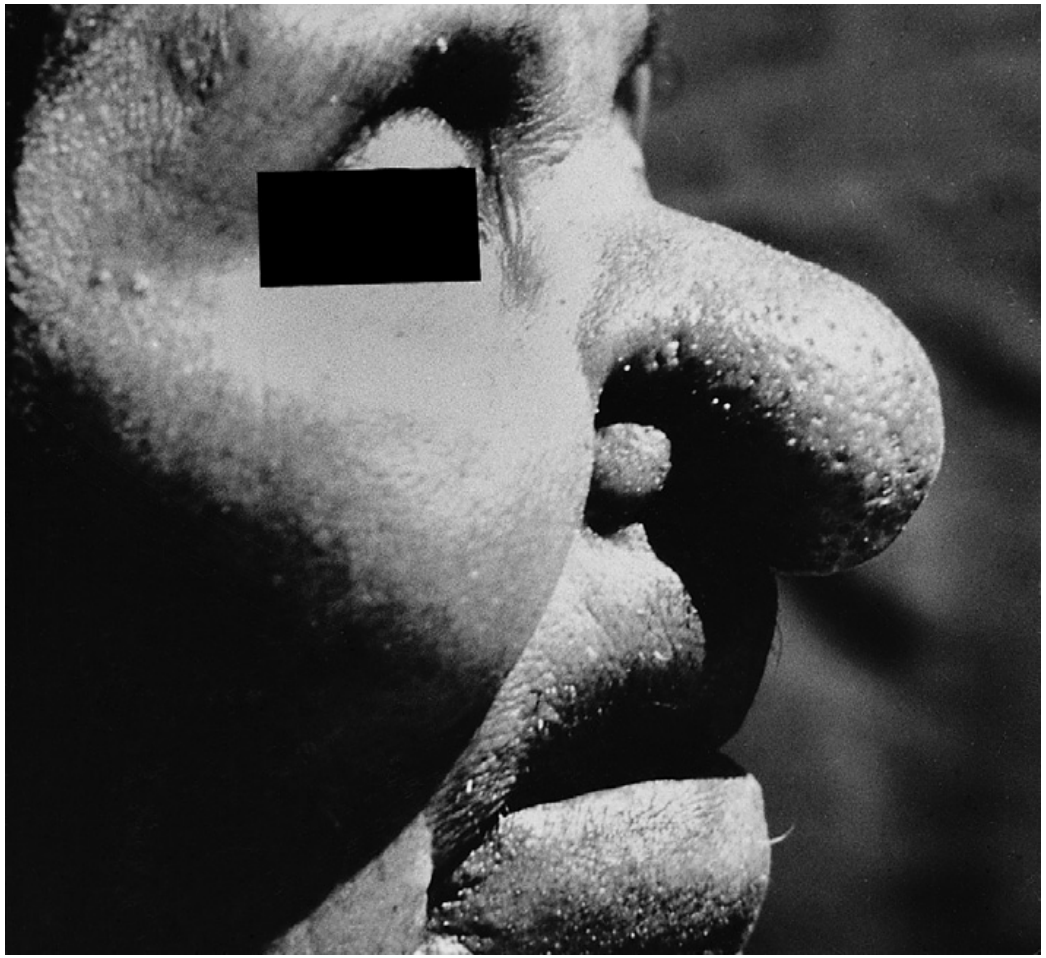




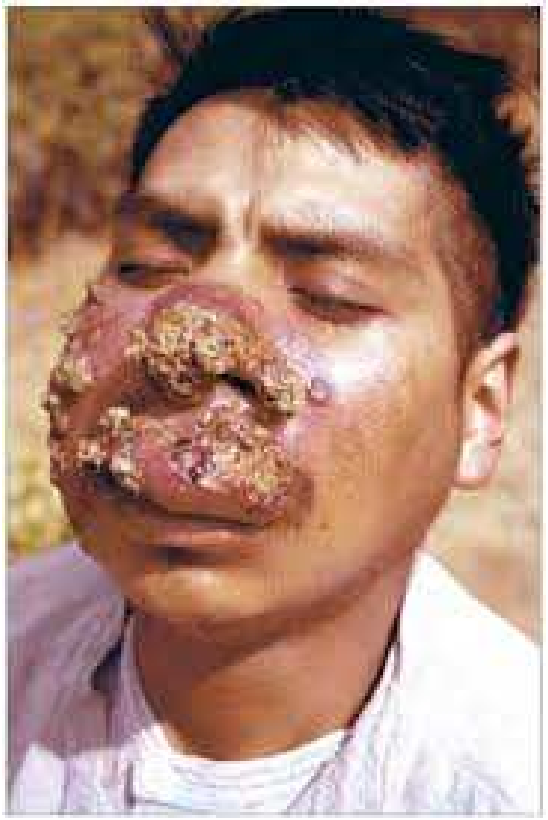


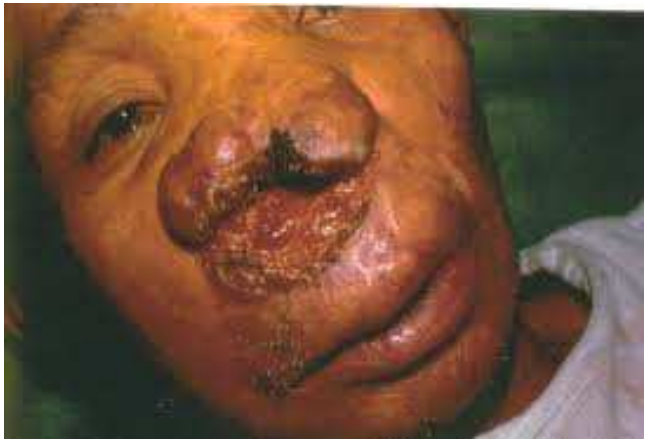
Mucocutaneous leishmaniasis: ‘tapir nose’.

(From Manson’s Tropical Diseases, 22nd edition)



Mucocutaneous leishmaniasis





Leishmaniasis Diagnosis 1

- **Based on clinical presentation, epidemiology but confirmed by direct detection of parasites or presence of specific Ab**
- **Sample collection:**

VL	CL & MCL
• Bone marrow/ spleen aspiration • Splenic puncture • Lymph node aspiration • Parasite detected in peripheral blood	• Skin material by superficial scraping, needle aspiration or biopsy punch • Site is important & depends on the clinical type of lesion

- **The collected material can be smeared on slide, cultures, fixed or used for PCR**
- **Staining used is May Grünwald- Giemsa**

Leishmaniasis Diagnosis 2

- Direct observation: sensitivity is low
- Culture in blood agar NNN: higher sensitivity & allows for parasites identification by isoenzymes electrophoresis, mononuclear Ab, specific probes
- Recent: molecular diagnosis (detection of parasite DNA through PCR. High sensitivity, high specificity
- Immunological diagnosis:
  - In VL, DCL: humoral response → high level of specific Ab in serum. May be absent in immunocompromised
  - In CL, MCL: cell-mediated → delayed hypersensitivity test → several tests ***

Leishmaniasis Treatment 2

- **Treatment according to clinical features. Case to case!**

TYPE	MANAGEMENT/TREATMENT
VL	Tx as soon as diagnostic is made Mainly antimonials & Amphotericin B Correct nutritional deficiencies if anaemia & wasting BUT resistance to antimonials. Combinations of drugs not tested yet Leishmaniasis in HIV + is non responsive to drugs & more side effects
LCL	Mild forms: untreated (*L. major, L. peruviana*) or local antimonials Large lesions: antimonials (20d)
DCL	Once established, resistant to Tx Antimonials may improve evolution for a while Need for tests of new formulations
MCL	Tx of primary lesions with antimonials (20d) Tx fast to avoid mutilations Amphotericin B used but few reports