Tropical diseases - parasites

Parasites

1. protozoa (one - cell microorganism)
    - intestinal (amoeba, giardia, balantidium, kryptosporidium)
    - blood (malaria, babezia, trypanosoma, leishmania)
    - others (toxoplazma, pneumocystis)
2. helmints (worms)
    1. Nematodes = roundworms
        - intestinal (askaris, ancylostoma, enterobius, trichiuris, strongyloides)
        - tissue (trichinella, toxocara, filariasis)
    2. Cestodes = tapeworms
        - Intestinal (taenia, difylobotrium, hymenolepis)
        - tissue (cysticercosis, echinococus)
    3. Trematodes = flatworms. flukes (schistosoma, fasciola, clonorchis, paragonimosis) v EU rare

Diagnosis od parasites

- Sample of stool - 3x, after 2 days
  - Macroscopy - helmints
  - Microscopy- Protozoa, warm's eggs
- “tape test” – Enterobius - is done by firmly pressing the adhesive side of transparent tape to the skin around the anus. The eggs stick to the tape and the tape can be placed on a slide and looked at under a microscope
- Thick and thin blood smears – blood parasites
- Serology– tissue parasites, malaria, leishmania
- PCR

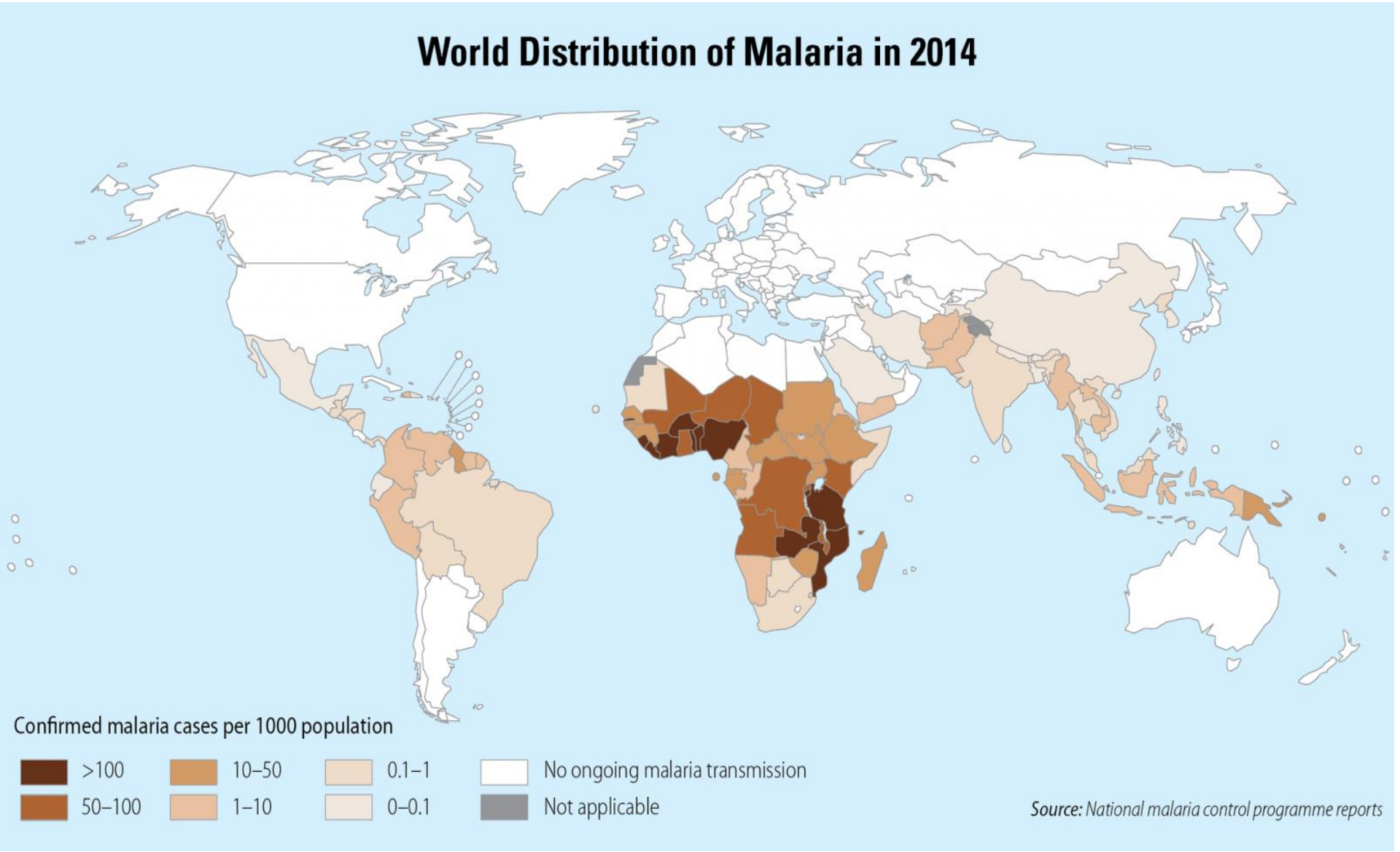
Malaria

Malaria incidence

- **40%** of world populations live in endemic area
  - Subsaharian Africa, Asia, Latin America
- **Incidence in 2000:** 500 mil**.** new cases yearly
- **Mortality: 2 mil.** death yearly, mostly children - mostly in sub-Saharan Africa
- In **2015**, an estimated 214 million new cases of malaria occurred, with approximately 438,000 deaths from the disease.

Malaria

- Febrile human illness
- Ethiology: plasmodia
- Vector: female mosquito anopheles (400 types)
  - Range: 1,5 km lenght, altitude : up to 1 500 m.n.m.,
- Natural conditions: stagnant freshwater areas


World Distribution of Malaria in 2014
Confirmed malaria cases per 1000 population
>100
50–100
10–50
1–10
0.1–1
0–0.1
No ongoing malaria transmission
Not applicable
Source: National malaria control programme reports

Ethiology

Species	**Periodicity**	**Persistent in liver?**
Plasmodium vivax	tertian	yes
Plasmodium ovale *(80%)*	tertian	yes
Plasmodium falciparum	tertian	no
about 10%, but the most severe diseases-tropical malaria		
Plasmodium malariae	quartan	no
Plasmodium knowlesi	(SE Asia, macacus)	

Clinical symptoms

- **IP:** *Pl.ovale* a *vivax* 9-16 days, *Pl.falciparum* 8-20, *Pl.malariae* 3-6 weeks
- **Prodromal stadium:** muscle and back pain, fatigue, vomiting, diarhoea
- **Malaria attack** (releasing of pyrogens): fever up to 41 °C, chills, after attack sweating
  - periodicity á 48 hr (ovale, vivax), á 72 hr (malariae)
  - **Pl. Falciparum malaria** – á 24 hod.
- other symptoms: hepatosplenomegaly, anemia, hemolytical icterus
- Nearly all death from severe malaria result from infections with *Pl. falciparum*

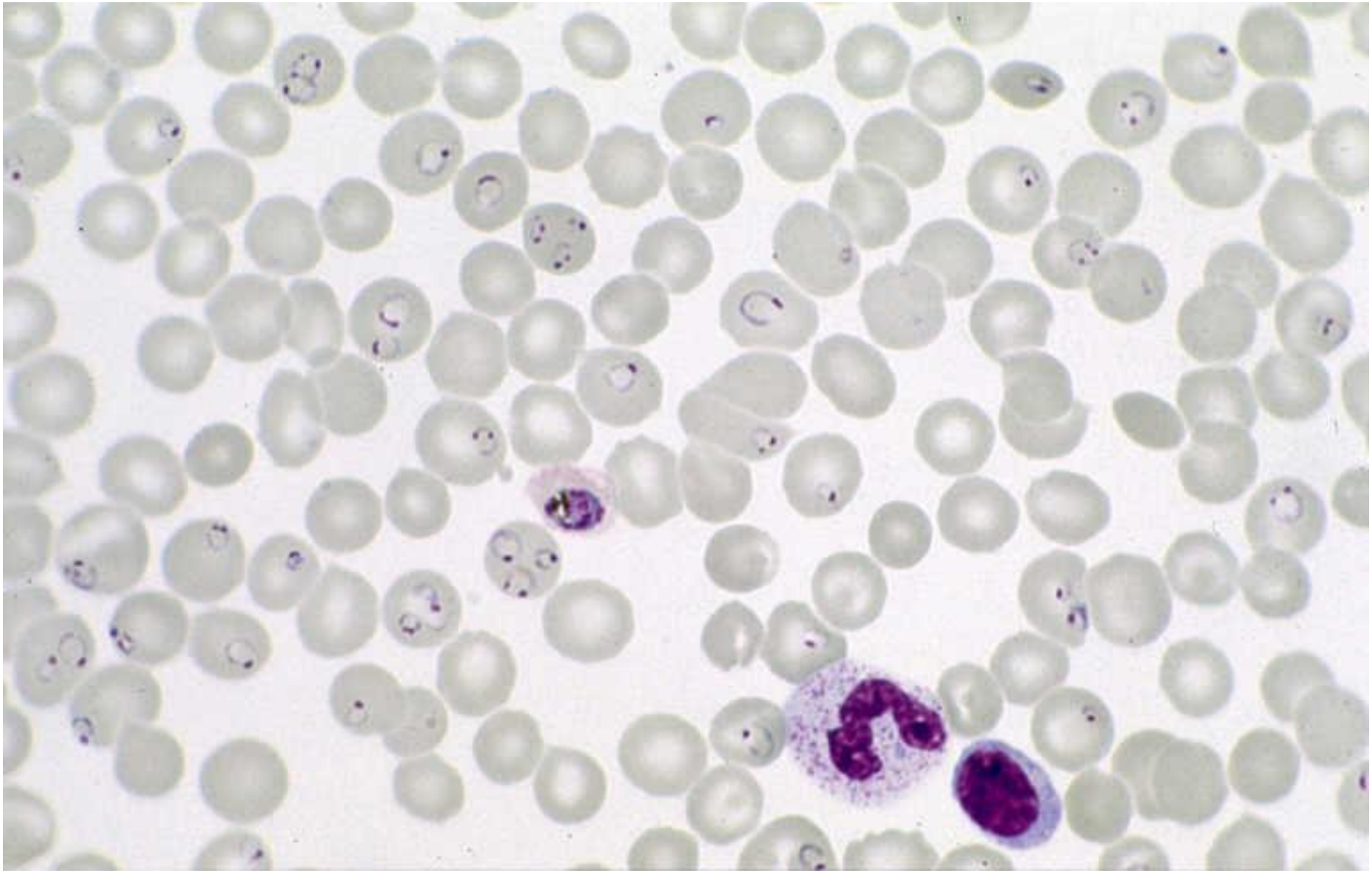
Symptoms of severe pl. Falciparum malaria

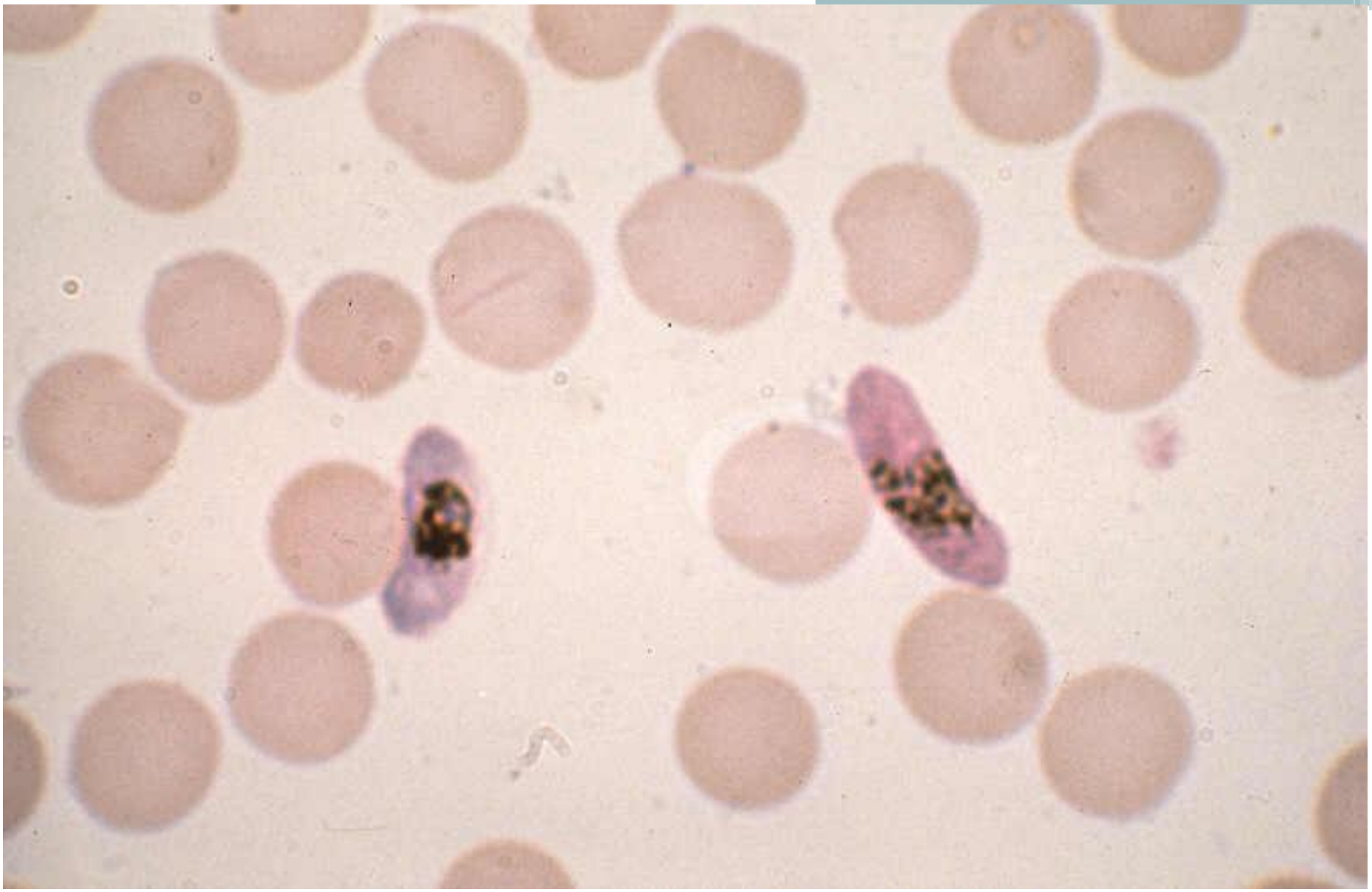
Vital organ dysfuntion:

- Impaired consciousness
- Prostration/obtundation i.e. generalised weakness
- Multiple convulsions
- Deep breathing and respiratory distress (acidotic breathing)
- Acute pulmonary oedema and ARDS
- Circulatory collapse or shock: SBP < 80 mm Hg
- Acute kidney injury
- Clinical jaundice + evidence of other vital organ dysfunction
- Abnormal bleeding

Diagnosis

- Thick and thin blood smears are gold standard
  - Identify species and quantify density
  - If can not identify species, treat for P.f.
    - Re-examine smears or use alternative diagnostic tool
- Suspect P.f. if
  - If critically ill, suspect P.f.
  - If returned from Sub-Saharan Africa, > 95 % chance of P.f. pure or mixed infection
  - Parasitemia > 1%
  - Doubly infected cells





Drugs Used to Treat Malaria

- Chloroquine (Aralen®, Dawaquine®)
- Amodiaquine (Camoquine®)
- Quinine and Quinidine
- Sulfa combination drugs (Fansidar®, Metakelfin®)
- Mefloquine (Lariam®)
- Halofantrine (Halfan®)
- Atovaquone-proguanil (Malarone®)
- Atemisin derivatives

Drug resistance is increasing

Therapy

- Standard therapy for other then *Pl. falciparum* malaria: increasing resistence
  - 4-aminoquinolins: (chloroquin)
    1.day → 600mg (4tbl.)
    á 6hod. → 300mg (2tbl.)
    2.-5.day →300mg (2tbl.)
- Antirelapse therapy (*pl. vivax, ovale*):
  - 8-aminoquinolins (Primaquin)
    2 x 7,5mg of base → 14 days
- Chloroquine combined with primaquine is the treatment of choice for chloroquine-sensitive *pl. vivax* infections.

WHO Guidelines for the treatment of Malaria 2015

Treating uncomplicated *P. falciparum* malaria

Treatment of uncomplicated P. falciparum malaria

Treat children and adults with uncomplicated *P. falciparum* malaria (except pregnant women in their first trimester) with one of the following recommended artemisinin-based combination therapies (ACT):

- artemether + lumefantrine
- artesunate + amodiaquine
- artesunate + mefloquine
- dihydroartemisinin + piperaquine
- artesunate + sulfadoxine–pyrimethamine (SP)

Strong recommendation, high-quality evidence

Duration of ACT treatment

ACT regimens should provide 3 days' treatment with an artemisinin derivative.
Strong recommendation, high-quality evidence

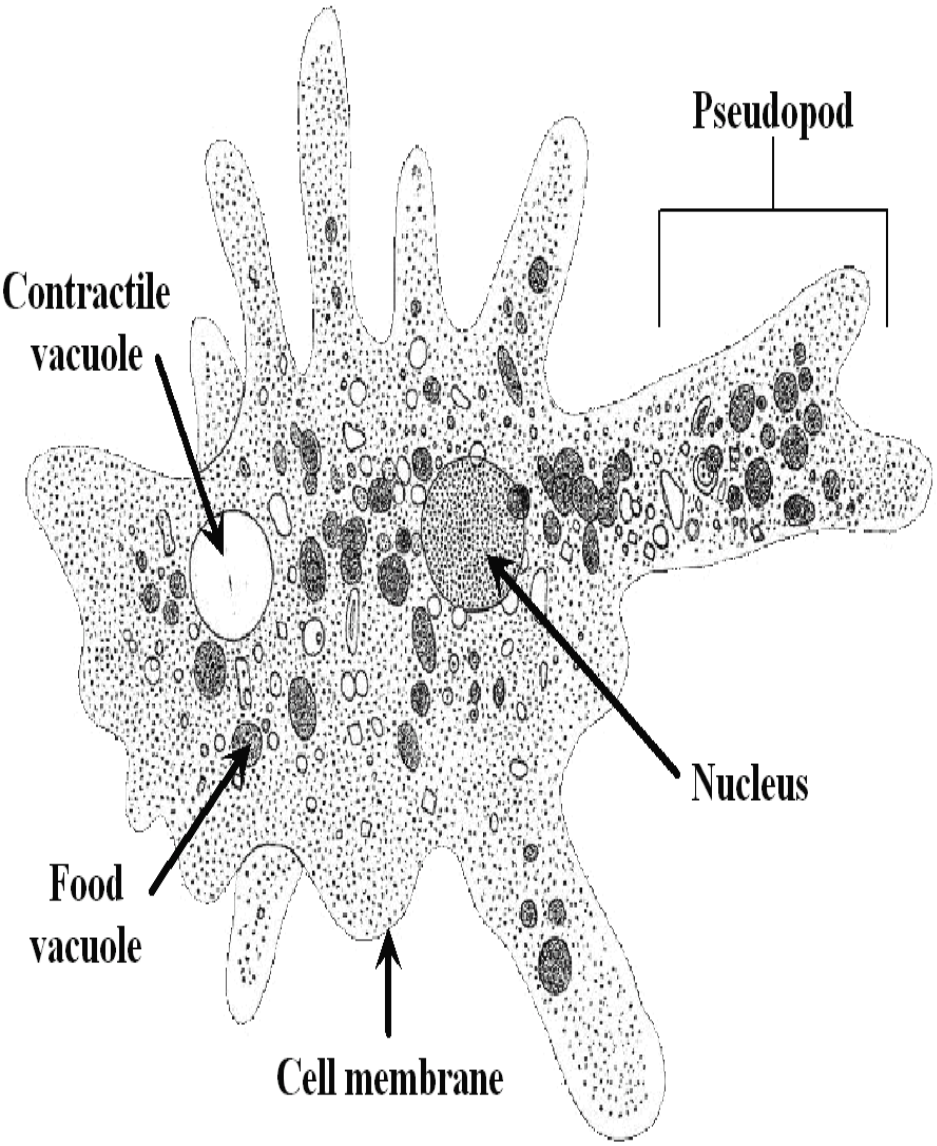
Chemoprophylaxis of malaria

- Chemoprophylaxis is based on current drug resistance patterns
- MEFLOQUINE first line prophylaxis
  - Mefloquine 250 mg po q week, 1-2 wks prior to 4 wks after
- DOXYCYCLINE as second line drug
  - Doxy 100 mg po qd, 2 days prior to 4 wks after
- Atovaquone-proguanil (Malarone)
- PRIMAQUINE
  - 30 mg* po qd x 14 days terminal prophylaxis
  - *15 mg per FDA and drug product information insert

Prevention

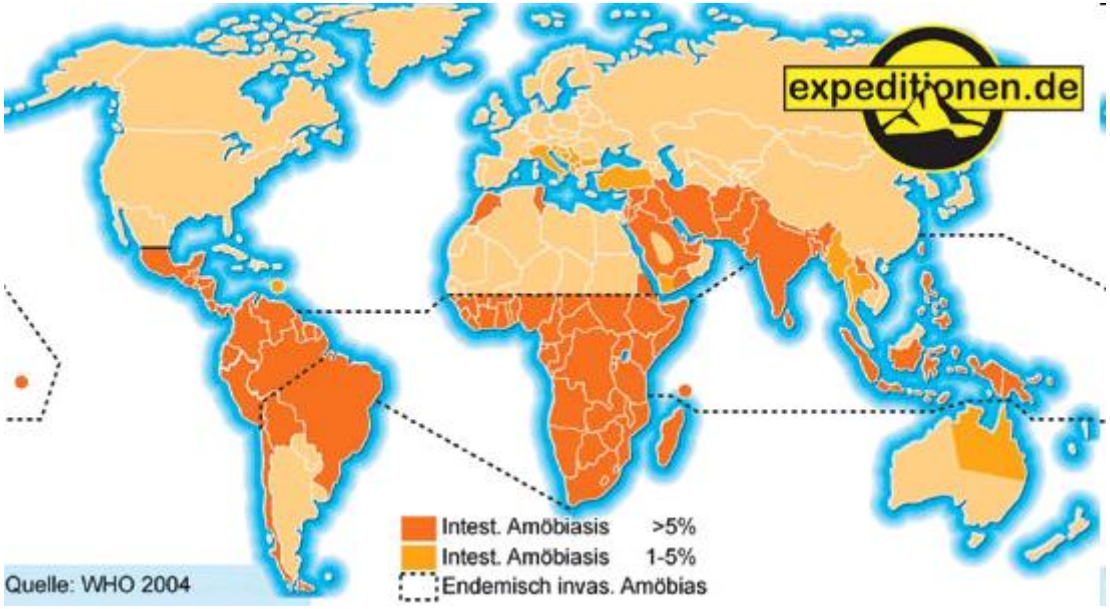
- Insecticide-treated bednet (ITNs) have been by "far the most important intervention" across Africa, and account for the prevention of 68% of malaria cases since 2000
- Artemisinin-based combination therapies and indoor residual spraying resulted in 22% and 10% of cases prevented (WHO report)

Amebiasis



- caused by a one-celled parasite *Entamoeba histolytica*
- Endemic in tropical areas with poor sanitary conditions

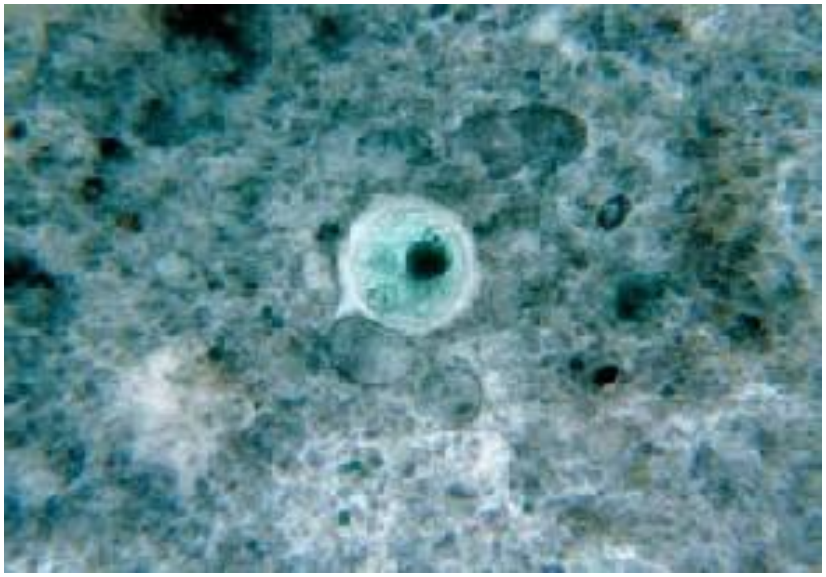
Trends of Amoebiasis



Transmission of Amebiasis

- Fecal – oral way
- contamination of drinking water and foods
- direct contact with dirty hands
- sexual contact.

Amebiasis – clinical symptoms



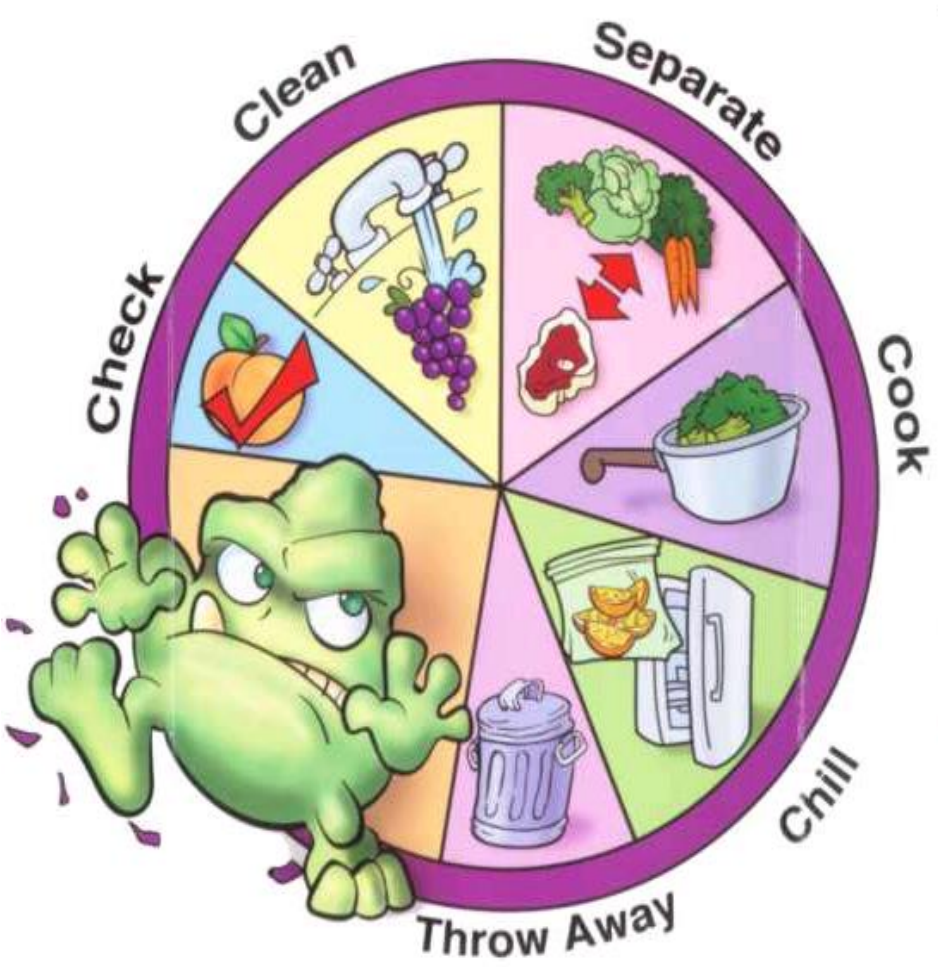
- **Asymptomatic inf. – 90%**
- **Invasive infection – 10%**
  - acute amoebic dysentery
  - amoebic colitis, appendicitis
  - toxic mega colon
  - Chronic amebiasis
  - amebomas
  - invasive extra intestinal amebiasis
    - liver abscess
    - Peritonitis
    - pleuropulmonary abscess
    - cutaneous and genital amoebic lesions

Treatment of amebiasis

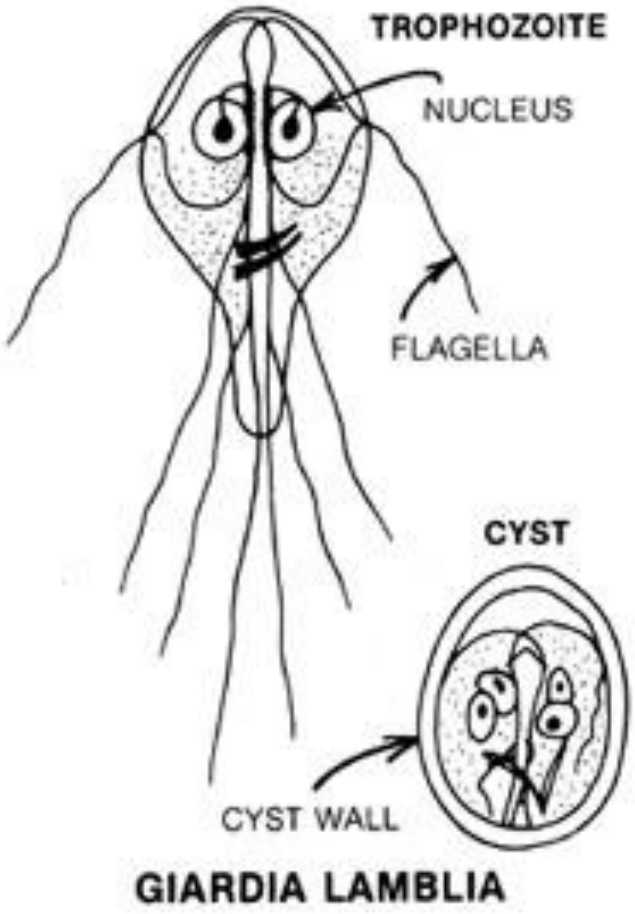
- metronidazole (Flagyl)
- tinidazole (Fasigyn)
- Chloroquine
- emetine
- doxycyklin

Prevention

- Wash your hands
- Wash vegetables and fruits before eating
- cook all raw foods
- Food safety



Giardiosis I.



- **ethiology: Giardia (Lamblia) intestinalis**
  - flagellated protozoan parasite
  - trofozoit – pear shape
  - cystic form
- **Source of infection: people, animals**
- **trnasmission: fecal - oral way, sexual contact, flys**
- Giardia cyst can survive for weeks to months in cold water

Giardiosis II.

Clinical symptoms **90% asymptomatic**

1. intestinal form (30%)
   - diarrhea
   - malaise
   - excessive gas, flatulence
   - steatorrhoea (pale, foul smelling, greasy stools)
   - epigastric pain
   - nausea, vomiting which is often violent
   - weight loss
2. hepatobiliar form (50%) – cholecystohepatitis
3. mixed form

diagnosis: **microscopy in stool and duodenal fluid**

treatment : **metronidazol, ornidazol**

Schistosoma

- Intermediate host –water snails
- Contamination of fresh water by human waste

- A genus of trematodes
- commonly known as blood-flukes
- Named also bilharzia
- Schistosomiasis is considered by the WHO as the second most important parasitic disease
  - next only to malaria
- with hundreds of millions infected pepole worldwide

Schistosomiasis=bilharsiosis

200 million people infected
flukes –sexual worms 1cm lenght

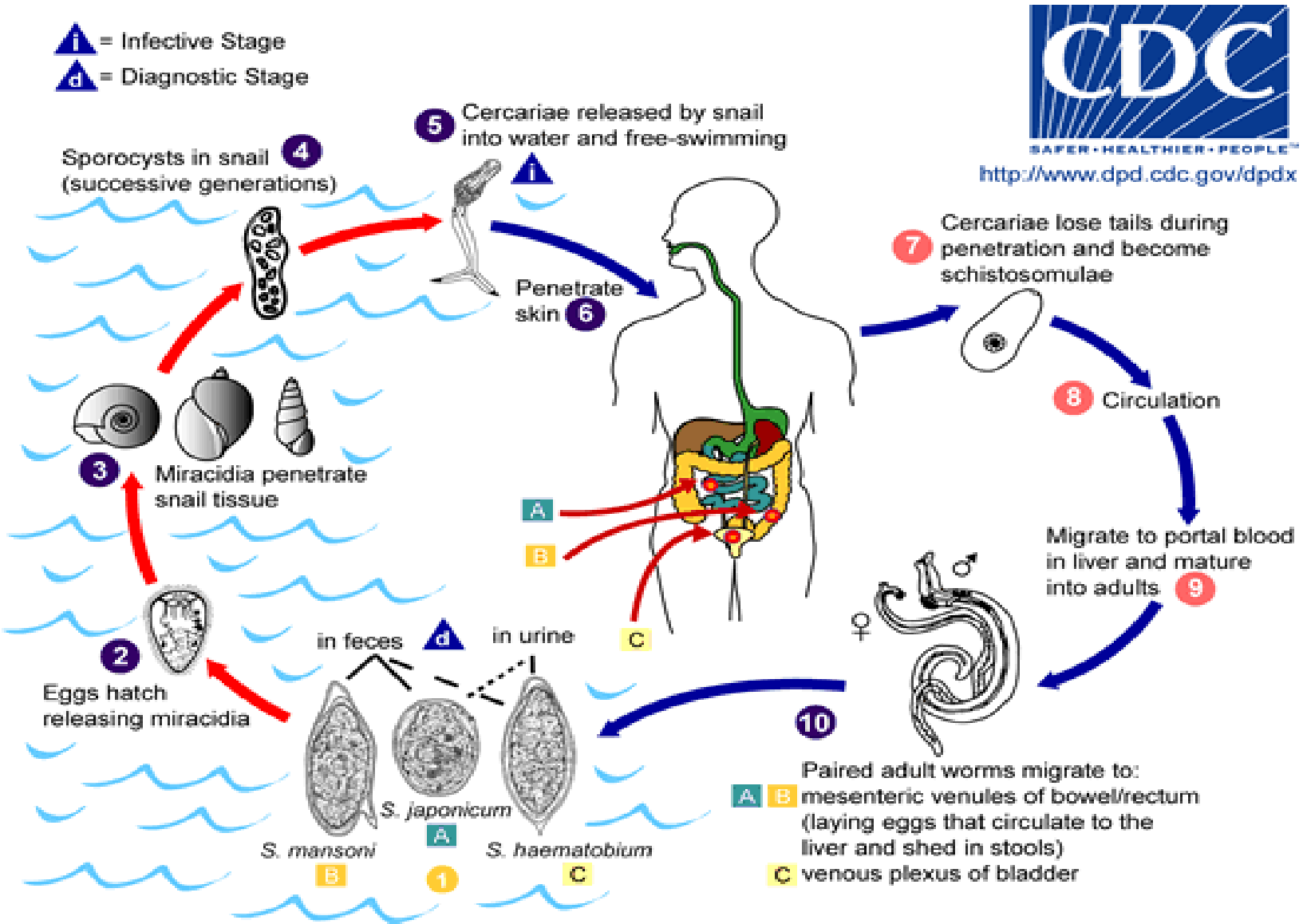
Each species has a specific geographical location:

- Schistosoma haematobium
  - Africa, Middle East
- Sch. mansoni
  - Arabia, Africa, South America, Carribean
- Sch. japonicum
  - Far East
- Sch. Mekongi
  - Southeast Asia
- Sch. Intercalatum
  - West and cetral Africa

Schistosomiasis

- Way of transmission: skin exposure to water contaminated with infected fresh water snails
- Adult worms parasitize
  - mesenteric blood vessels
  - or venous plexus of bladder
- Organs affected:
  - intestine, liver, spleen, lungs, skin,
  - kidneys, bladder, ureters
- Diagnostic specimen: urine, stool

Schistosomiasis



Clinical features – acute diseases

1. Early reaction /swimmers´ itch):
   - Cercariae penetrate the skin → dermatitis – pruritic papular rash with oedema. Resolve spontaneusly
2. Acute toxoaemic schistosomiasis „Katayama fever“
   - Rare, but severe → 1-3 months after inf.:
   - fever, chills, sweating, headache, caugh, diarrrhoea, ↑H,L, LU, eosinophilia – usually resolve
   - Usually no ova or only scanty ova in specimens

Clinical features – chronic diseases

- Occurs in patients with heavy infestation
- production of large number of eggs induce granulomatous inflammation and fibrosis which may affect many organs
    1. Genitourinary tract
    2. bowels
    3. Liver
    4. Rarely
        - CNS, spinal cord
        - Lung, others

Urinary schistosomiasis

- Chronic sequelae of *Sch. haematobium* infection (Africa)
- Bladder fibrosis and calcification –
- ureteric obstruction, hydronephrosis
- Hematuria
- Increased risk of squamous cells carcinoma of the bladder

Intestinal schistosomiasis

- *Sch. mansoni, Sch. japonicum, Sch. mekongi*
- Eggs reach mesenteric venous plexuses
- Chronic inflammation of small and large bowel
- Clinical symptoms:
  - Fatigue, colicky abdominal pain
  - Intermitent bloody diarrhoea, tenesmus, pseudopolyps, malabsorption, hypalbuminaemia, anemia
  - Dif.dg. Ulcerative colitis

Hepatic schistozomiasis

- *also Sch. Mansoni, Sch. Japonicum, Sch. Mekongi*
- Eggs reach portal venous system⇒periportal fibrosis ⇒ collateral circulation
- Sympotms: hepato-splenomegaly, portal hypertension, oesophageal varices, ascites
- Hypersplenism ⇒ pancytopenia

Schistozomiasis Dg a Th

Diagnosis:

- clinical signs + history of exposure
- Diagnostic specimen: urine, stool – microscopic demonstrations of eggs
- Urine dipstick for blood - screening
- Serologic tests

Therapy: praziqantel

Leishmaniasis

Mammalian Hosts Vectors

- Rodents
- Bats
- Primates
- Dogs
- Foxes
- humans

Phlebotomine Sandflies

Clinical Disease

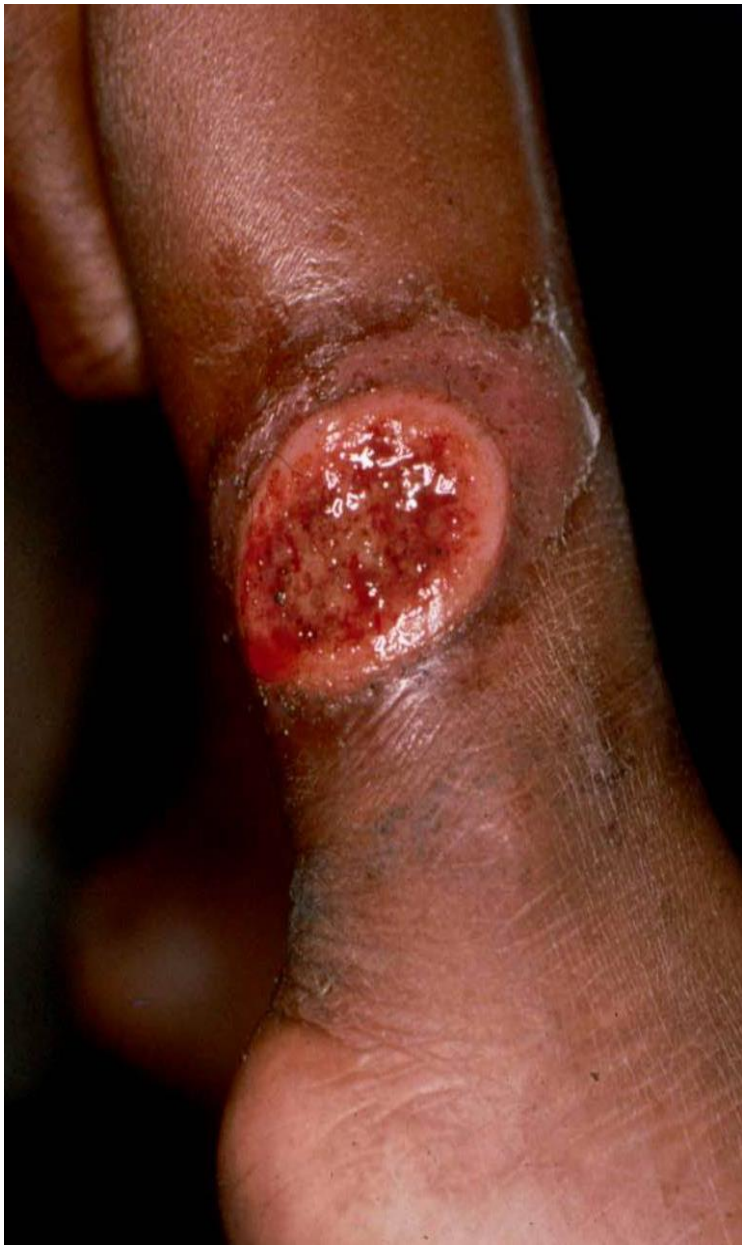
- **Visceral**
  - Fatal (90% untreated)
  - Liver
  - Spleen
  - Bone marrow
- **Cutaneous**
  - Generally Self- healing
  - Skin
  - Mucous membranes

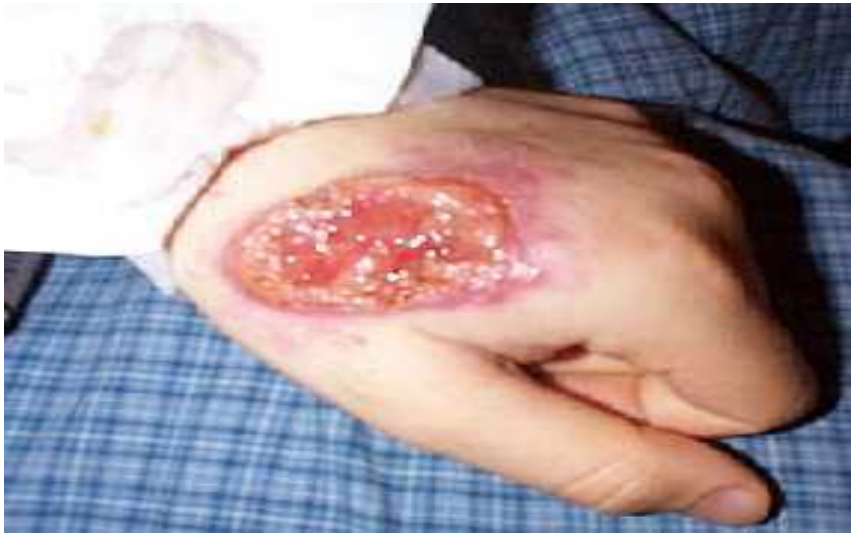
Cutaneous leishmaniasis

- localized or diffuse infections - skin reactions
- the most common is the *Oriental Sore* (caused by Old World species *L. major*, *L. tropica*, and *L. aethiopica*
- in the New World, the most common culprits is *L. mexicana*
- Cutaneous infections are most common in Afghanistan, Brazil, Iran, Peru, Saudi Arabia and Syria

Cutaneous leishmaniasis

- Symptoms:
- hypo-pigmented macules, papules, nodules, or facial erythema
- macular, depigmented eruption found mainly on the face, arms, and upper part of the trunk



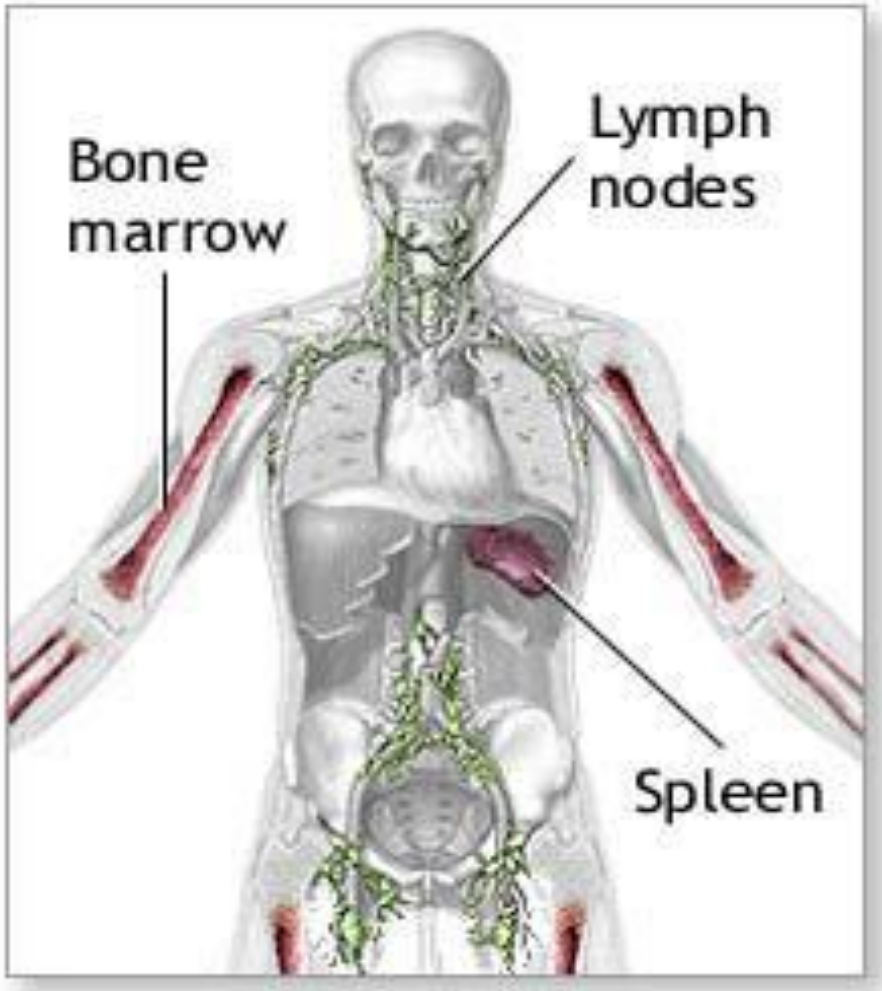


Visceral leishmaniasis

- kala-azar, black fever, and Dumdum fever
- caused exclusively by species of the *L. donovani* complex (*L. donovani*, *L. infantum* syn. *L. chagasi*)
- visceral infections are most common in Bangladesh, Brazil, India, Nepal and Sudan

Visceral leishmaniasis

- the parasite migrates to the internal organs such as liver, spleen and bone marrow, and, if left untreated, will almost always result in the death of the host (up to 3 years)
- symptoms include fever, weight loss, mucosal ulcers, fatigue, anemia and substantial swelling of the liver and spleen



A.D.A.M.

Diagnosis

Clinical signs & symptoms

Hypergammaglobulinemia

- Serology

Bone marrow biopsy

Spleen or liver biopsy

Culture & Histology

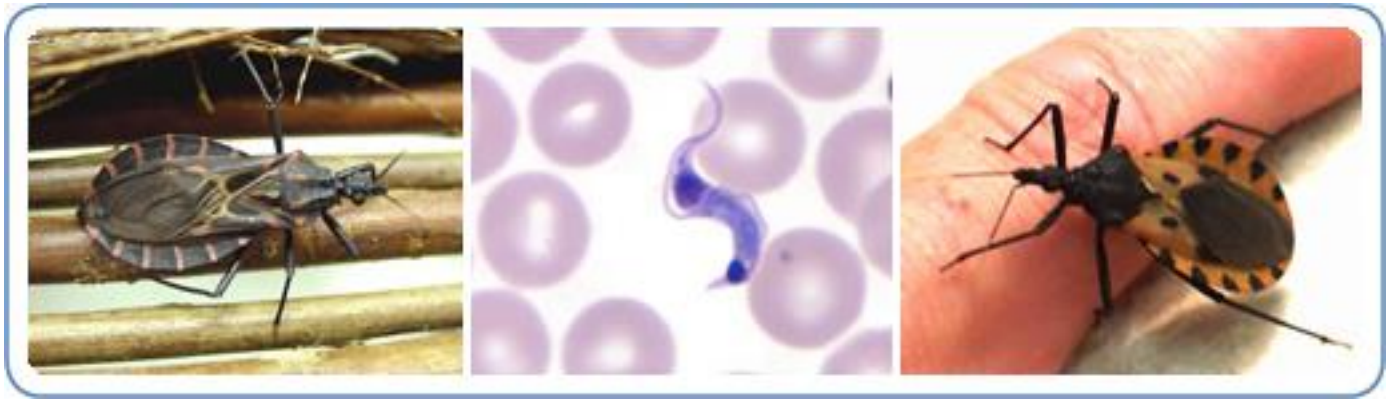
PCR

Treatment

- Good nursing
- Diet
- Pentavalent antimony
- Pentamidine
- amphotericin B
- Antibiotics - paromomycin (a parenteral aminoglycoside)
- miltefosine

- New drugs - New delivery

American trypanosomiasis - Chagas' disease



American trypanosomiasis

- Agent: protozoan *Trypanosoma cruzi*
- Transmission: through feces of an infected triatomine insect "kissing bug"
  - if bug bite is scratched or
  - by consuming contaminated food or beverages - rare
  - through blood transfusion or organ transplantation
  - from mother to infant.
- is found only in the Americas - mainly, in rural areas of Latin America

American trypanosomiasis

- Chagas' disease is the third most common parasitic disease globally, after malaria and schistosomiasis
- An estimated 6 to 7 million persons are infected, and 36,800 new cases occur each year.

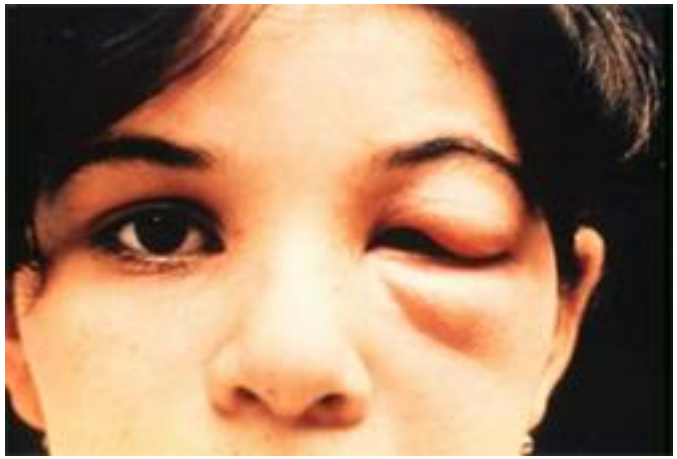
Chagas disease

- acute phase
- chronic phase
  - prolonged asymptomatic form
  - Organomegaly
  - Cardiomyopathy

- If untreated, infection is lifelong

Acute Chagas disease

- occurs immediately after infection
- may last up to a few weeks or months
- parasites may be found in the circulating blood.
- Symptoms:
  - Usually mild or asymptomatic
  - fever and swelling around the site of inoculation
  - Rarely, acute infection may result in severe myocarditis or the meningoencephalitis



Romaña's sign, the swelling of the child's eyelid, is a marker of acute Chagas disease. The swelling is due to bug feces being accidentally rubbed into the eye, or because the bite wound was on the same side of the child's face as the swelling.

Chronic Chagas disease

- Many people may remain asymptomatic for life
- 20 - 30% of infected people will develop Chagas-related symptoms:
  - Organomegaly
  - Cardiomyopathy
  -

Chagas´chronic cardiomyopathy

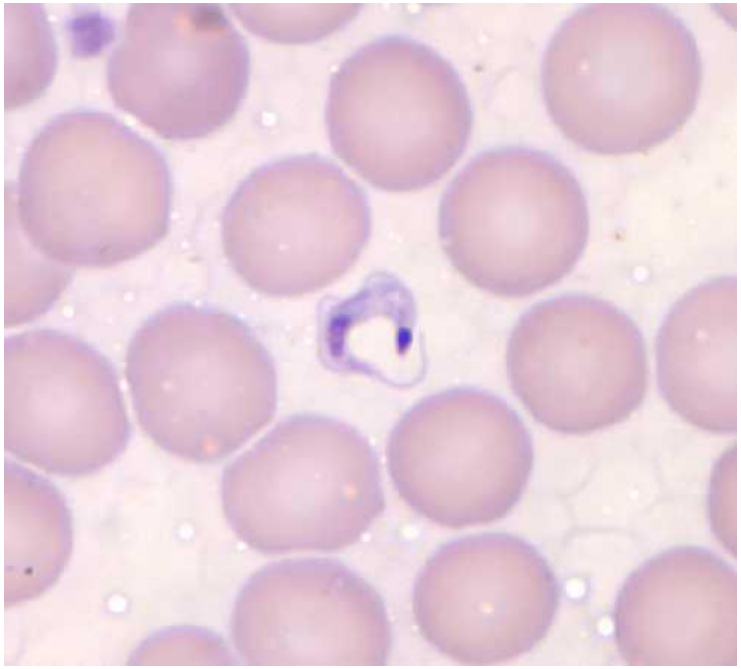
- the most common form of nonischemic cardiomyopathy
- one of the leading causes of complications and death in Latin America.
- develops in approximately 25% of patients infected with Trypanosoma cruzi
- is associated with malignant arrhythmias, conduction disturbances, heart failure, and pulmonary and systemic embolism

Diagnosis

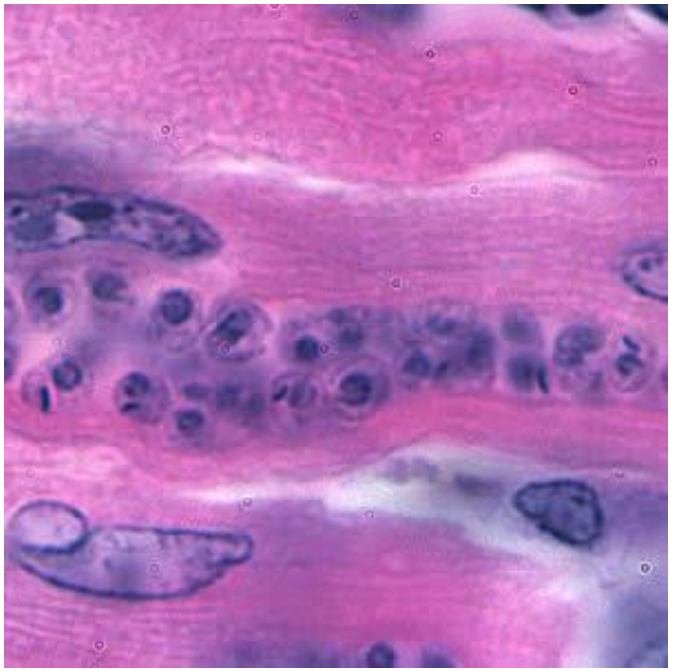
- Microskopy – thick and thin blood smear
  - In the acute stage of the disease in blood or CSF
  - During the chronic stage - trypomastigotes are usually not found circulating in blood
  - Amastigotes may be found in biopsy specimens
- serologic testing is recommended in chronic stage
- Molecular testing - PCR

Tripanosoma cruzi

trypomastigote in a thin blood smear stained with Giemsa



amastigotes in heart tissue



Treatment

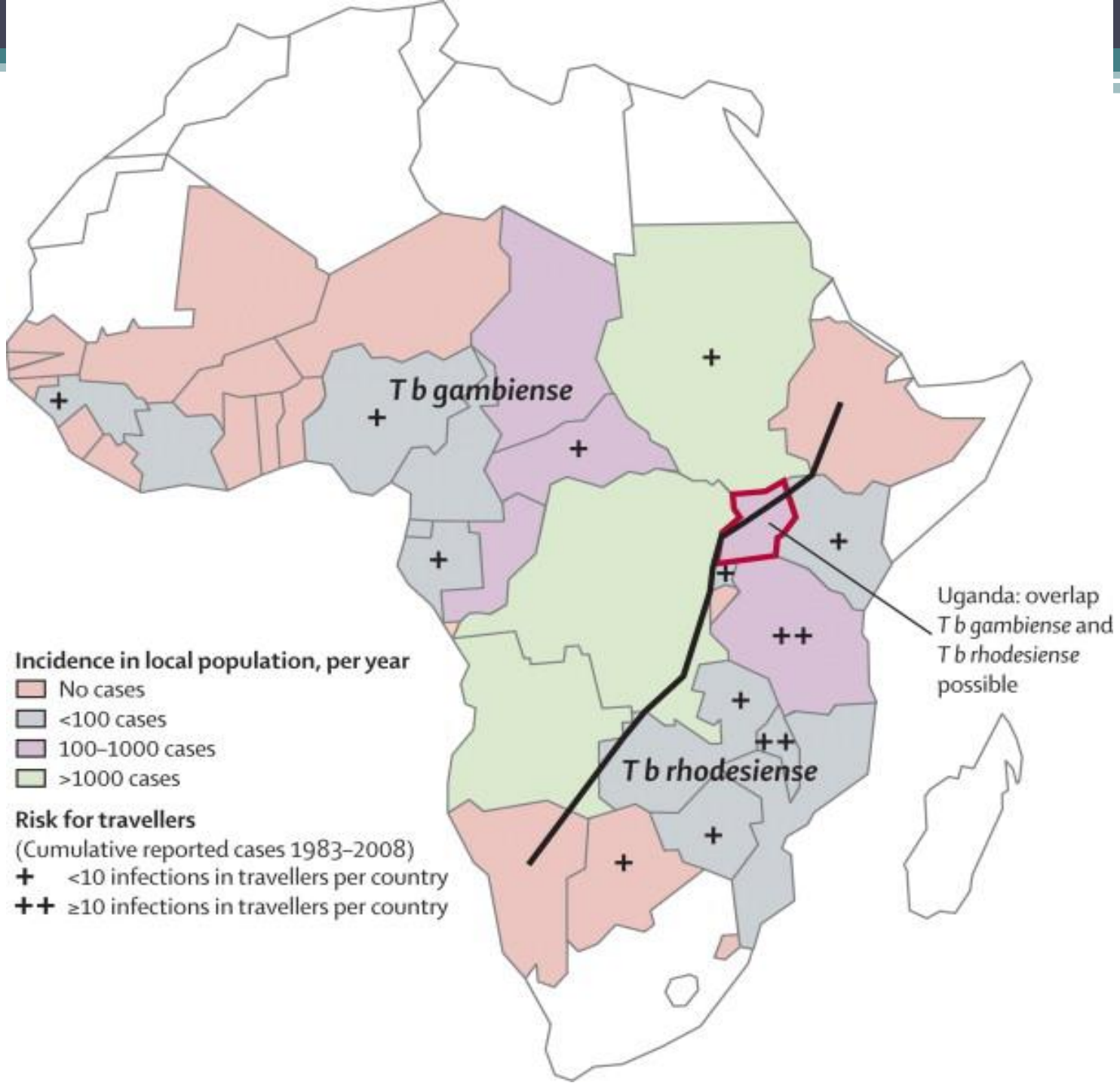
- Antiparasitic treatment –
  - nifurtimox and benznidazole
    - is indicated for all cases of acute or reactivated Chagas disease and for chronic *Trypanosoma cruzi* infection in children up to age 18.
    - for adults up to 50 years old with chronic infection who do not already have advanced Chagas cardiomyopathy

Chagas´cardiomyopathy - Th

- acute disease, can be cured with trypanocidal treatment
- in chronic cardiomyopathy, the role of the parasite is debated
- the effect of trypanocidal treatment is unclear
- autoimmune mechanisms were implicated as potential causes of late cardiac injury
- parasite persistence may be an important factor that, in conjunction with individual host factors, triggers the inflammatory process
- benznidazole treatment significantly reduced the detection of circulating parasites but did not reduce cardiac clinical progression

African trypanosomiasis

- sleeping sickness - endemic to sub-Saharan Africa
- transmitted to human hosts by bites of infected tsetse flies.
- caused by 2 subspecies of the flagellate protozoan *Trypanosoma brucei*
  - East African or Rhodesian trypanosomiasis –
    - ***T. brucei rhodesiensae***
    - is a zoonotic infection with animal vectors - antilope
  - West African or Gambian trypanosomiasis –
    - ***T. brucei gambiensae***
    - the reservoirs of infection are exclusively human


T b gambiense
T b rhodesiense
Uganda: overlap
T b gambiense and
T b rhodesiense
possible
Incidence in local population, per year
No cases
<100 cases
100–1000 cases
>1000 cases
Risk for travellers
(Cumulative reported cases 1983–2008)
+ <10 infections in travellers per country
++ ≥10 infections in travellers per country

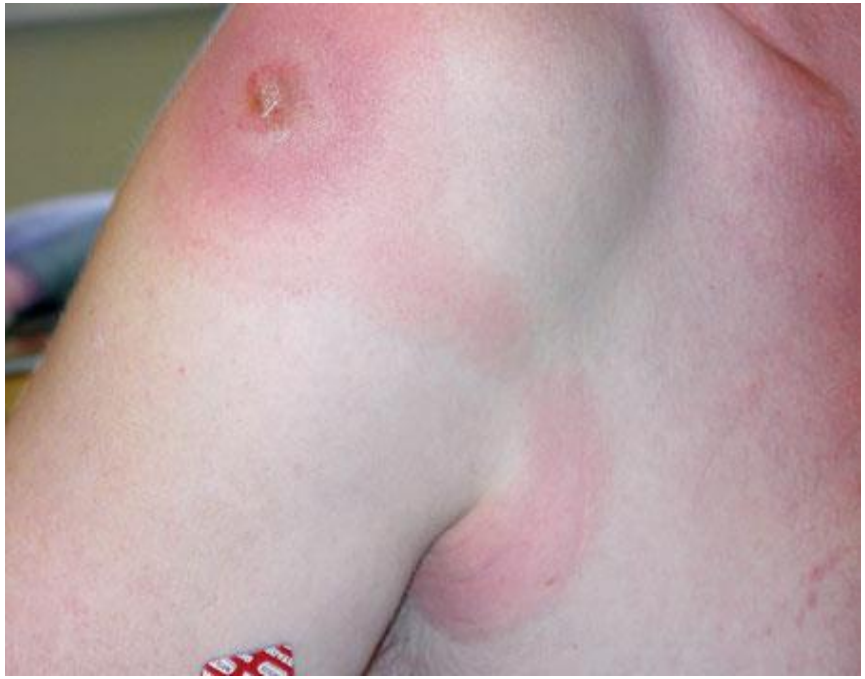
Clinical signs

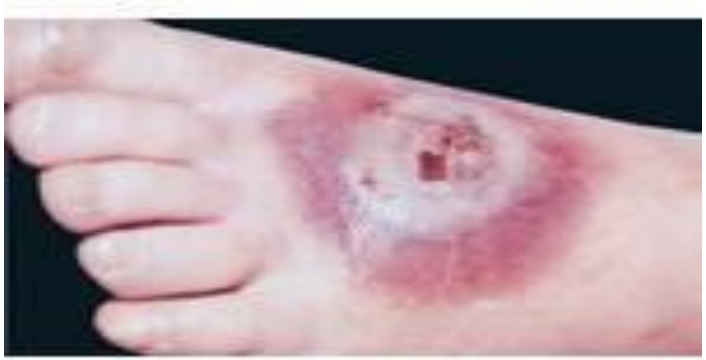
- Two stages:
  - 1. early or hemolymphatic stage
  - 2. late or neurologic stage
- Death if untreated - is usually due to aspiration or seizures caused by CNS damage.
  - after 2-4 month in East Africa
  - after 3 years in West Africa

Clinical signs - 1. early or hemolymphatic stage

- Chancre -painless skin induration at bite site
  - appears about 5-15 days after the bite
  - resolve spontaneously
- Intermittent fever - 3 weeks after the bite
- malaise, myalgia, arthralgias, and headache
- Generalized or regional lymphadenopathy
- Splenomegaly
- hypersensitivity reaction - 6-8 weeks after onset
  - Facial edema
  - Transient urticarial rashes - Skin lesions (trypanids)

Chancre at bite site





Clinical signs – 2. late or neurologic stage

- Persistent headaches (refractory to analgesics)
- Daytime somnolence followed by nighttime insomnia
- Behavioral changes, mood swings, or depression
- Loss of appetite, wasting syndrome, and weight loss
- Seizures (more common in children)
- Psychosis
- Stupor and coma
- Meningismus is rare

Diagnosis

- microscopic examination of
  - Blood
  - CSF
  - lymph node aspirate
  - biopsy of a chancre
- serology

Treatment

Table. Medications Recommended for Treatment of African Trypanosomiasis

Type of Trypanosomiasis	Stage 1 (Early or Hemolymphatic Stage)	Stage 2 (Late or Neurologic Stage)
East African trypanosomiasis (caused by *Trypanosoma brucei rhodesiense*)	Suramin 100-200 mg IV test dose, then 1 g IV on days 1, 3, 7, 14, 21	Melarsoprol 2-3.6 mg/kg/day IV for 3 days; after 1 week, 3.6 mg/kg/day for 3 days; after 10-21 days, repeat cycle
West African trypanosomiasis (caused by *Trypanosoma brucei gambiense*)	Pentamidine isethionate 4 mg/kg/day IM for 10 days *or* Suramin 100-200 mg IV test dose, then 1 g IV on days 1, 3, 7, 14, 21	Nifurtimox-eflornithine combination therapy (NECT): Nifurtimox 5 mg/kg PO q8h for 10 days and eflornithine 200 mg/kg IV q12h for 7 days *or* Eflornithine 400 mg/kg/day IV in 2 divided doses for 14 days *or* Melarsoprol IV for 10 days