PARASITIC DISEASES

1. Toxoplasmosis

a) cerebral toxoplasmosis
b) extracerebral toxoplasmosis

2. Leishmaniosis

a) Cutaneous and mucocutaneous leishmaniosis
b) Visceral leishmaniosis

3. Trypanosomiasis

a) The American trypanosomiasis
b) The African trypanospmiasis
    West African trypanosomiasis
    East African trypanosomiasis

Svatava Snopková, 4/2020

TOXOPLASMOSIS

DEFINITION

- An acute or chronic infection caused by the obligate intracellular protozoan ***Toxoplasma gongii***

In immunocompetent human

- Infection is usually **asymptomatic**

In immunocompromised patient

- symptoms occur, they range from a mild, self-limited **to a fulminant disseminated disease**

SYMPTOMS

Usually involve the following:

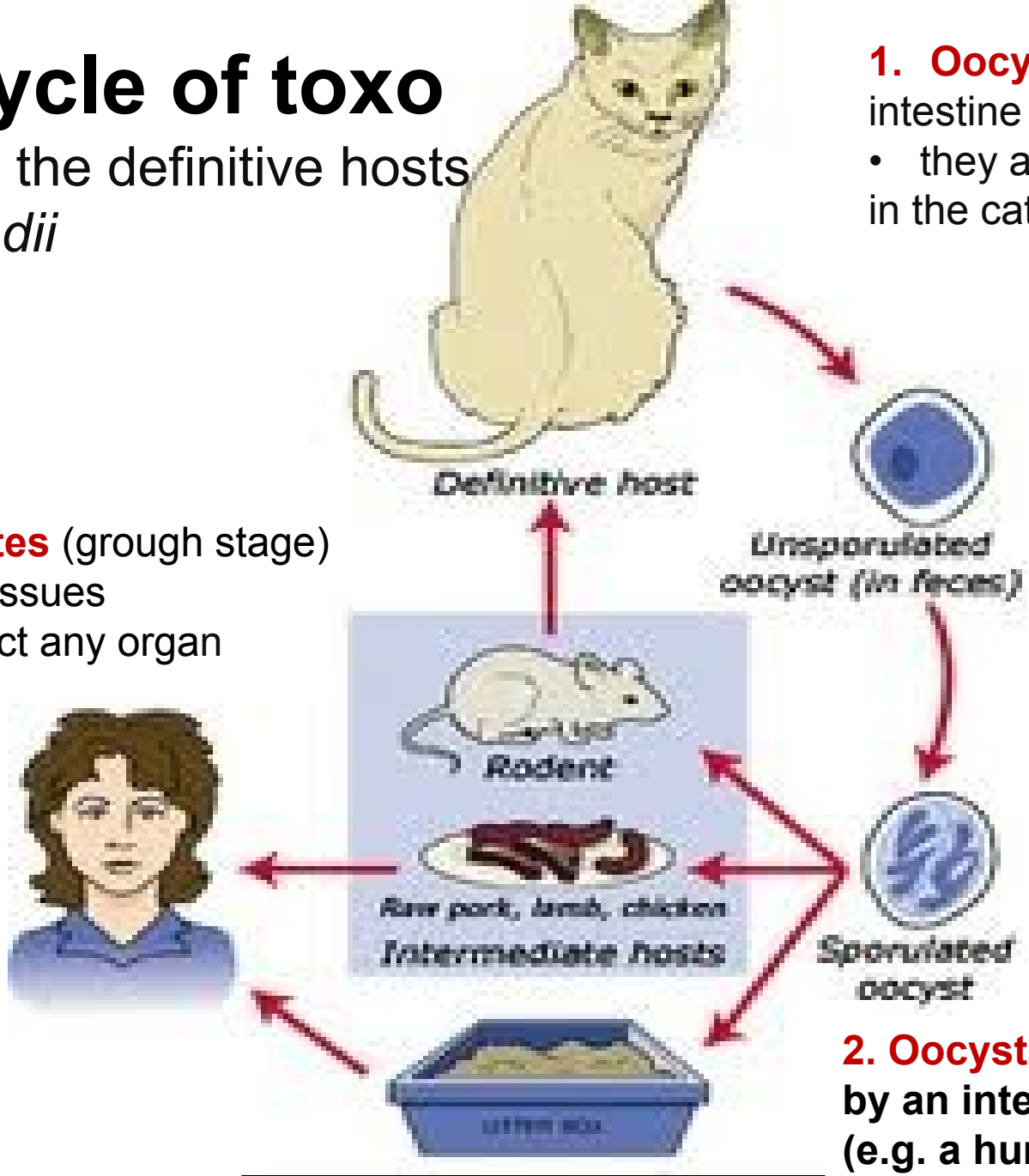
- Central nervous system, eyes
- Skeletal or cardiac muscles
- Lymph nodes, Liver, Lungs

Severe diseminated diseases (infections)

- In an **immunocompromised patients**
- By the transplcental passage of parasite
  from an infected mother to the fetus
  (congenital toxoplasmosis)

Life cycle of toxo

- cats are the definitive hosts for *T. gondii*

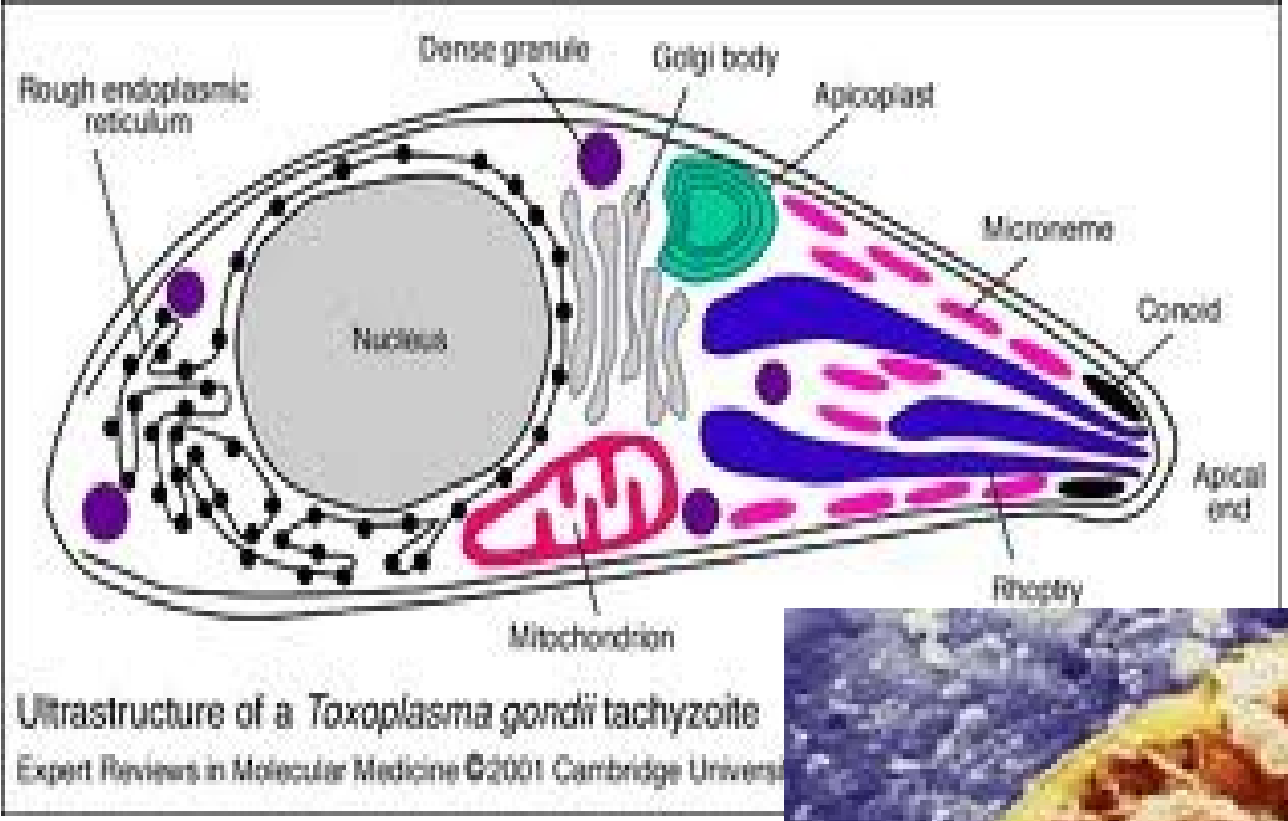


1. Oocysts in the cat s intestine are created

- they are excreted in the cat feces

2. Oocysts are ingested by an intermediate host (e.g. a human)

3. Tachyzoites (grough stage) migrate to tissues and can infect any organ

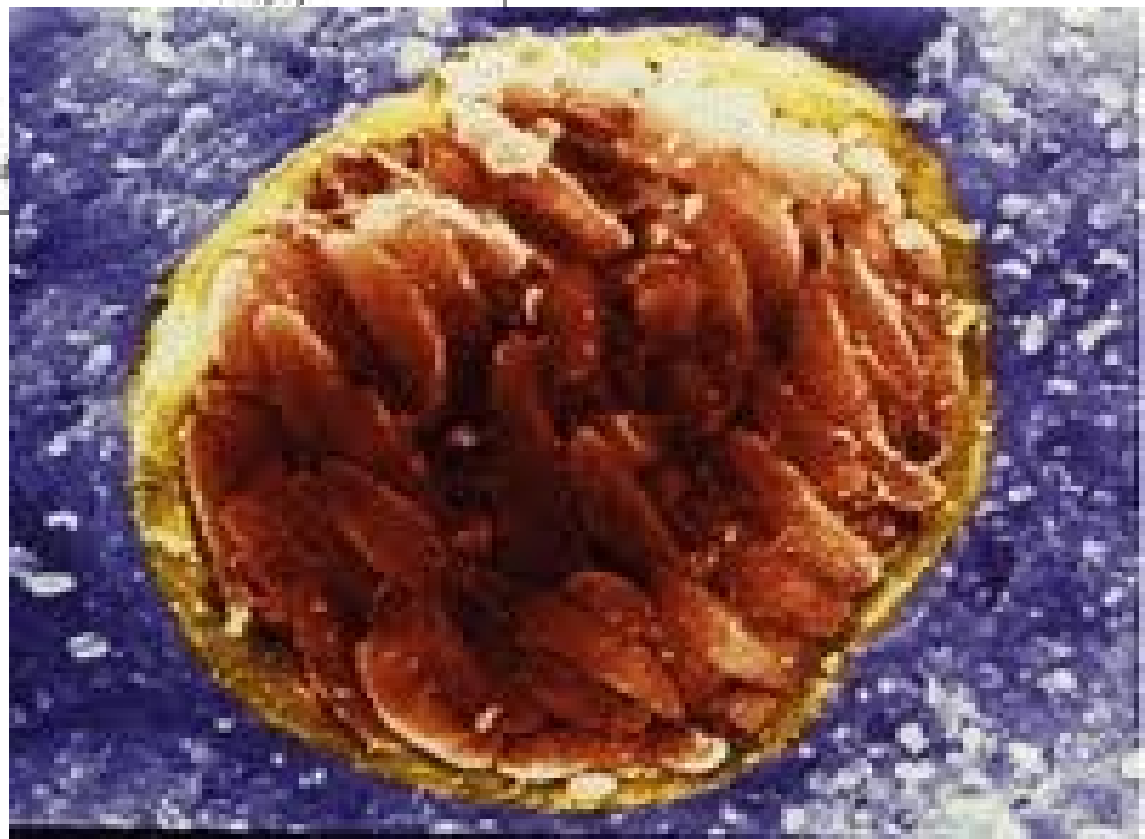


Ultrastructure of a *Toxoplasma gondii* tachyzoite

Expert Reviews in Molecular Medicine ©2001 Cambridge Universi

Tachyzoites

- grouwth stage of toxoplasma
- migrate and form cysts in various tissues



Epidemiology

The seroprevalence of toxo depends on geografic location:
US – between 3-67% tropical countries – up to 90%

Risk for toxoplasmosis

- eating undercooked meat

Risk – steak tartare

Epidemiology

Risk

- contaminated vegetables

Ingestion of oocysts from contaminated soil

TOXOPLASMOSIS

- Immune responses are able to eliminate most of the tachyzoites when immune systém is sufficient and competent
- Therefore **80 – 90%** of cases in immunocompetent persons are **asymptomatic**

- the greatest incidence of toxo is seen among patients with a low CD4 count

  <100 cells/mm^3 due to immunoderficiency
- In areas with high seroprevalence for toxoplasmosis, **25% to 50% of all AIDS** patients, who are not receiving antiretroviral therapy, will develop **CNS toxoplasmosis**

Toxo in immunocompromised patients

The infection usually involves the **CNS**

Clinical manifestations of cerebral toxoplasmosis infection include the following:

- Headache, seizures,weakness
- Cranial nerve abnormalities, Visual field defects
- Mental status changes
- Cerebellar signs
- Speech abnormalities, Meningism
- Sensory or motor disorders, Disorientation, Hemiparesis
- Convulsions, Coma and death

EXTRACEREBRAL TOXO

- Less common among patients with immunodeficiency
- The prevalence is estimated

  at 1,5% to 2,0%

  - **lungs** (pneumonitis)
  - **eye** (chorioretinitis)
  - **heart**

Cases of gastrointestinal, liver, skin, or multiorgan involvement also have been reported

Extracerebral toxoplasmosis

retinochoroiditis

- Involving other organs among patients is rare
- Dg. is usually based on biopsy

OCULAR TOXOPLASMOSIS

- Is usually based on a suggestive **ophthalmoscopic picture**
- Histopathologic identification of *T.gondii*

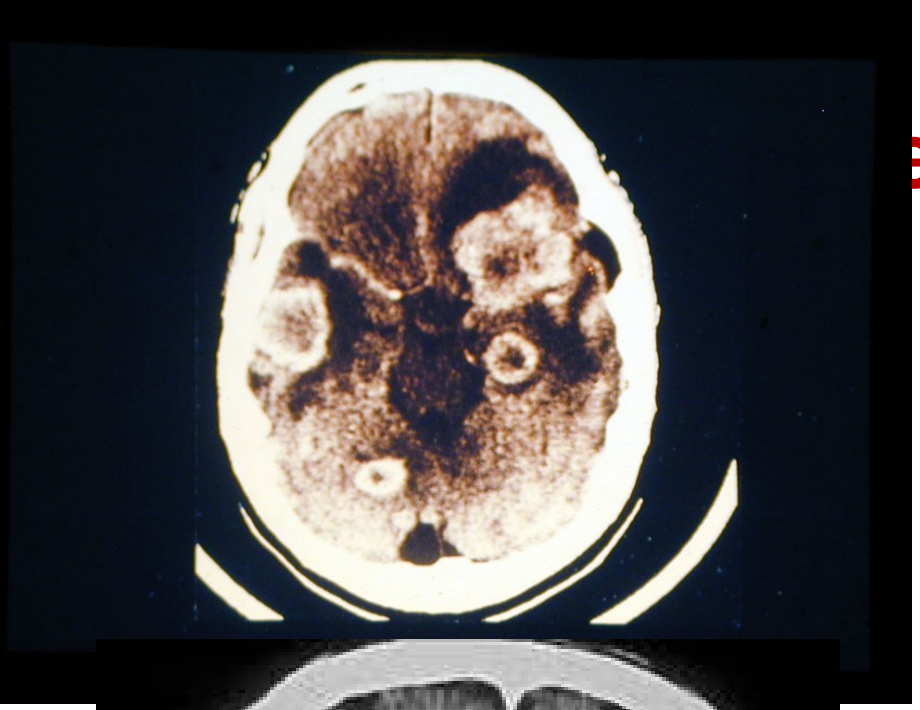
  in the eye can establish the diagnosis

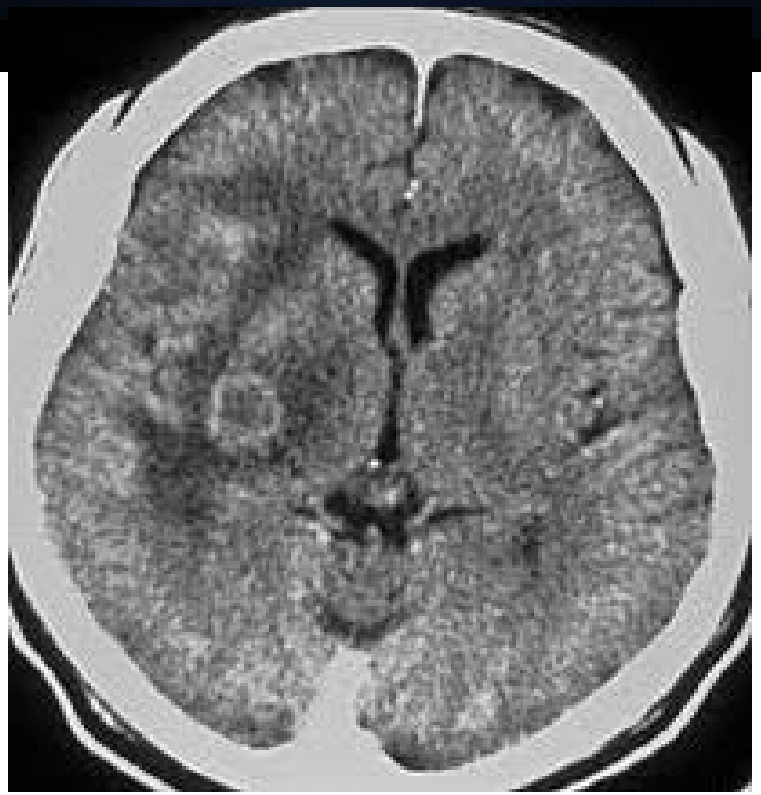
DIAGNOSIS

Is based on:

- **Compatible clinical picture**
- **Neuroimaging findings**
- **Serology**

Definitive diagnosis is based on **pathology.**





euroimaging (CT, MRI)

The **abscesses** of cerebral toxoplasmosis are typically

- Multiple
- Located in the cortex or deep nuclei (thalamus and basal ganglia)
- Surrounded by edema
- Enhance in a ringlike pattern with contrast

SEROLOGY

- Approx. **20%** of patients

  have no detectable antibodies
- Titer of antibodies does not always rise during infection
- Negative serology does not rule out infection
- But a rising titer may be of diagnostic significance

OTHER LABORATORY METHODS

PCR (polymerase chain reaction)

in blood samples suggest that

- This modality has limited diagnostic value in cases of cerebral toxoplasmosis

CSF (cerebrospinal fluid)

- Is also nonpathognomonic and reveals **elevated protein** and **mild pleocytosis**

MAIN TREATMENT

The regimen of choice for acute therapy

- **Pyrimethamine** 50 to 75 mg/d

  + **sulfadiazine** 4 to 8 g/d

- Leucovorin – coadministtered to prevent the folinic acid deficiency and ameliorate the hematologic toxicity of pyrimethamine
- Duration of treatment

  – usually **for 6 to 8 weeks**

ALTERNATIVE TREATMENT

- Pyrimethamine + clindamycin
- Atovaquone (alone)
- Atovaquone + pyrimethamine
- Clarithromycin
- Clarithromycin + pyrimethamine
- Azithromycin + pyrimethamine
- Trimethoprim-sulfamethoxazole

PATIENT FOLLOW-UP

After induction treatmen

- Patients with immunodeficiency schould receive lifelong **suppression therapy**

  pyrimethamine 25-50 mg/d

  + sulfadiazine 2-4 g/d

PROPFYLAXIS FOR HIV+ INDIVIDUALS

***Toxoplasma*-seropositive**

- With CD4 counts less than 100 cells/mm3 should receive **prophylaxis against toxoplasmosis** (the doses of TMP/SMX recommended for *P. carinii* pneumonia appear to be effective)

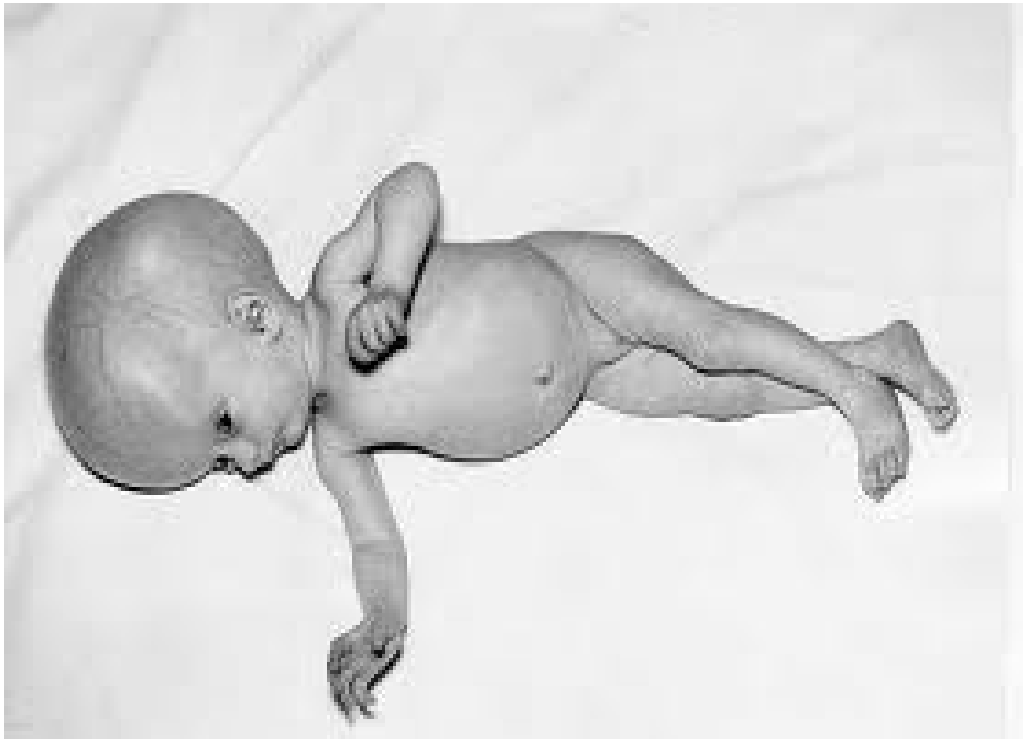
PREVENTION
FOR INDIVIDUALS AT RISK

- Not to eat raw or undercooked („pink“) meat
- Wash fruits and vegetables
- Wash hands after contact with raw meat
  and after contact with soil
- Wash hands after changing a cat litter box

PRIMARY PROPHYLAXIS for HIV-positive people

conditions	pathogen	drug
CD4+ any + TB exposure	*M. tuberculosis*	isoniazid (+pyridoxin), rifampicin, pyrazinamid, ethambutol
CD4+ < 200/mm3	*Pn. carinii jiroveci*	co-trimoxazol, pentamidine (aerosol), dapson
CD4+ < 150/mm3 + antibody to *Toxoplasma* positive	*Toxoplasma gondii*	co-trimoxazol, dapson, pyrimethamin(+folinat)

CONGENITAL TOXOPLASMOSIS

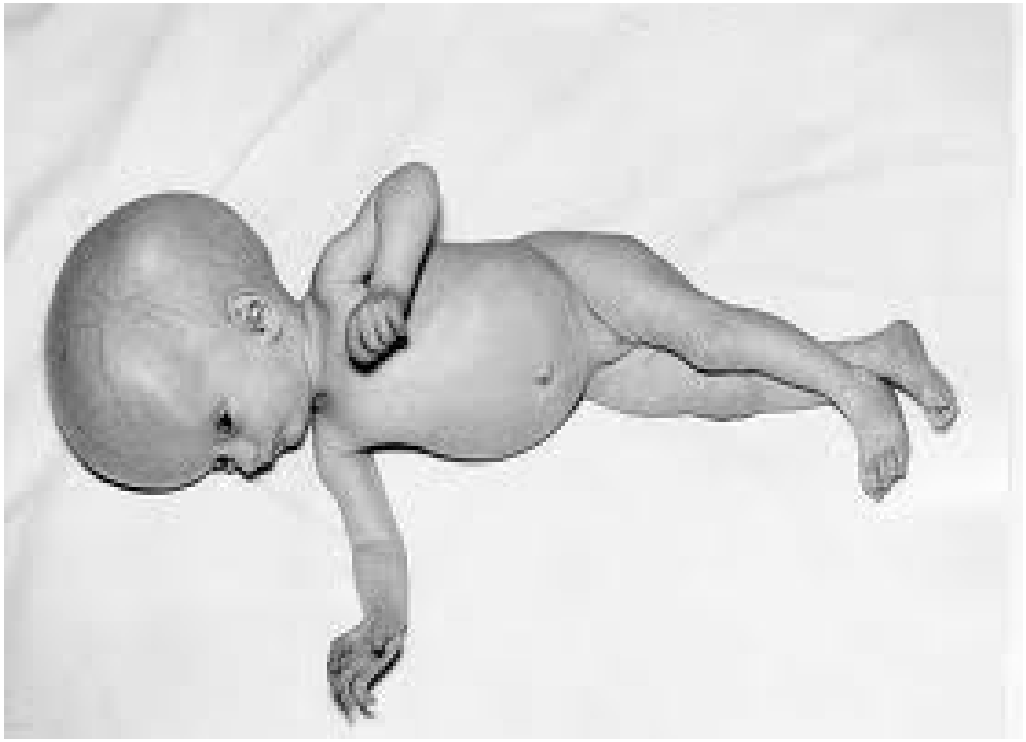


Sabin tetrade

- classic tetrade of signs

1. Retinochoroiditis
2. Hydrocephalus
3. Convulsions
4. Intracerebral calcifications

CONGENITAL TOXOPLASMOSIS



- Clinical findings are variable

  There may be **no sequelae**, or sequelae may develop at various times after birth

  Premature infants may present with CNS or ocular disease

  Full-term infants usually develop milder disease, with hepatosplenomegaly and lyfadenopathy

Immunocompromised patients

Intimate contact with cats is risk for acquering of toxo

for pregnant woman

and for immunocompromised patients

LEISHMANIASIS

Leishmaniasis

- Leishmaniasis refers to the spectrum of diseases caused by the **protozoa *Leishmania* spp.**
- Protozoa are transmitted by **a sandfly vector**
- Clinically, leishmaniasis is divided into:
  - **Cutaneous**
  - **Mucocutaneous**
  - **Visceral**

Epidemiology - incidence

- Leishmania infection is among the most common parasitic diseases

- Currently, leishmaniasis occurs in four continents
- Is considered to be **endemic in 88 countries**
- 72 of which are developing countries

- With about **10 million infected persons**
- **400 000 new infections every year** are referred globally
- In Europe, infections ***L. major*** and ***L. tropica*** are increasingly occuring due to travel and immigration

Old World cutaneous leishmaniasis

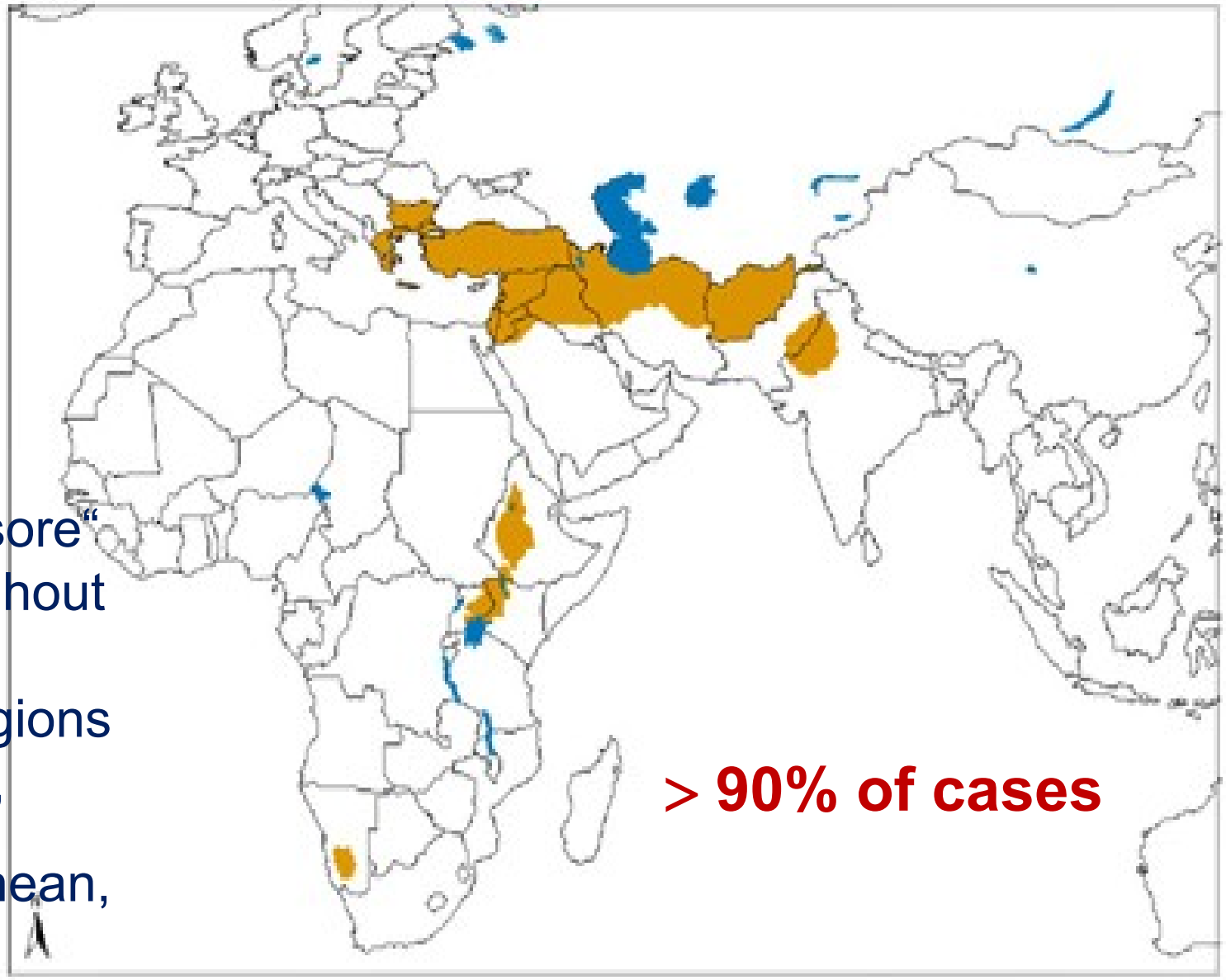
- ***L. tropica***

and related species

- ***L. aethiopica***

The „oriental sore“ occurs throughout tropical and subtropical regions in Asia, China,

the Mediterranean, and Africa



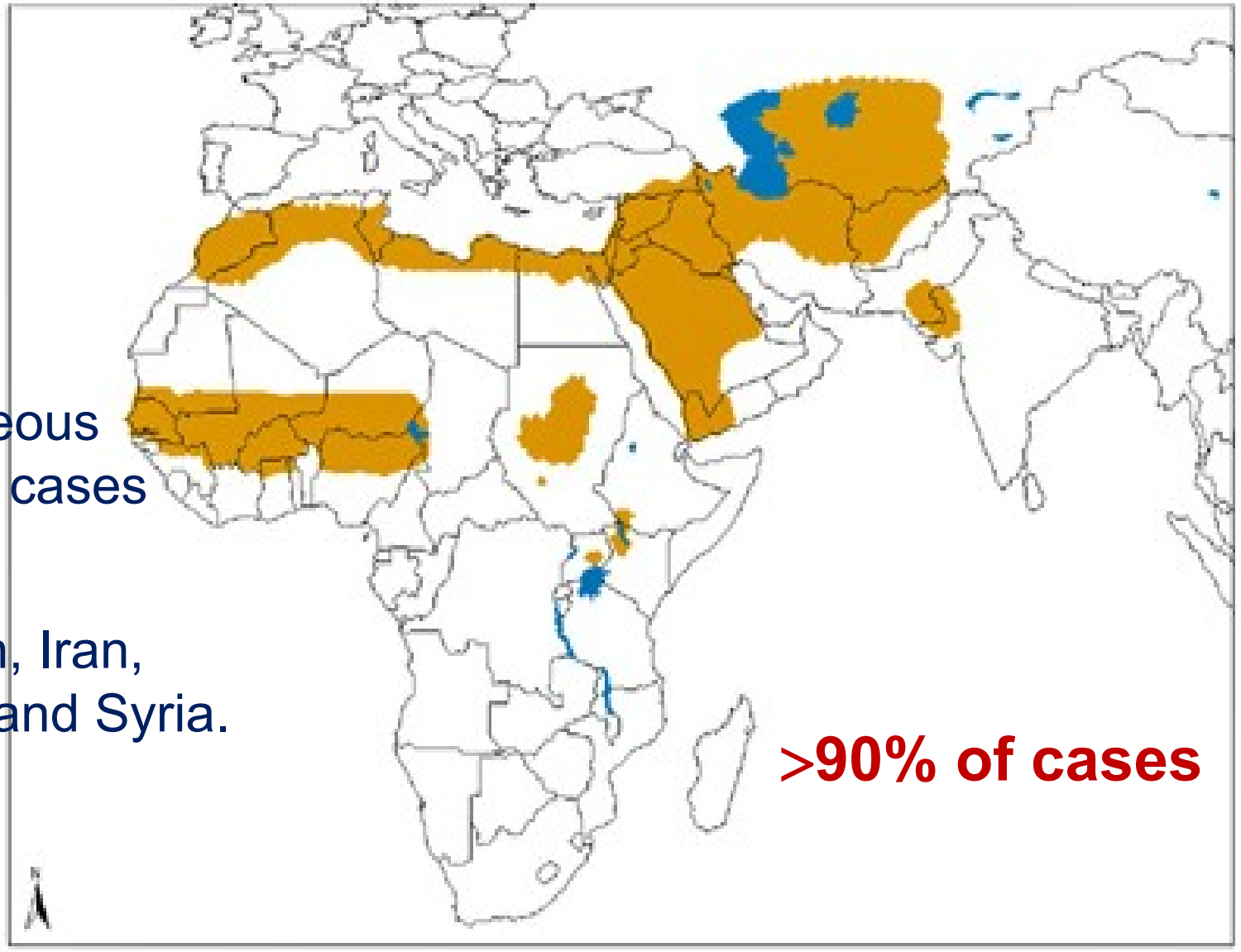
> 90% of cases

Old Word cutaneous leishmaniasis

- ***L. major***

90% of cutaneous leishmaniasis cases occur

in Afghanistan, Iran, Saudi Arabia and Syria.

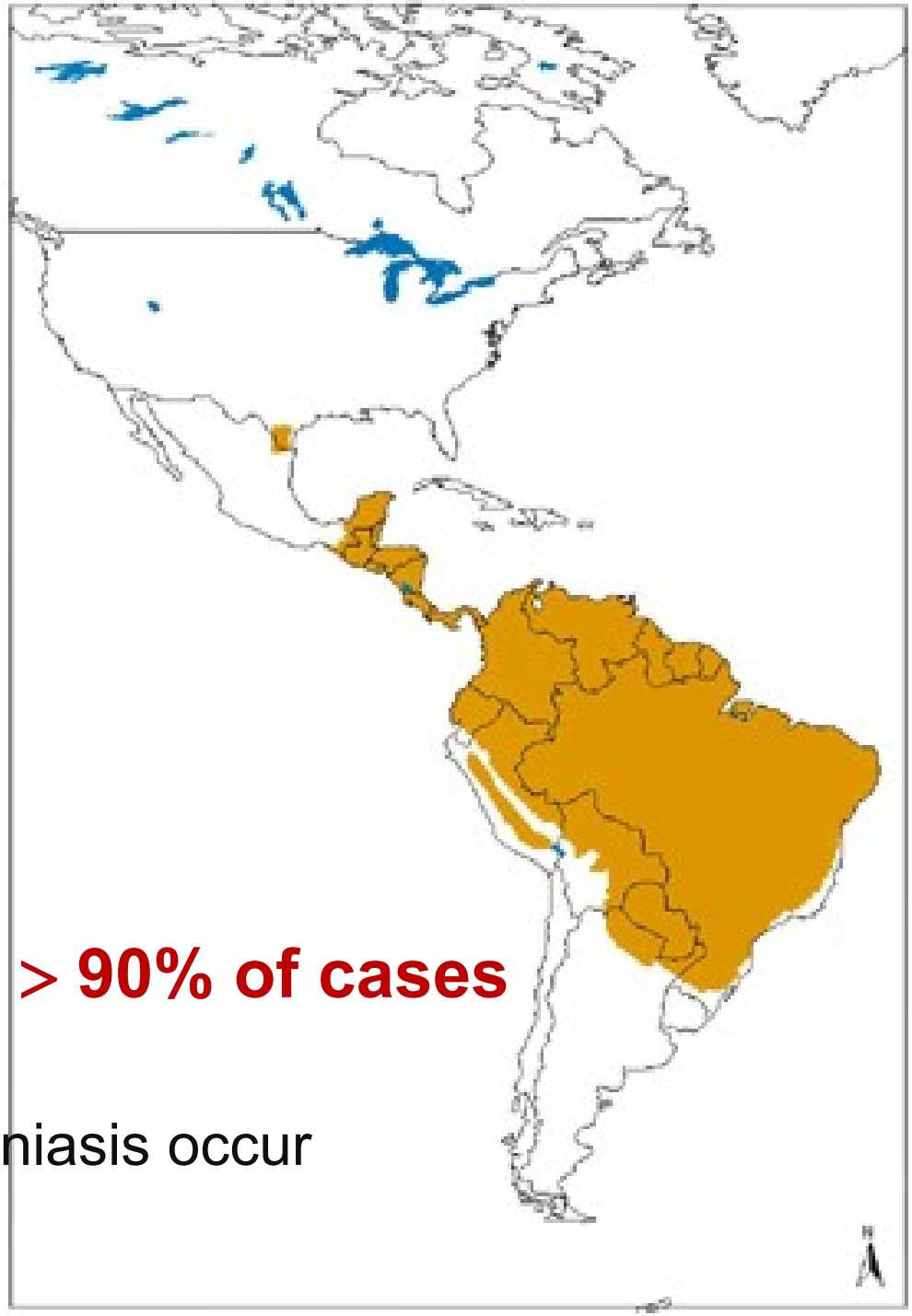


New World cutaneous and mucocutaneous leishmaniasis

- ***L. brasiliensis***
- ***L.chagasi***
- ***L. mexicana***

Widespread

in Latin America



90% of mucocutaneous leishmaniasis occur in Bolivia, Brazil and Peru

Geographical distribution of visceral leishmaniasis in the Old and New world

90% of all visceral leishmaniasis cases occur in Bangladesh, Nepal, India, Sudan and Brazil

Typical risk factors for Leish.

1. **Children and young adults**
   are the most frequently affected
2. Leishmaniasis remains an important problem for **military personnel operating** in endemic regions
3. Visceral leishmaniosis is more common among **immunocompromised persons,** such as thous with HIV infection, or after organ transplantation

Transmission of *Leishmania* spp.

In most areas,

the *Leishmania* spp. are inoculated

1. When the **sandfly vector attempts to feed**

(person is infected when bitten by mosquitoes)

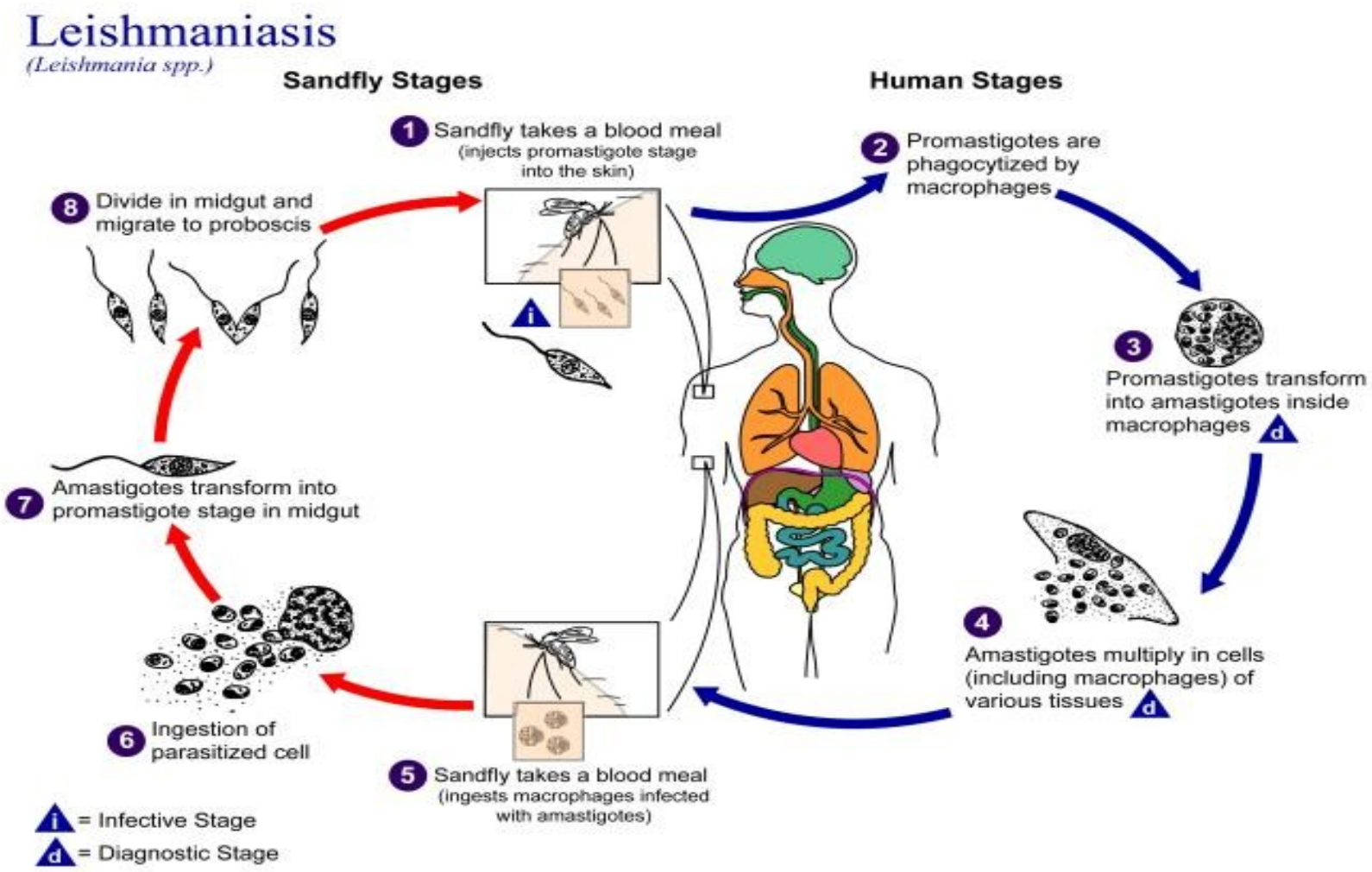
2. Through **contact with infected animals**
3. Transmission **from human to human** is possible

Sand Fly
Phlebotomus
is vector
of *Leishmania* spp.

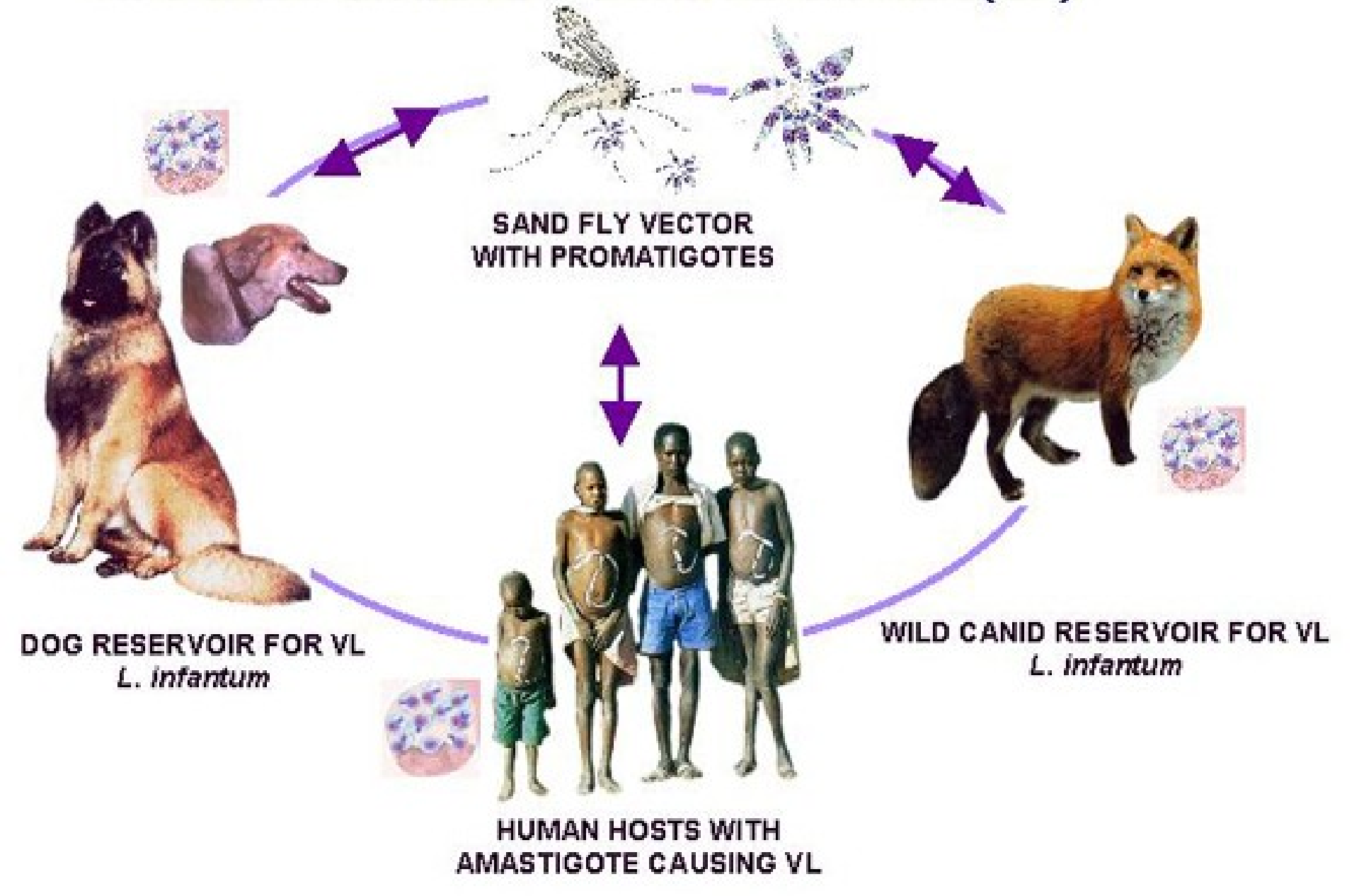
Leishmania spp.

- Have **a dimorphic life cycle**
  - **Promastigotes** (flagellum)
    - Infective stage for humans
  - **Amastigotes** (flagellum-free)
    - They live in macrophages of the host

- Leishmania spp. occurs in the body of mosquito as promastigotes (flagella form),
  In animals, which are a reservoir (canids, rodents, cattle) and human - protozoa proliferate as amastigotes (flagellum-free form)



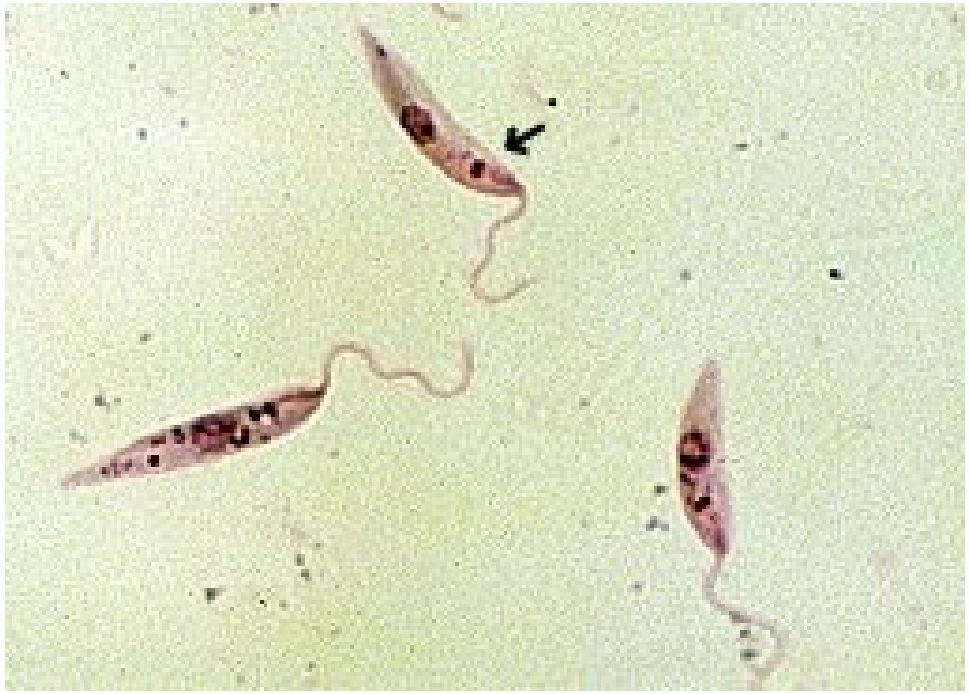
LIFE CYCLE OF *LEISHMANIA* CAUSING VISCERAL LEISHMANIASIS (VL)



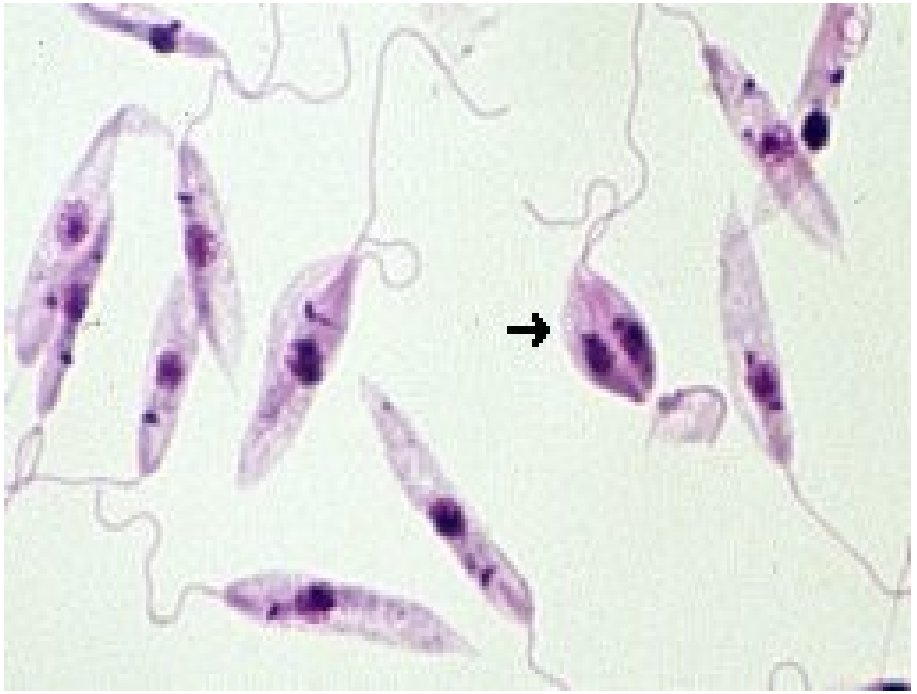
Promastigotes of *Leishmania spp.*

- they are the infective stage for hunans

They are characterized by a flagellum and a kinetoplast-DNA (arrow) anterior to the nucleus.



The multiplication of promastigotes
by longitudinal fission (arrow) that occurs naturally in the gut of sandfly vectors.



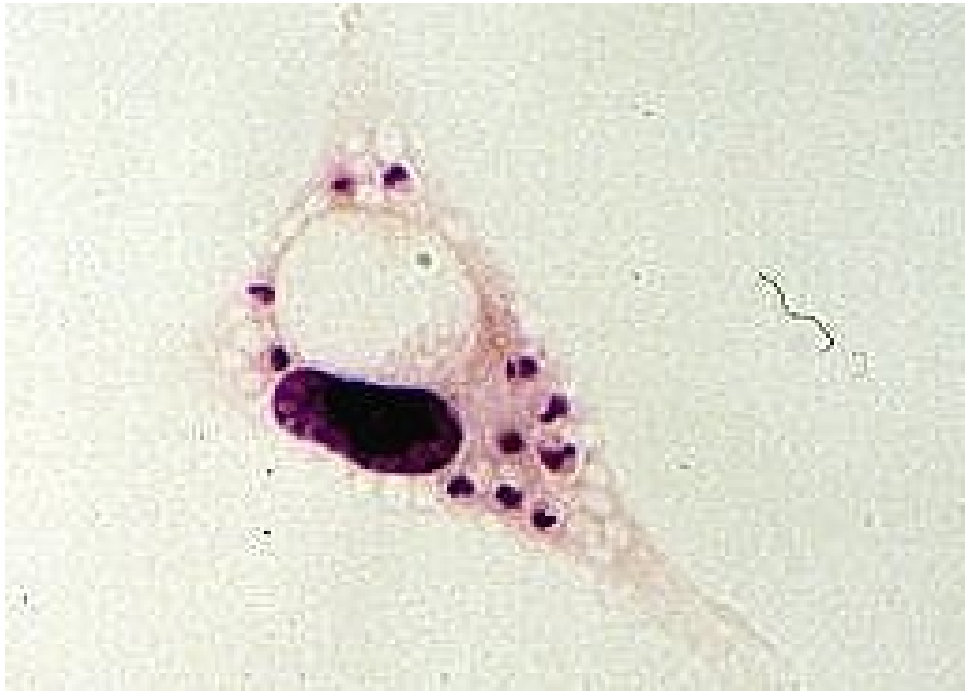
Amastigotes of *Leishmania spp.*

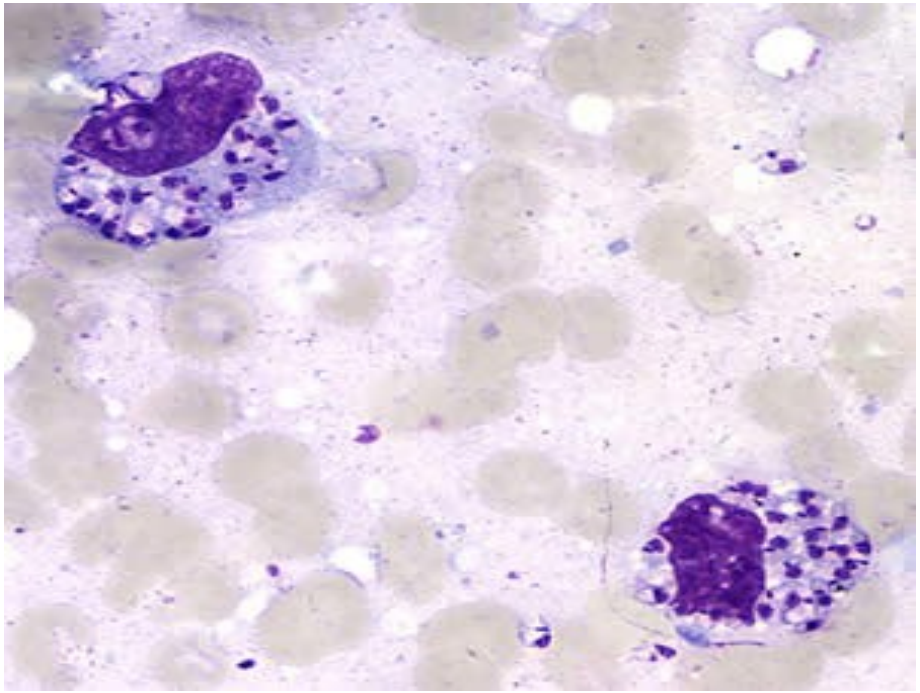
- macrophages are filled with amastigotes

Amastigotes are formed after the macrophage phagocytizes an infective promastigote and are spherical to ovoid

The organisms reside in macrophages of the host and can be found throughout the body (in various tissue).

They measure 1-5 μm long by 1-2 μm wide.





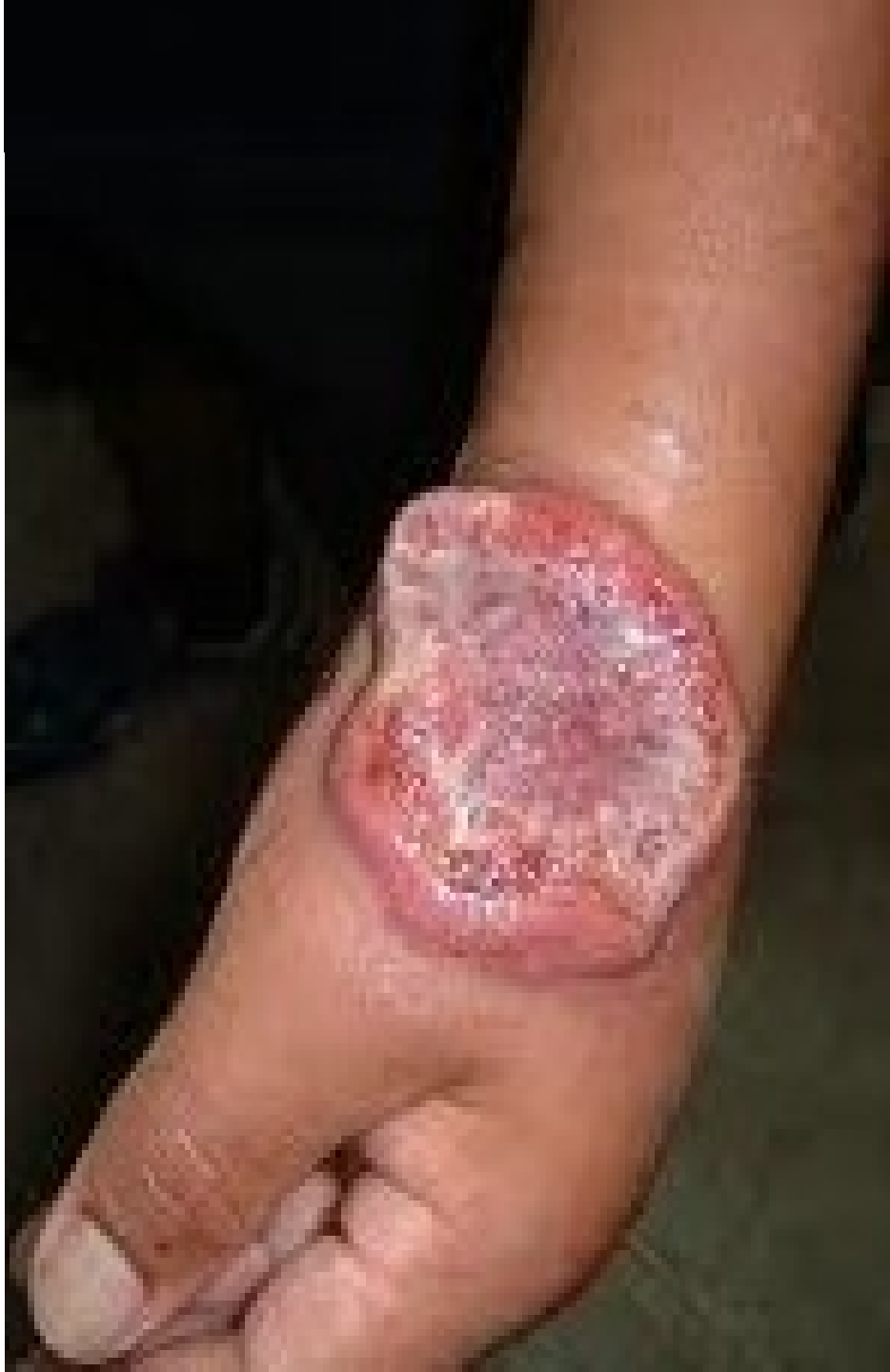
Cutaneous leishmaniasis

- **The incubation period** varies
  - From **a few weeks to several months**
  - In some cases, **up to years**
- **Initial lesion**
  - Usually appears 2 to 8 weeks after the sandfly bite
- A local lesion that starts as a small, **erythematous papule**
- At the side where promastigotes are inoculated
- The papule gradually increases in size slowly to form **a typical leishmaniotic ulcer**
- Become **crusted,** and finaly **ulcerates**

Cutaneous leishmaniosis

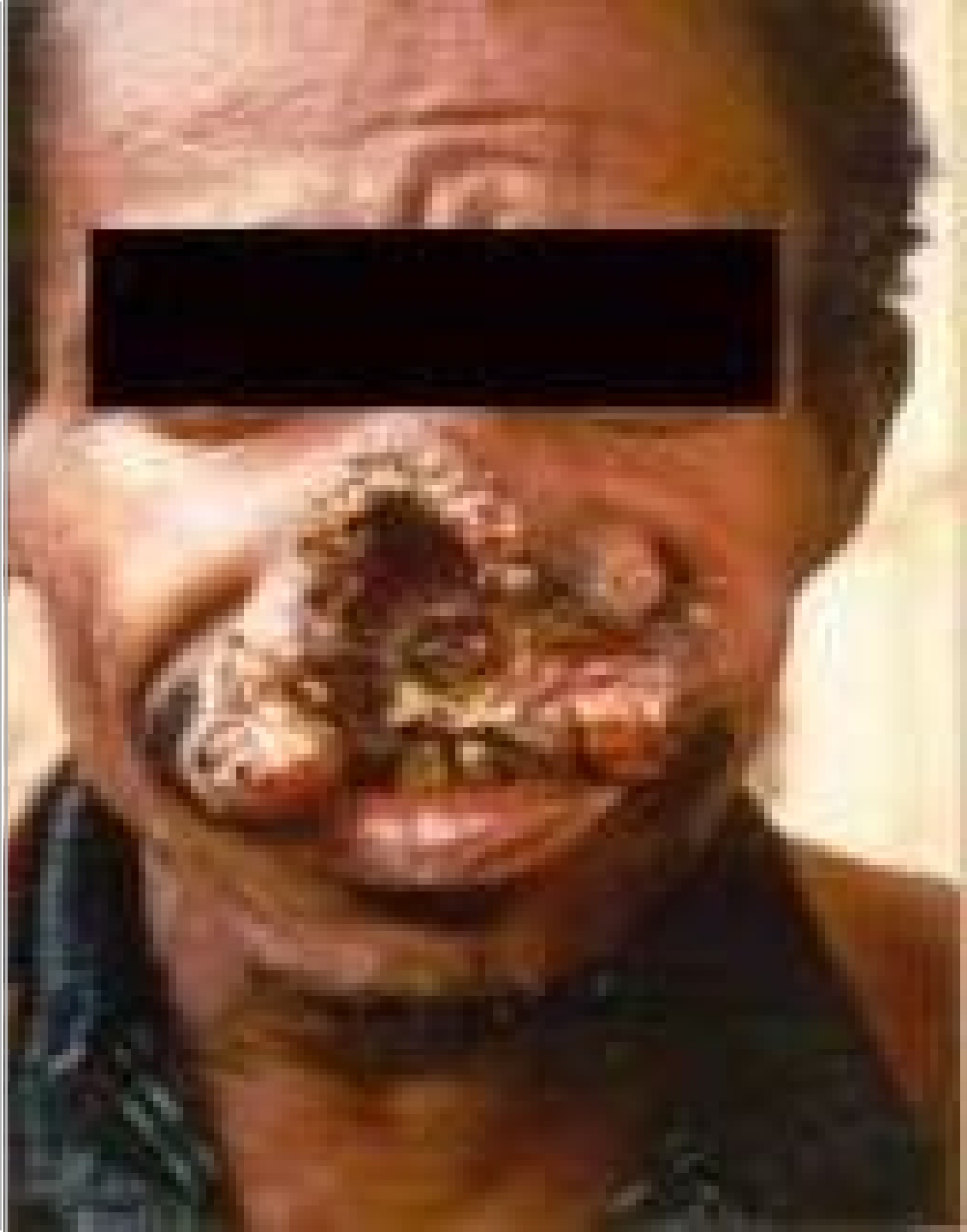
The ulcer is usually

- shallow and circular
- with well-defined, raised, erythematous borders
- and a bed of granulation tissue
- Round with raised borders and **a granulating base**
- and covered by exudate
- May persist for months to years

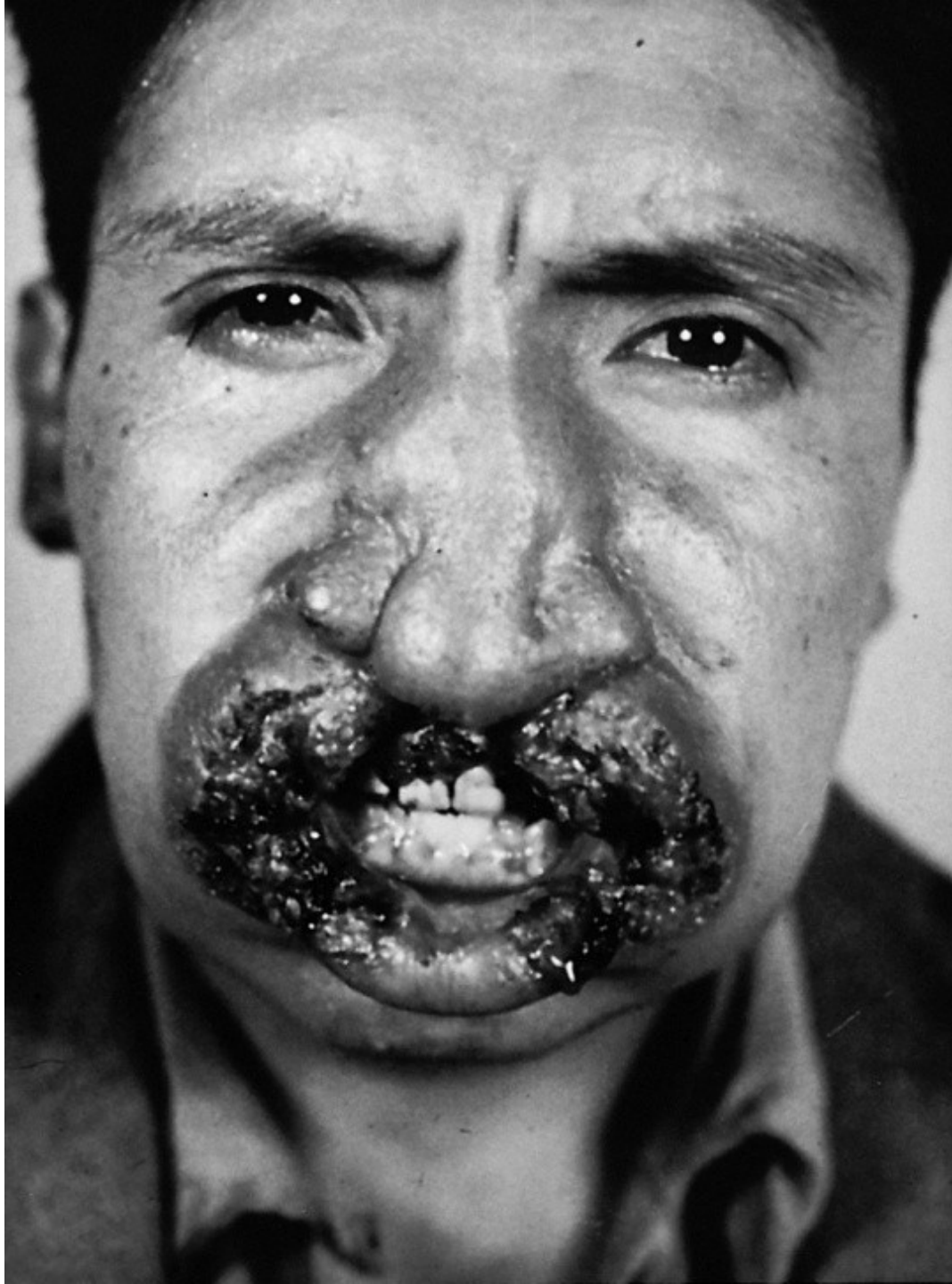


Leishmaniotic ulcer

- Gradually increases in size
- May reach a diameter of 2 cm or more
- **Satellite lesions** that fuse with the original ulcer may be present
- There is frequently a serous or seropurulent discharge



A wide variety
of skin manifestations,
ranging from small, dry,
crusted lesions
to large, deep,
mutilating ulcers,
which are seen
especially in American
cutaneous
leishmaniasis



Differential diagnosis of cutaneous leishmaniasis

Includes the following:

- Fungal infections
- Lupus vulgaris (skin tuberculosis)
- Mycobacterial infections of the skin (due to atypical mycobacteria, toberculosis, or leprosis)
- Neoplasms
- Syphilis

Visceral leishmaniasis („kala-azar“)

- **Causative agents** include:
  - *Leishmania donovani*
  - *Leishmania infantum*
  - *Leishmania chagasi*
- **Incubation period**
  - Varies and depends on the type of the infection
  - Can be up to **8 months or more**

Visceral leishmaniasis („kala-azar“)

Is characterised by:

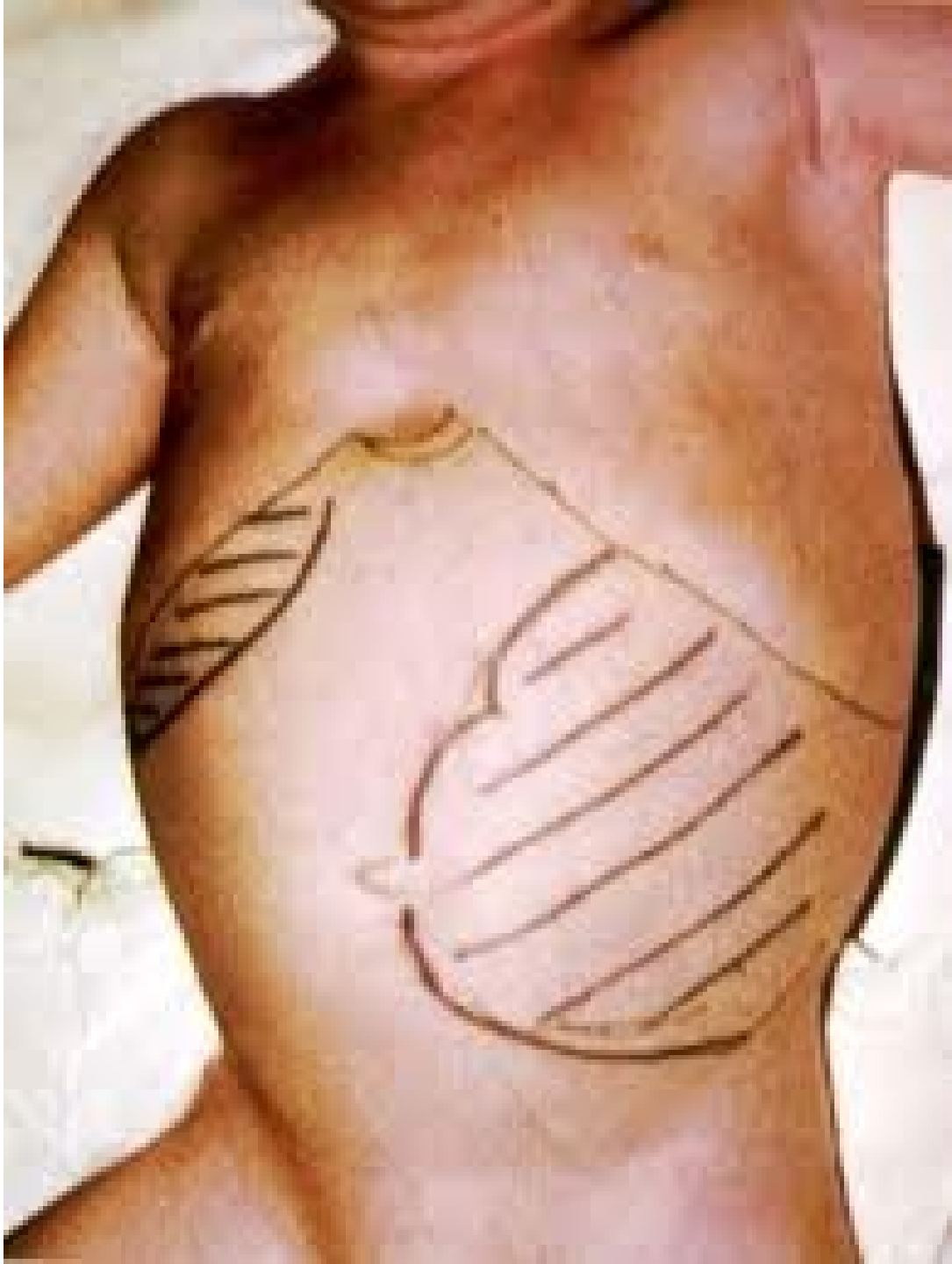
- The abrupt onset of fever
- Rigors
- Malaise
- And other **nonspecific symptoms**
- As early as 2 weeks after infection
  - Fever may be intermittent or continuous
  - Sweating with chills accompanies the temperature spikes

„Kala-azar“

As time passes,

the spleen and liver become enlarged

and fill the whole abdomen



„Kala-azar“ diff. dg.

Can present as:

- Organomegaly
- Fever
of unclear etiology
- Unexplained
chronic anemia
- Can mimic other infectious diseases (malaria, typhoid fever, brucellosis, etc.)

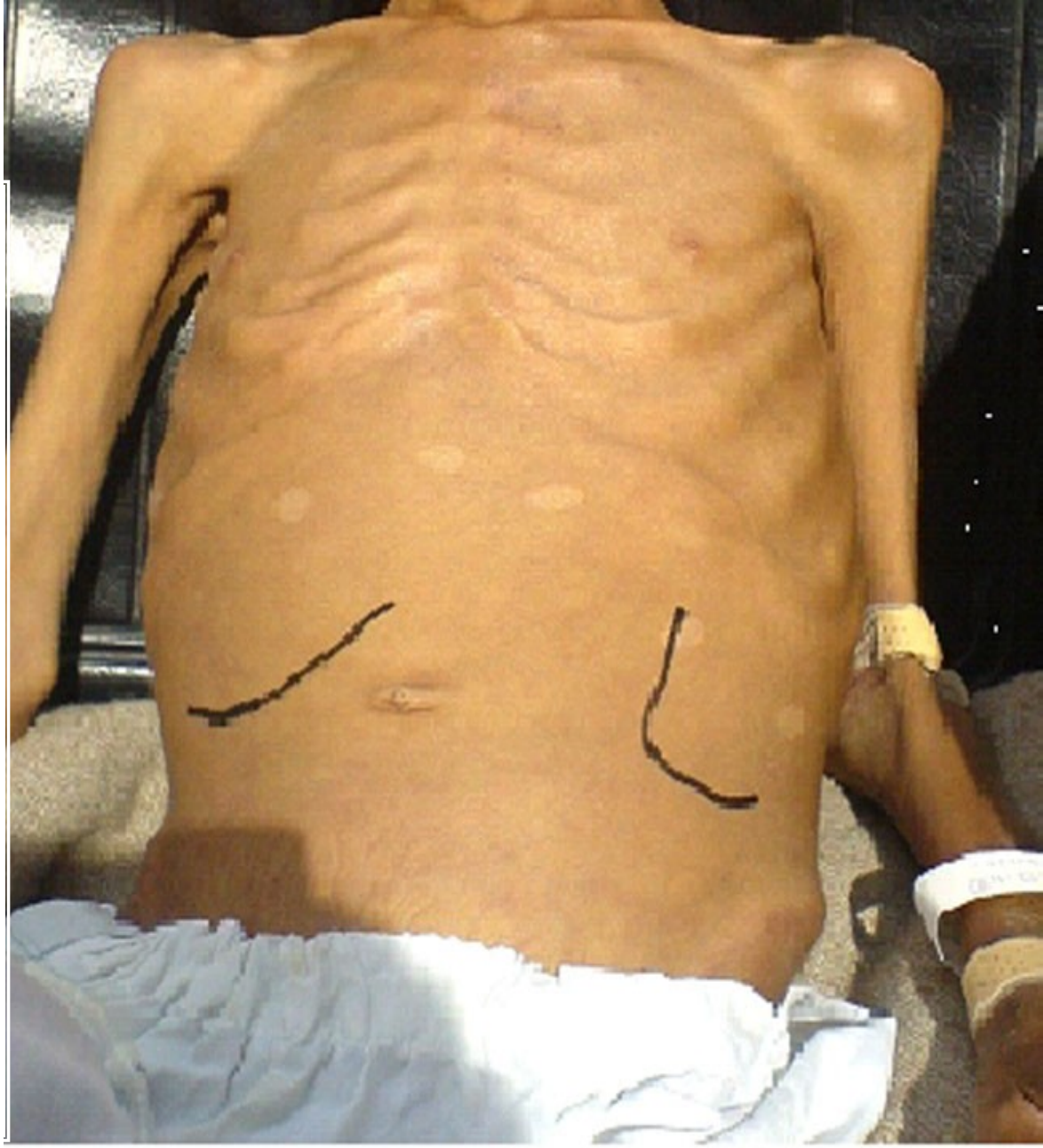


Figure-1 : Abdomen of first child showing massive hepatosplenomegaly. Also evident are the cachectic upper extremities.

Laboratory

In person with visceral leishmaniasis are present:

- **Anemia**
- **Leukopenia**
- **Hypergamaglobulinemia**

A definitive diagnosis depends on the demonstration

- Of amastigotes **in tissue**
- Or isolation of the organism **in culture**

Laboratory

Culture which may reveal the parasites are the most often:

- Bone marrow
- Liver, spleen
- Lymph node
- Blood (in some cases)

The most common diagnostic procedure for dg: „kala-azar“

- **Bone marrow aspiration**
- **Liver or spleen biopsy**

- **ELISA** (enzyme-linked immunosorbent assay)

  and **the indirect immunofluorescent antibody assay**
  - Can be used but are nondiagnostic procedures

Main treatment

Most commonly used for treatment are:

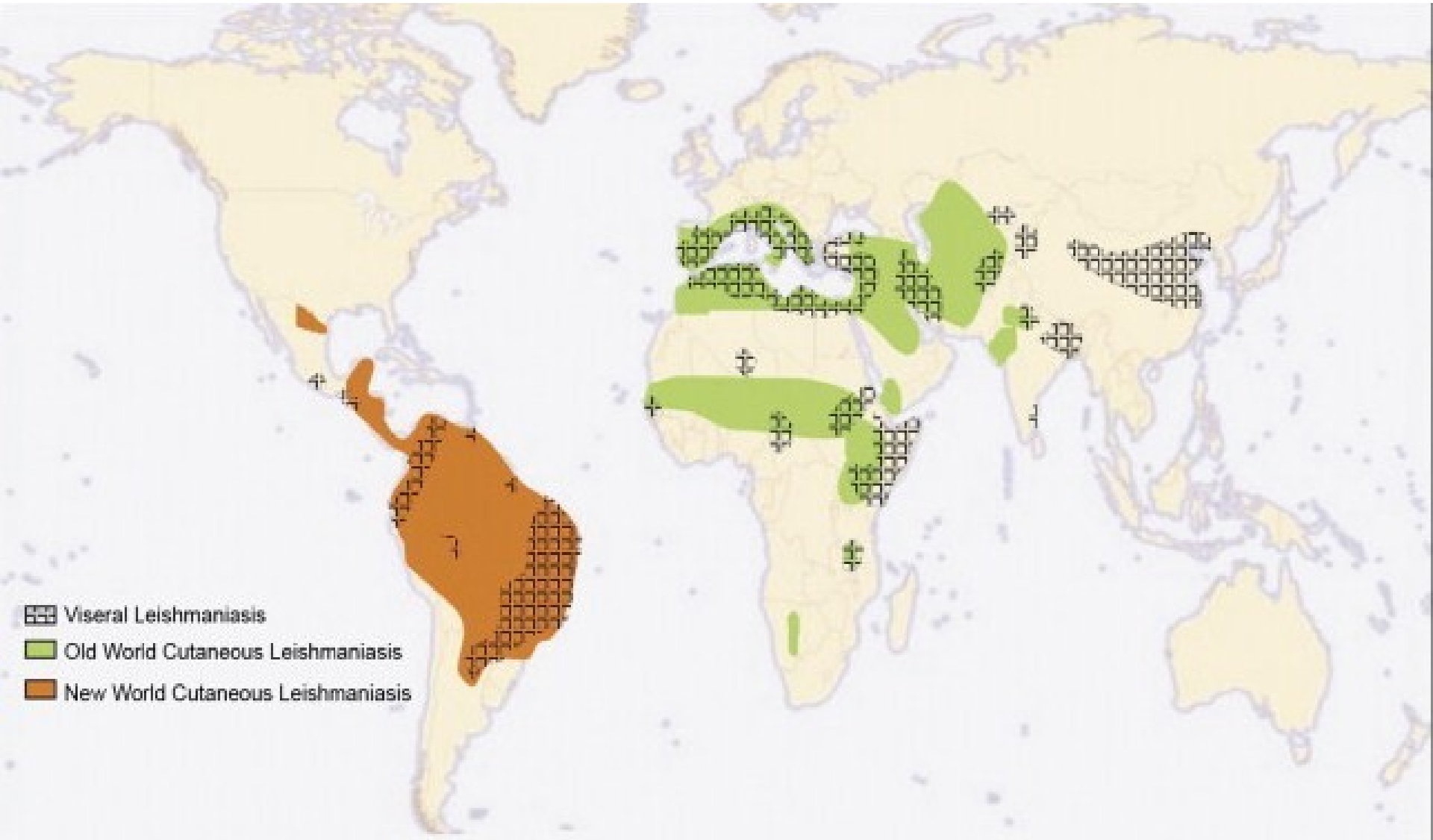
- **Pentavalent antimonial compounds**
  - Are most commonly used
- **Amphotericin B**
  - Has been used to treat patients who fail to respond or relapse with antimonials
- **Liposomal amphotericin B**
- **Pentamidine**
  - Is a less commonly used alternative

Prevention is non-specific

Includes non-specific measures:

- **Travelers** to endemic areas **should be educated** about the risk of leishmaniasis and the prevention of bites by sandflies
- Leishmaniasis remains an important problem for **military personnel operating** in endemic regions

Geografic distribution



TRYPANOSOMIASIS

Trypanosomiasis

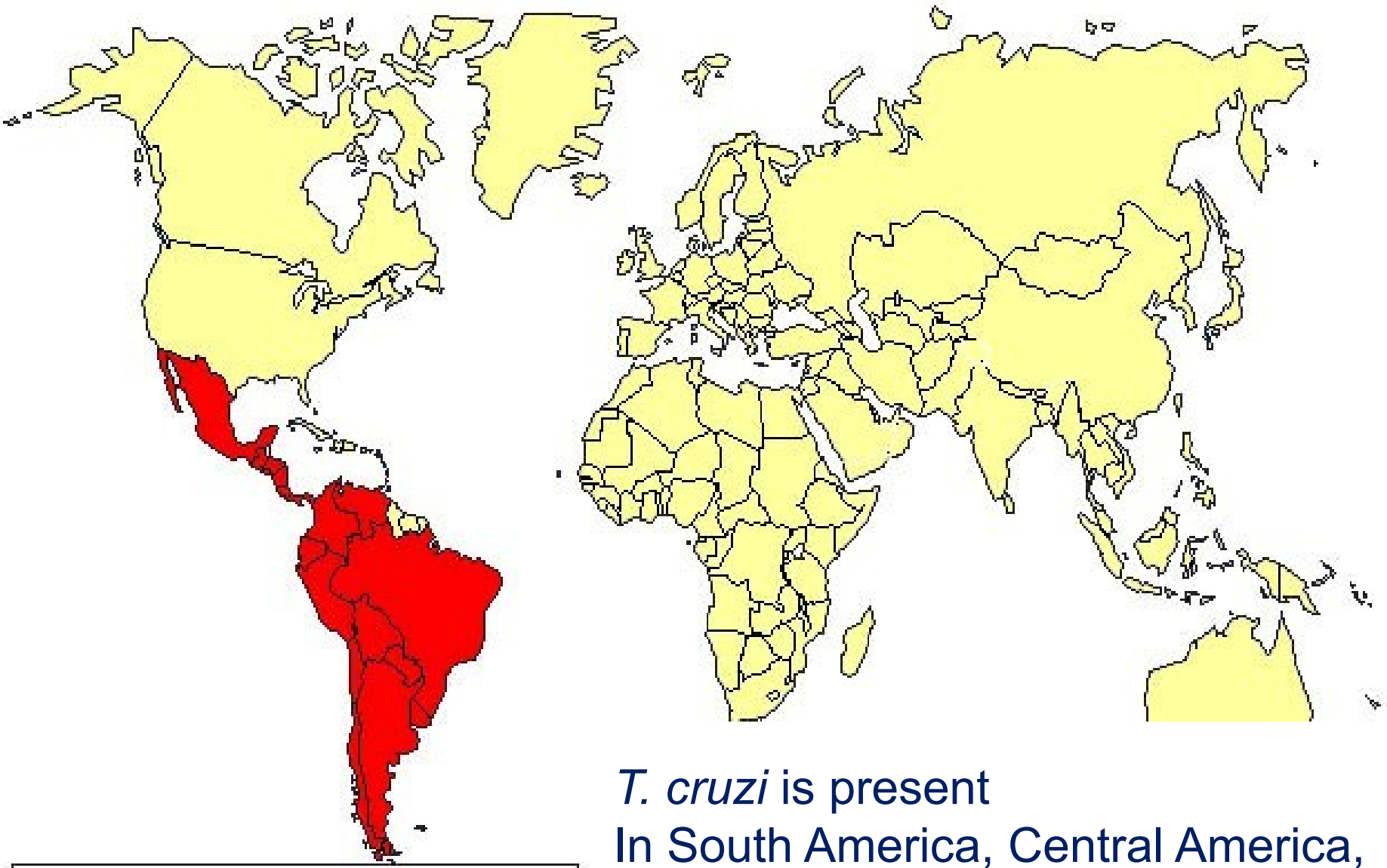
- A zoonotic **protozoal disease**
- Transmitted to humans
  via blood-sucking insect vectors
- It produces various
  acute and chronic diseases in humans
- Is divided into
  - The American trypanosomiasis
  - The African trypanospmiasis

American trypanosomiasis

„Chagas´ disease“

- Causative agent – ***Trypanosoma cruzi***
  (related to *Leishmania spp.)*
- 16 to 18 million people are currently infected in Latin America
- Is the most serious parasitic disease in Latin America
  and annually infected 700,000 new victims.

Chagas Disease



T. cruzi is present
In South America, Central America, Mexico

Epidemiology

Trypanosoma cruzi

- Is present in many species

  of **wilde and domestic mammals**
- Most cases in humans occur during childhood
- Disease is much more common in areas of **poverty and rural areas**

Transmission

T. cruzi is transmitted:

- Via blood-sucking insects (kissing bugs)
  - ***Triatoma***
- **Via blood transfusion**
- **In utero,** and is associated with fetal demise and fetal abnormalities

Main rout of transmission

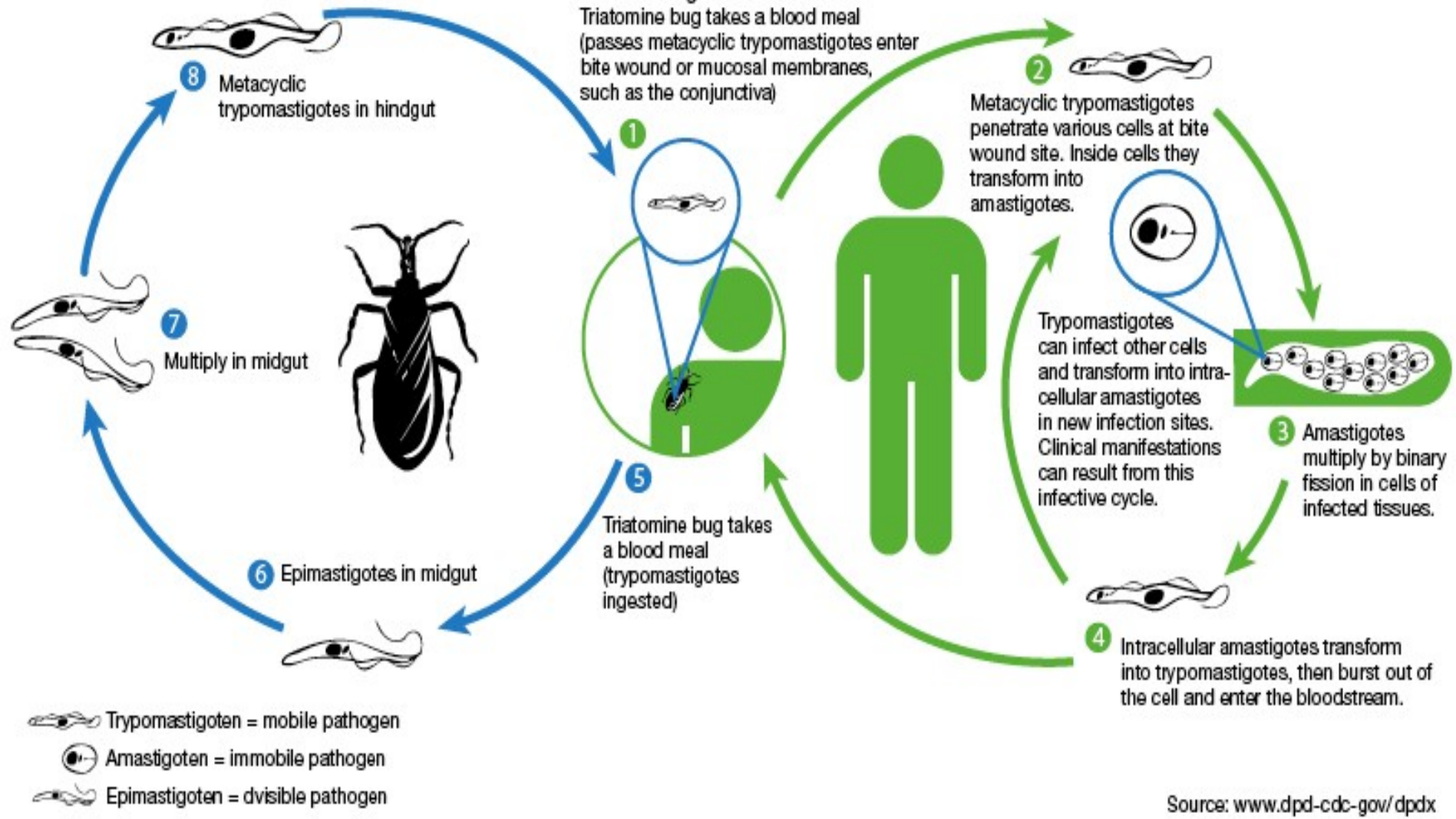
Via blood-sucking insects
(kissing bugs)

- ***Triatoma***
  - Is In the insects´ feces
  - From there, the infectious trypomastigotes enter

    the human body through breaks in the skin
  - Trypomastigotes are transformed into amastigotes (in human body)

Triatomine insect, which can transmit Chagas disease parasite. Photo: CDC/DPDx.

Infection cycles of Chagas disease

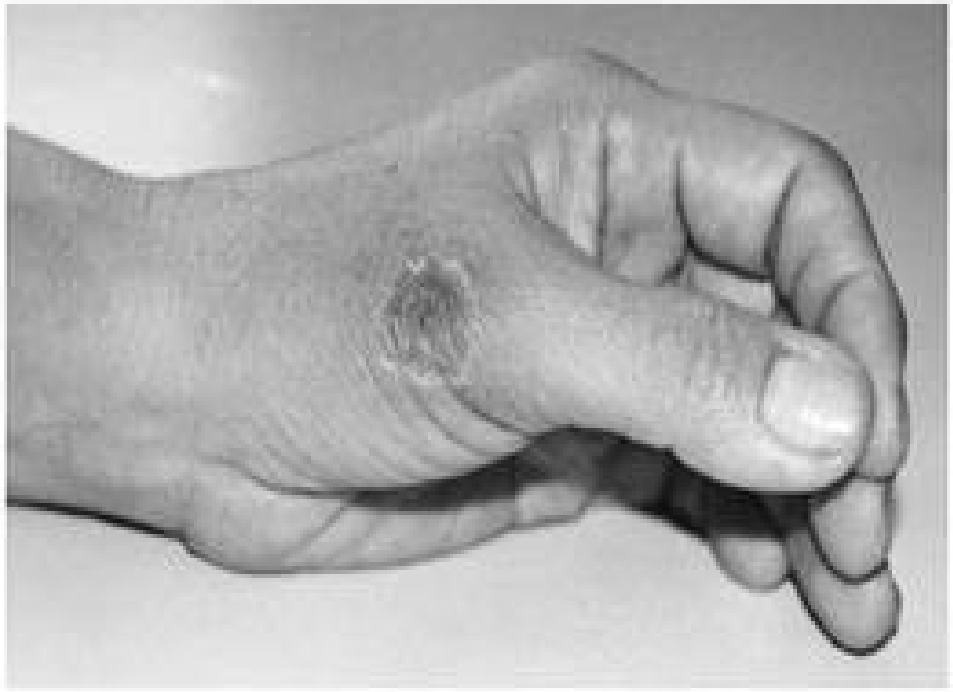


Source: www.dpd-cdc-gov/dpdx

Incubation

- **Acute symptoms** of Chagas´ disease
  - occur 1 week after contact with the parasite
- **Chronic symptoms** of Chagas´disease
  - take years to decades to cause significant illness

Acute Chagas´ disease



Chgoma

A small, indurated papule with erythema and local lymphadenopathy

Chagoma occurs at the site of invasion by the organism

Romaňa sign

- when contact is made from the organism to the conjunctiva, periocular edema occurs or swelling and closure of the eye

Acute Chagas´disease

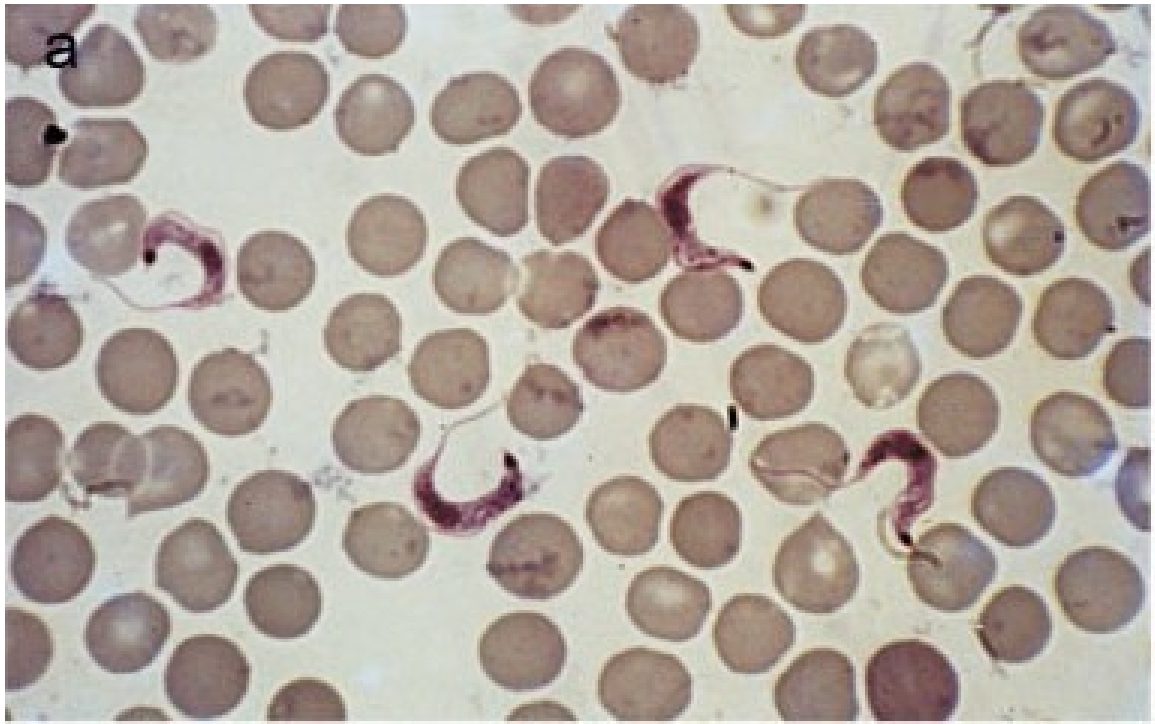
- **Fevers, constitutional symptoms, lymphadenopathy, and splenomegaly** can occur and usually resolve within weeks

- Central nervous system symptoms and myocarditis are rare complications at this stage

Diagnosis of acute Ch. disease

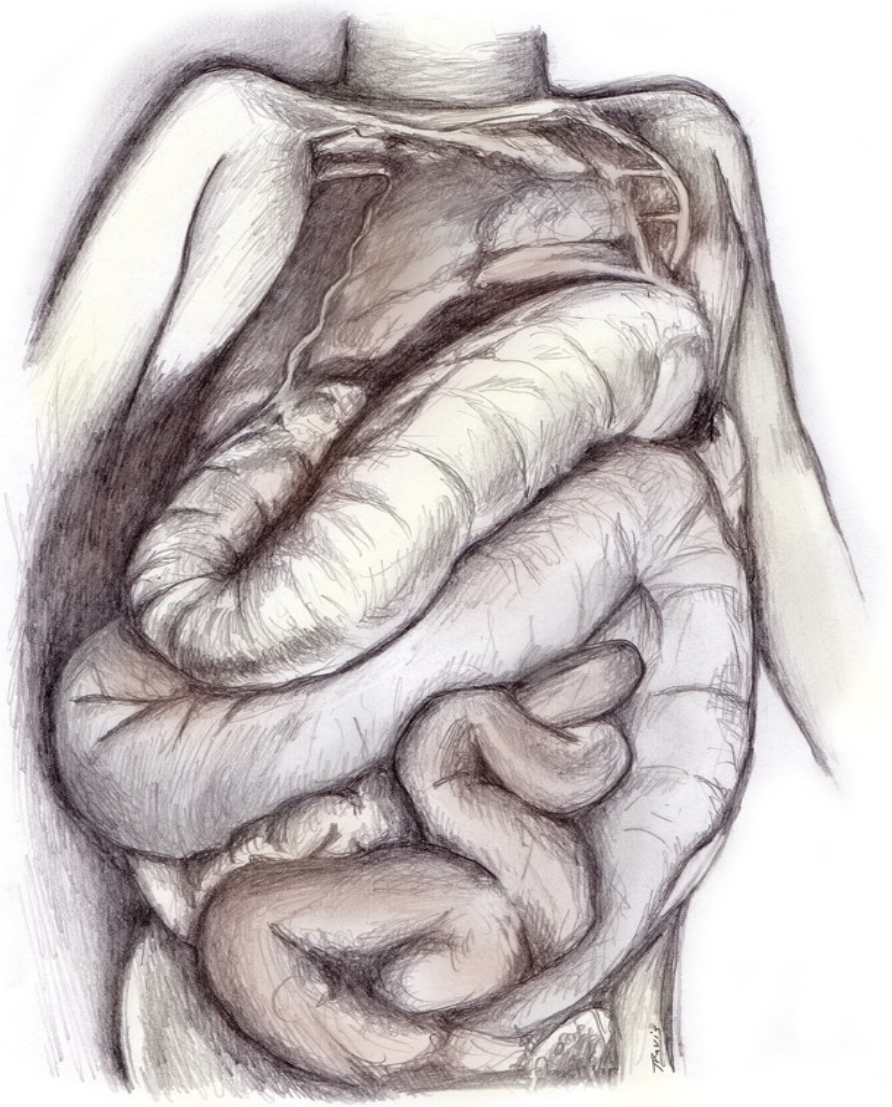
Finding circulating parasites in the blood is essential

- The organisms are motile
- Detection occurs 50% of the time of acute symptoms

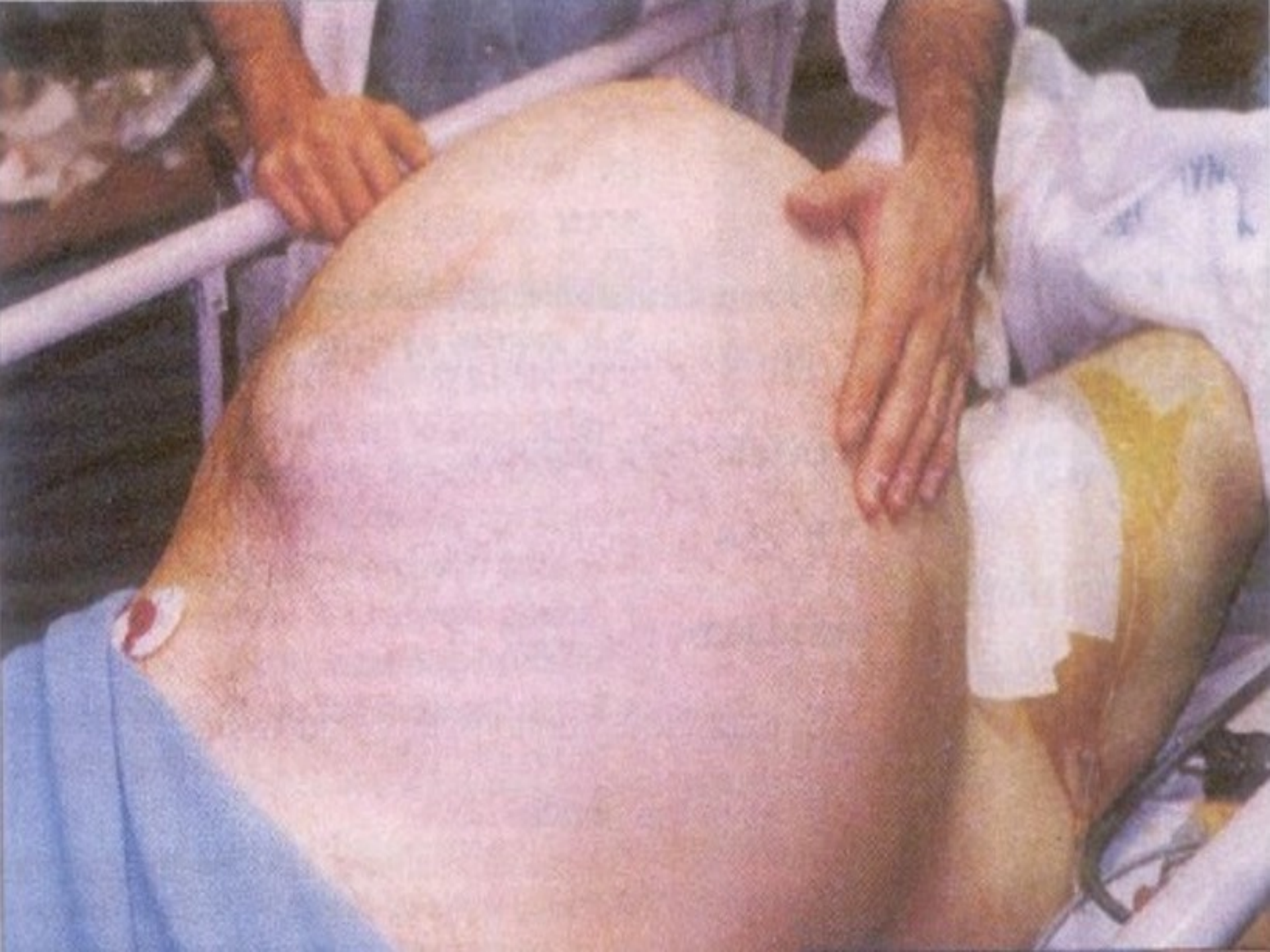


Trypomastigotes circulating among erythrocytes in blood during acute phase

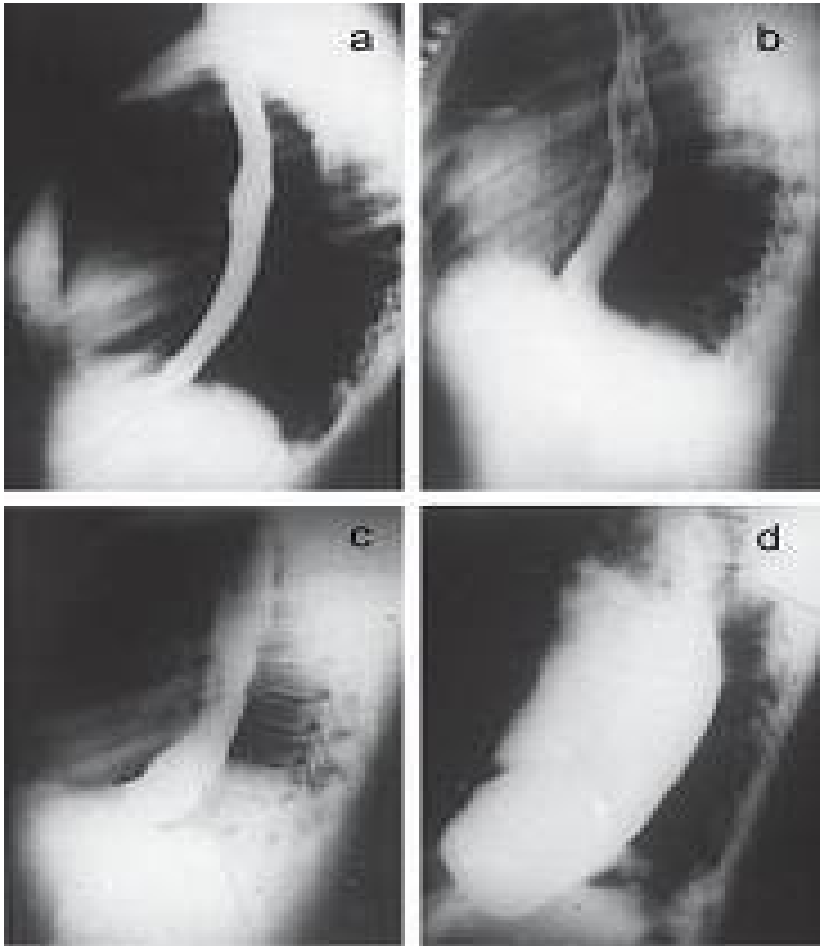
Chronic Chagas´disease



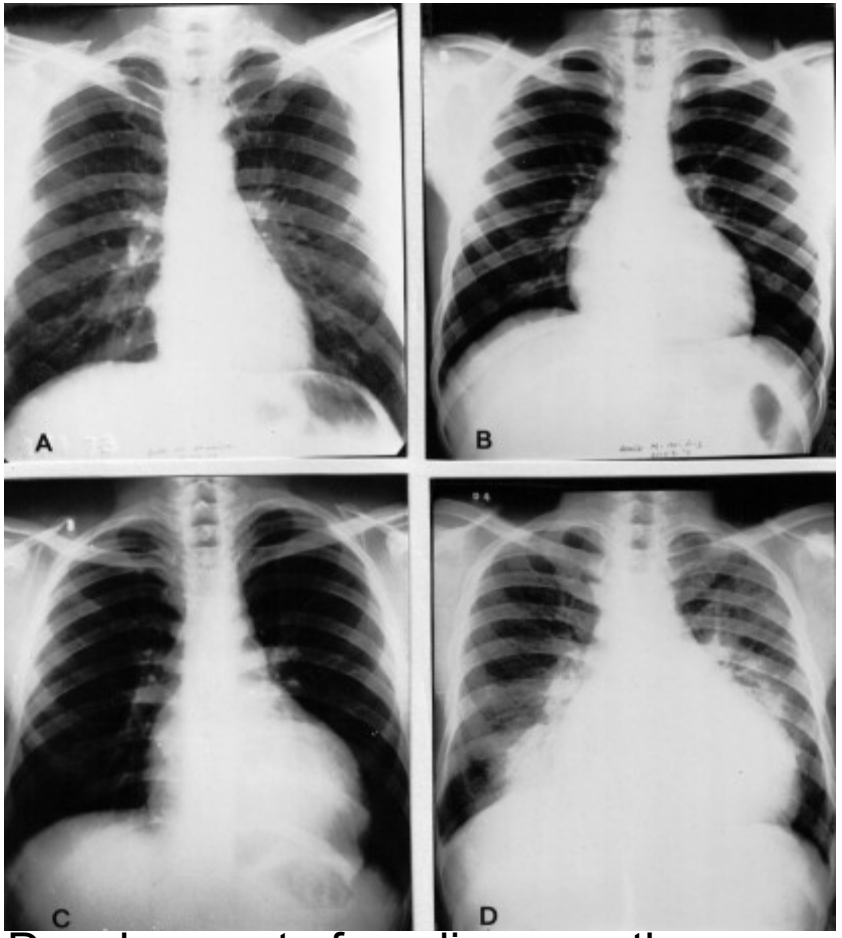
- Develops years after the initial infection
- Megaesophagus and dysphagia
- Aspiration is common
  - and due to aspiration pneumonia is a common complication
- Colonic dysfunction with megacolon occurs



Chronic Chagas´ disease



X ray - development of megaesophagus



Development of cardiomyopathy

is associated with heart failure

and/or arrhytmias, which are often fatal

Diagnosis of chronic Ch. disease

- **Serology** is used to detect antibodies to the organism
  - Many false-positive tests occur
- **Histologic examination** of affected tissue
  - Essential for diagnoses of chronic disease

The histological changes in the affected tissue

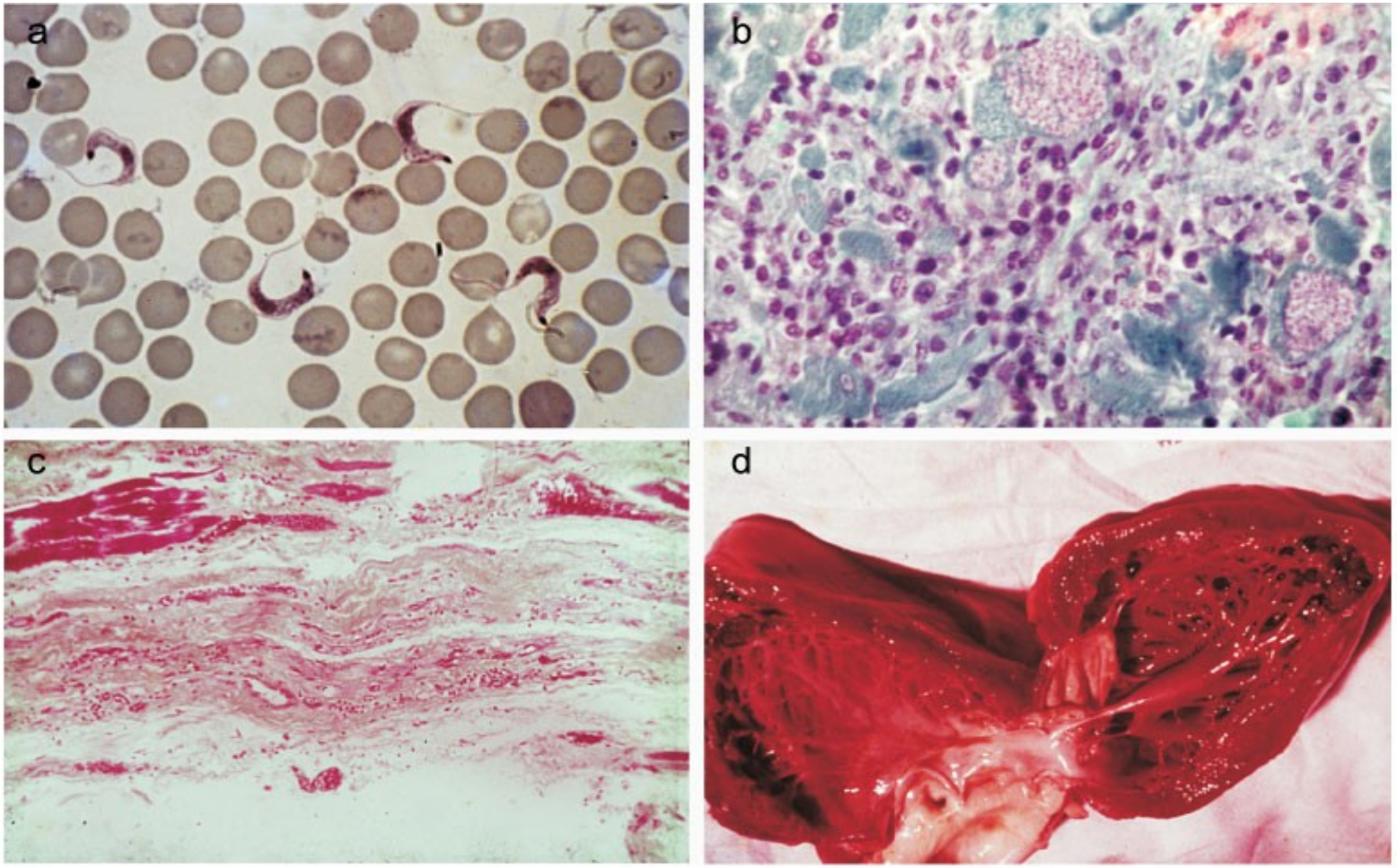


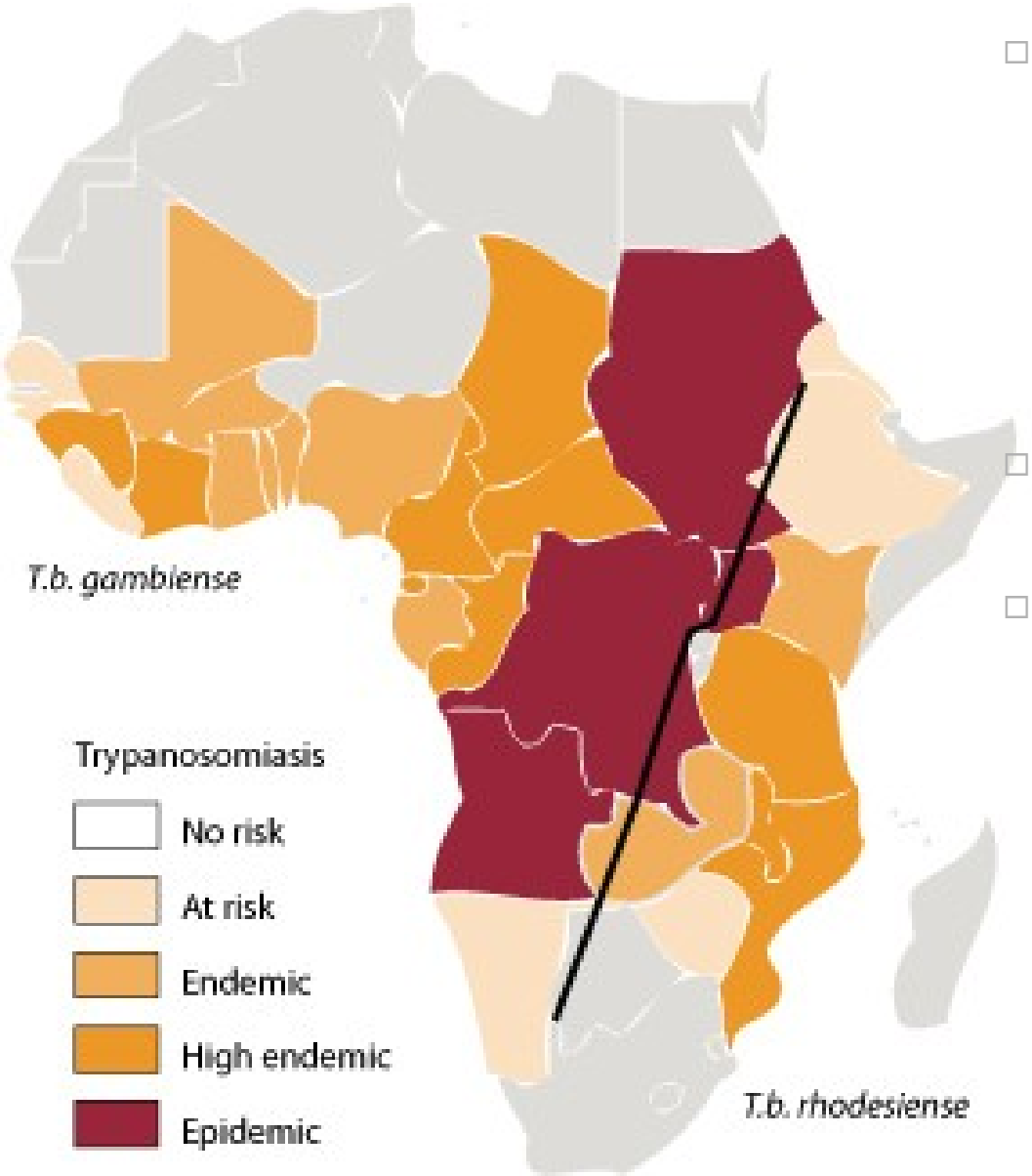
Fig. 2a: trypomastigotes circulating in blood during acute phase; b: pseudocysts of amastigotes in myocardial fibers in the acute phase of Chagas disease; c: fibrosis of the myocardial conducting system in chronic phase of Chagas disease; d: hipertrophy of myocardium and dilatation of the heart cavities with the presence of thrombi in chronic Chagas heart disease (Coura et al. 2007).

Treatmen of Chagas´disease

Acute or chronic disease:

- **Nifurtimox** orally over a 90 to 120 days
  - Side effects on CNS and GIT
- **Benzimidazol** orally for 60 days
- **Pacemaker** insertion is warranted
  - in patients with arrhythmias and heart block
- Management of **congestive heart failure** is important
- Treatment is insuficient

African trypanosomiasis

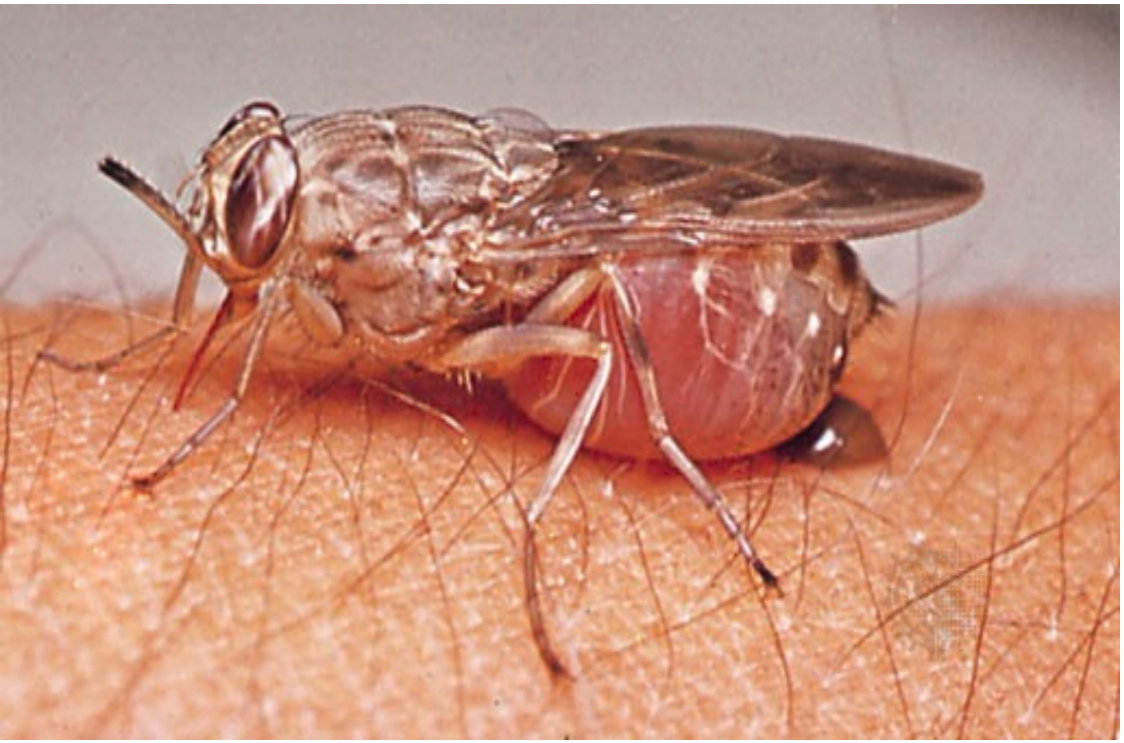


- Occurs in 36 countries in sub-Saharan Africa

  - Angola, Sudan, the Democratic Republic of Congo, Central African Republic, Chad, Uganda, Tanzania, Malawi, Coast Ivory…

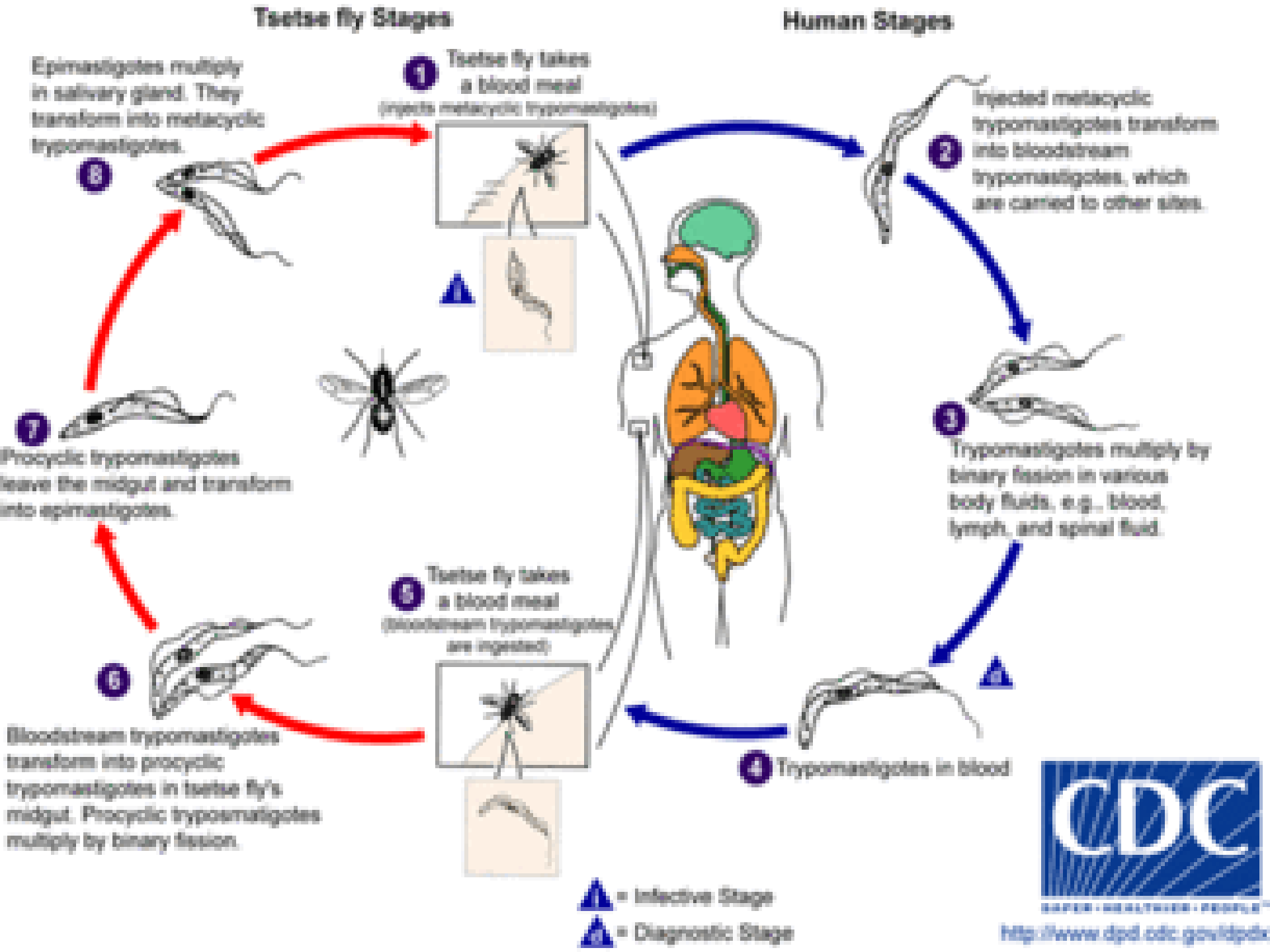
- 500 000 new infection every year is reported
- Is a zoonotic protozoal disease (as well as American trypanosimiasis)

Blood-sucking fly Tse-tse



- Genus *Glossina*
- Vector
- It transmits the parasite between reservoir animals (cattle, pigs, wild mammals, antelope…

Trypomastigotes are transmitted from the salivary glands of the fly to the human during a blood meal.


Tsetse fly Stages
Human Stages
Epimastigotes multiply in salivary gland. They transform into metacyclic trypomastigotes.
8
1 Tsetse fly takes a blood meal
(injects metacyclic trypomastigotes)
Injected metacyclic trypomastigotes transform into bloodstream trypomastigotes, which are carried to other sites.
2
3 Trypomastigotes multiply by binary fission in various body fluids, e.g., blood, lymph, and spinal fluid.
7 Procyclic trypomastigotes leave the midgut and transform into epimastigotes.
5 Tsetse fly takes a blood meal
(bloodstream trypomastigotes are ingested)
6 Bloodstream trypomastigotes transform into procyclic trypomastigotes in tsetse fly's midgut. Procyclic tryposmastigotes multiply by binary fission.
4 Trypomastigotes in blood
= Infective Stage
= Diagnostic Stage
CDC
SAFER · HEALTHIER · PEOPLE
http://www.dpd.cdc.gov/dpdx

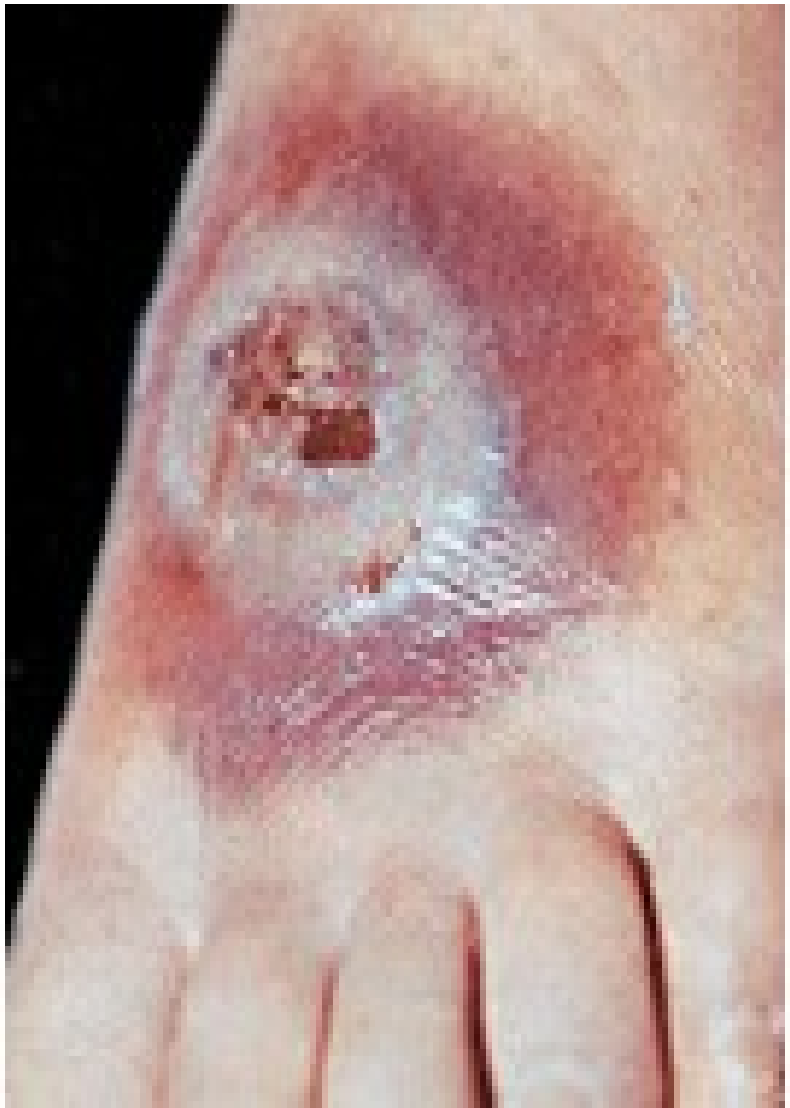
African trypanosomiasis

African sleeping sickness

West African trypanosomiasis

- Causative agent
  - ***Trypanososma brucei gambiense***
  - It is present in tropical rain forests and rural regions in Central and West Africa
- Outbreak of disease is greatest in the dry seasons

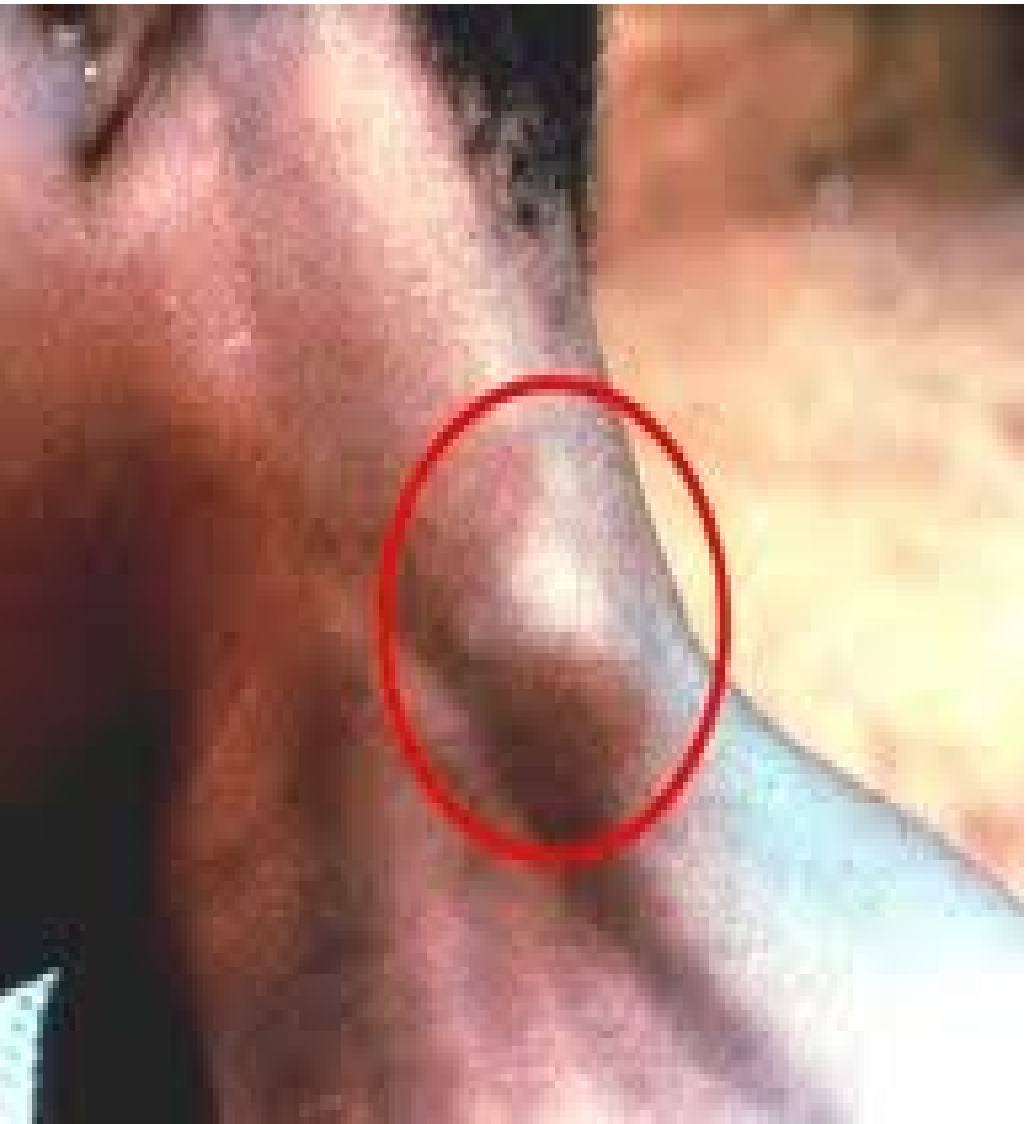
West African trypanosomiasis



Chancre

- Initial infection
- Develops within 1 to 2 weeks following the tsetse fly bite

West African trypanosomiasis



- Several weeks to several months after the initial infection, patients develop fevers associated with lymphadenopathy
- Massive enlargement of the cervical lymph nodes is seen

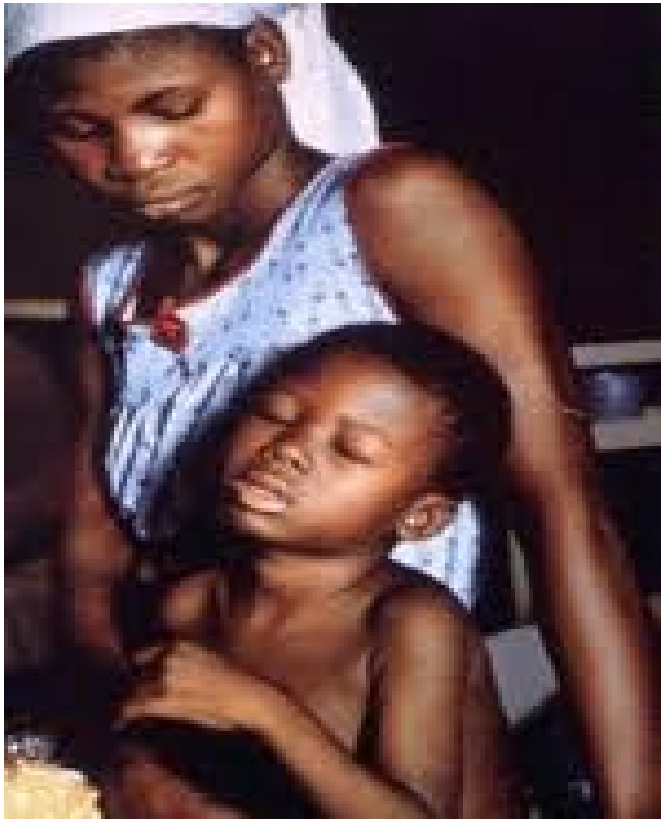
Winterbottom´s sign

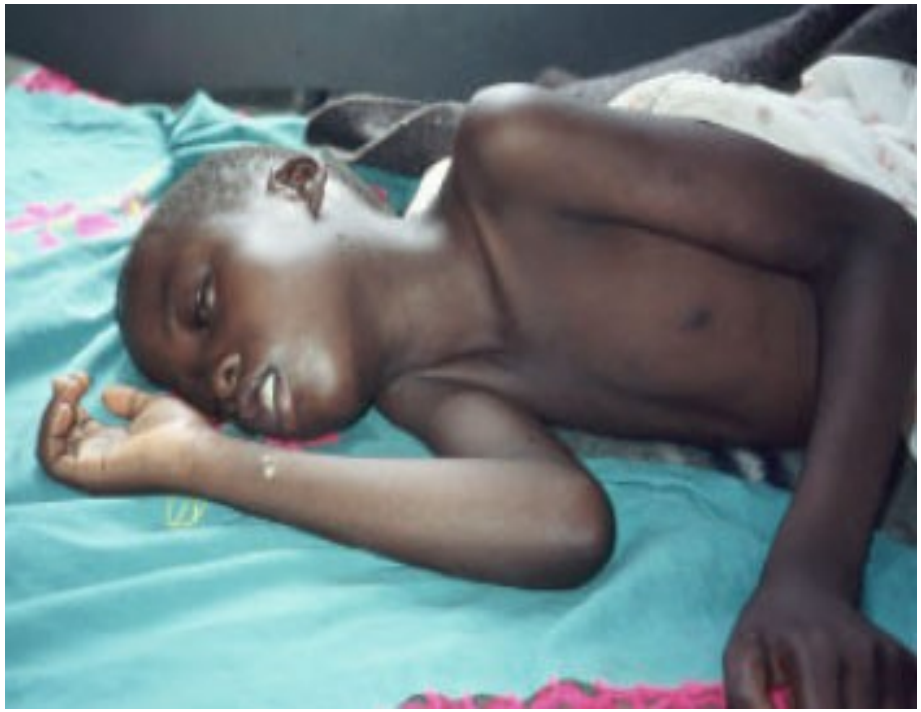
West African trypanosomiasis

Marked constitutional signs occur at this stage:

- Pruritus
- Arthralgias
- Transient edema of the face and extremities
- Erythematous rashes with internal clearing
- …

West African trypanosomiasis





- Several months to years after the initial infections, patients can develop CNS signs
  - of lethargy, somnolence, personality changes, ataxia, fasciculations, meningoencephalitis…
- **Progressive slow progression to stupor, coma and death.**

African trypanosomiasis

African sleeping sickness

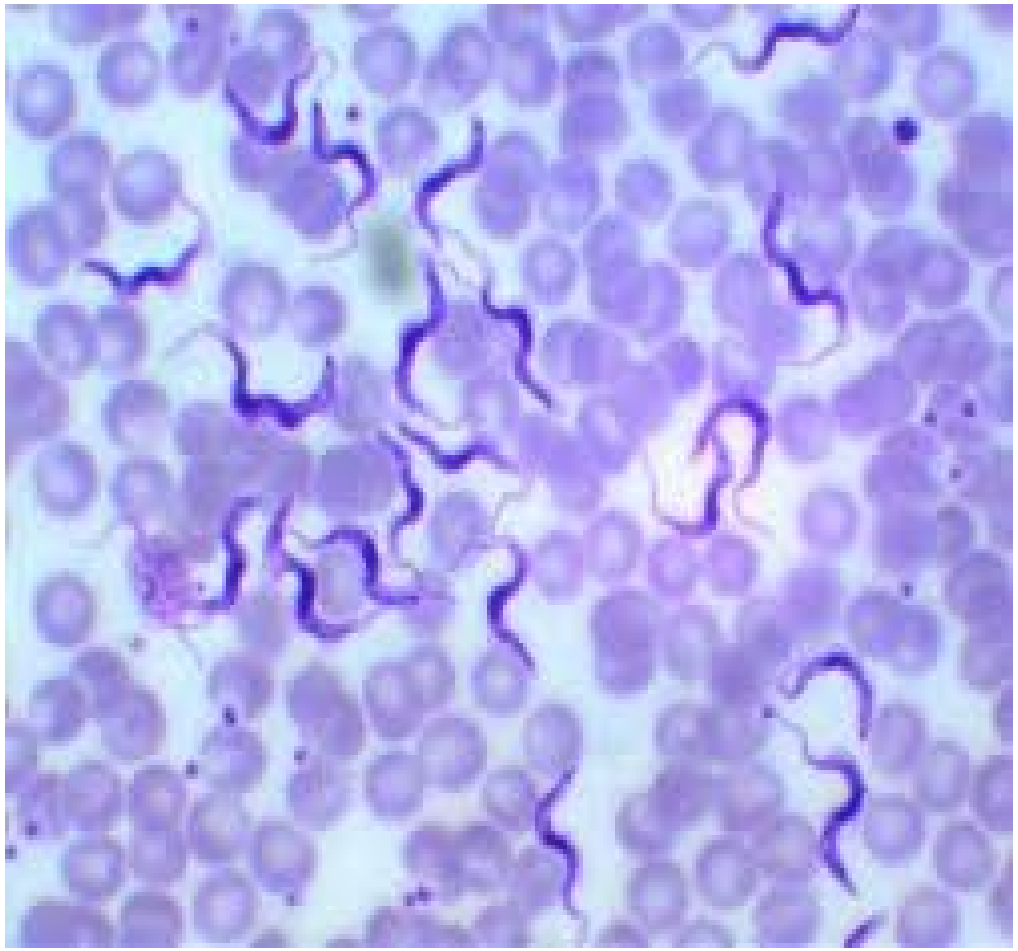
East African trypanosomiasis

- Is caused mostly by
  - ***Trypanosoma brucei rhodesiense***
- Reservoir of disease is mostly in wild game such as antelope
- infection in humans is limited

East African trypanosomiasis

- It follows that of the East African disease
  - It is much **more acute in nature**
- Symptoms occure **a few days** following the insect bite
- **Fever** and **rash** develop within weeks after the tse-tse fly bite, as opposed to months, such is in West African trypanosomiasis
- **Lymphadenopathy is less** apparent
- Patients often die of **cardiac failure** or **arrhythmias** due to pancarditis
- **CNS signs** may occur at the time that fevers are present

Diagnosis of African trypanosomiasis



Organism of *Trypanosoma brucei* can be seen in:

- Fluid from **chancres** or aspirate from **lymph nodes**
- **Blood**
- **Cerebrospinal fluid**

Treatment

- *T. brucei gambiense* infection
  - without CNS abnormalities
    - **Suramin**
    - **Pentamidine**
  - With or without CNS involvement
    - **Eflornithine**
    - **Tryparsamide**
- *T. brucei rhodesiense* infection
    - **Suramin, pentamidine, melarsoprol**

- Thank you for your attention…