

Importované parazitární infekce a možnosti jejich diagnostiky

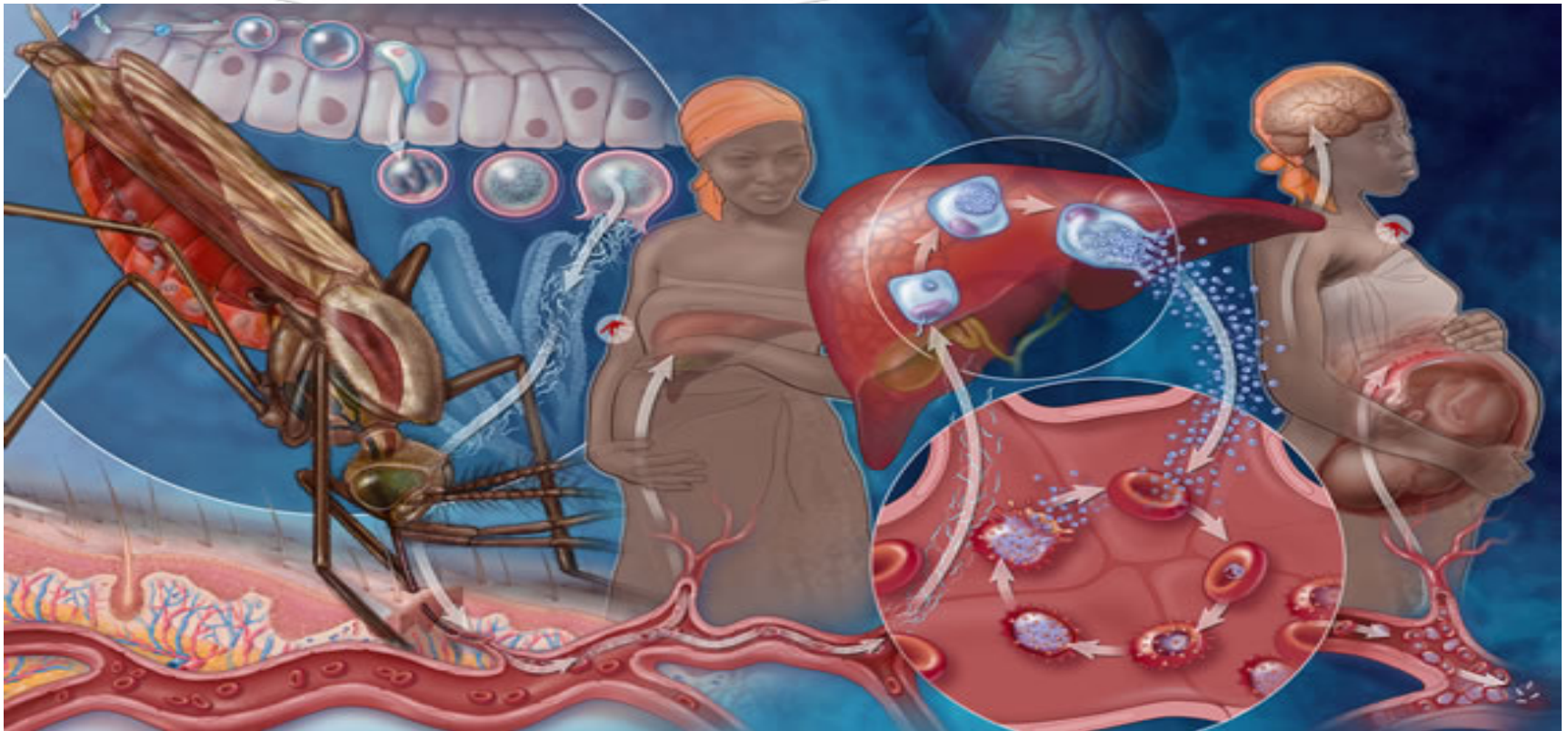
Lenka Richterová

NRL pro diagnostiku tropických parazitárních infekcí, FNB

Specializační kurz: Lékařská parazitologie – novinky

19. 9. - 21. 9. 2023

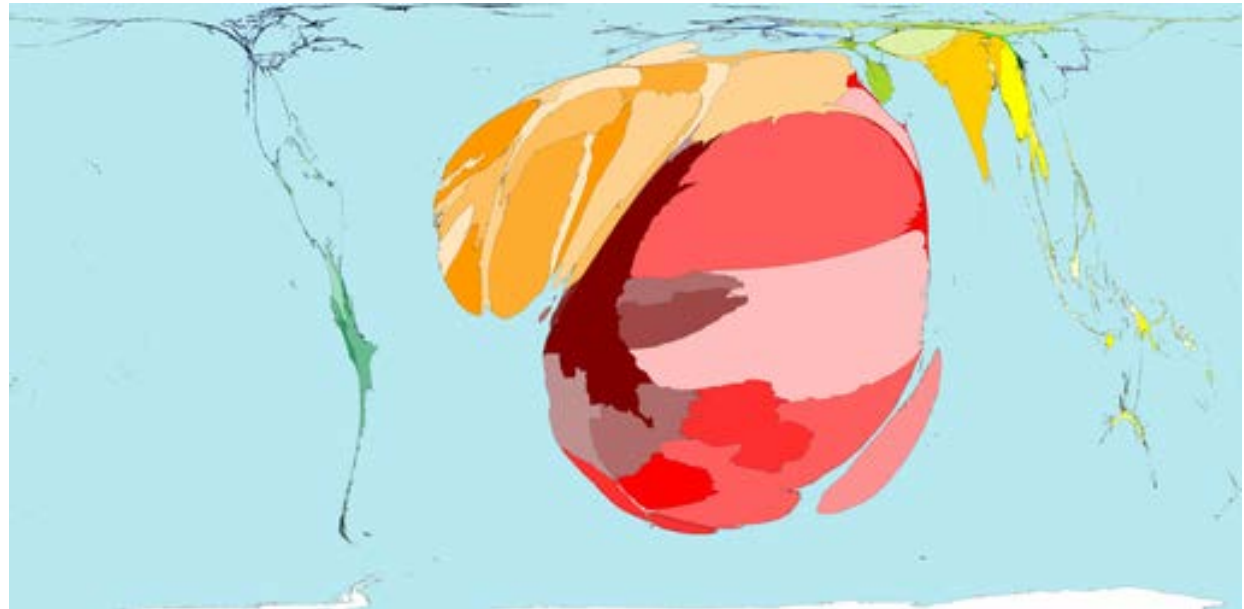
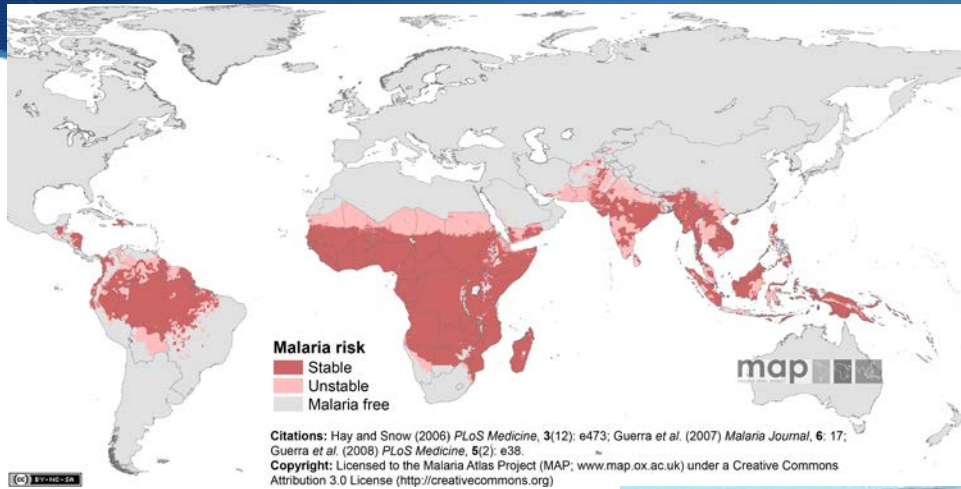
Plasmodium falciparum - životní cyklus



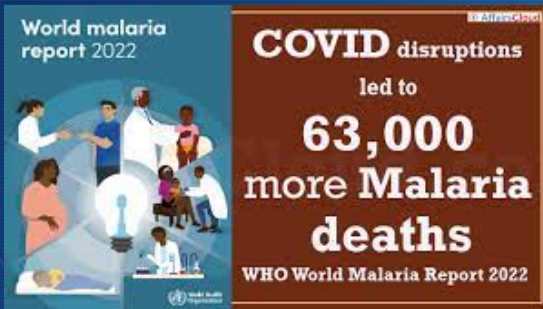
Malaria Clinical presentation

- ◆ symptoms of **uncomplicated** malaria can be rather **non-specific**
- ◆ **untreated** malaria can progress to severe forms that may be rapidly (**<24 hours**) **fatal**
- ◆ most frequent symptoms include **fever** and **chills**, which can be accompanied by **headache, myalgias, arthralgias, weakness, vomiting, and diarrhoea**
- ◆ Other clinical features include **splenomegaly**, anemia, **thrombocytopenia**, hypoglycemia, pulmonary or renal dysfunction, and neurologic changes

Malaria Epidemiology



World malaria report 2022



2016 prvně po více než 20ti letech, kdy byl nárůst počtu případů!!!

Venezuela
1 mil 2018

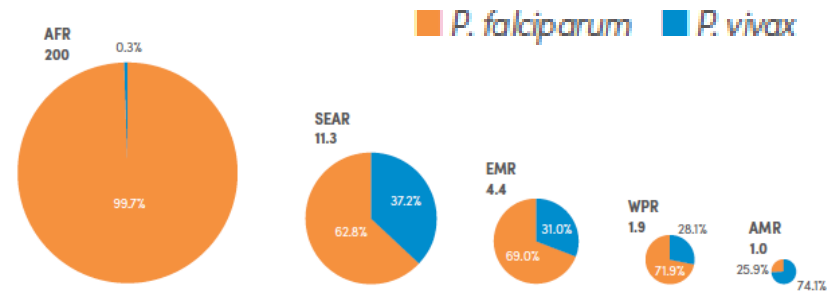
Burundi
7,2 mil 2019

Countries with indigenous cases in 2000 and their status by 2017 Countries with zero indigenous cases over at least the past 3 consecutive years are considered to be malaria free. All countries in the WHO European Region reported zero indigenous cases in 2016 and again in 2017. In 2017, both China and El Salvador reported zero indigenous cases. Source: WHO database



- One or more cases in 2017
- Zero cases in 2017
- Zero cases (≥ 3 years) in 2017
- Certified malaria free since 2000
- No malaria
- Not applicable

Estimated malaria cases (millions) by WHO of the estimated number of cases in each region



AFR: WHO African Region; AMR: WHO Region of the Americas; EMR: WHO Eastern Mediterranean Region; *P. falciparum*: *Plasmodium falciparum*; *P. vivax*: *Plasmodium vivax*; SEAR: WHO South-East Asia Region; WHO: World Health Organization; WPR: WHO Western Pacific Region.

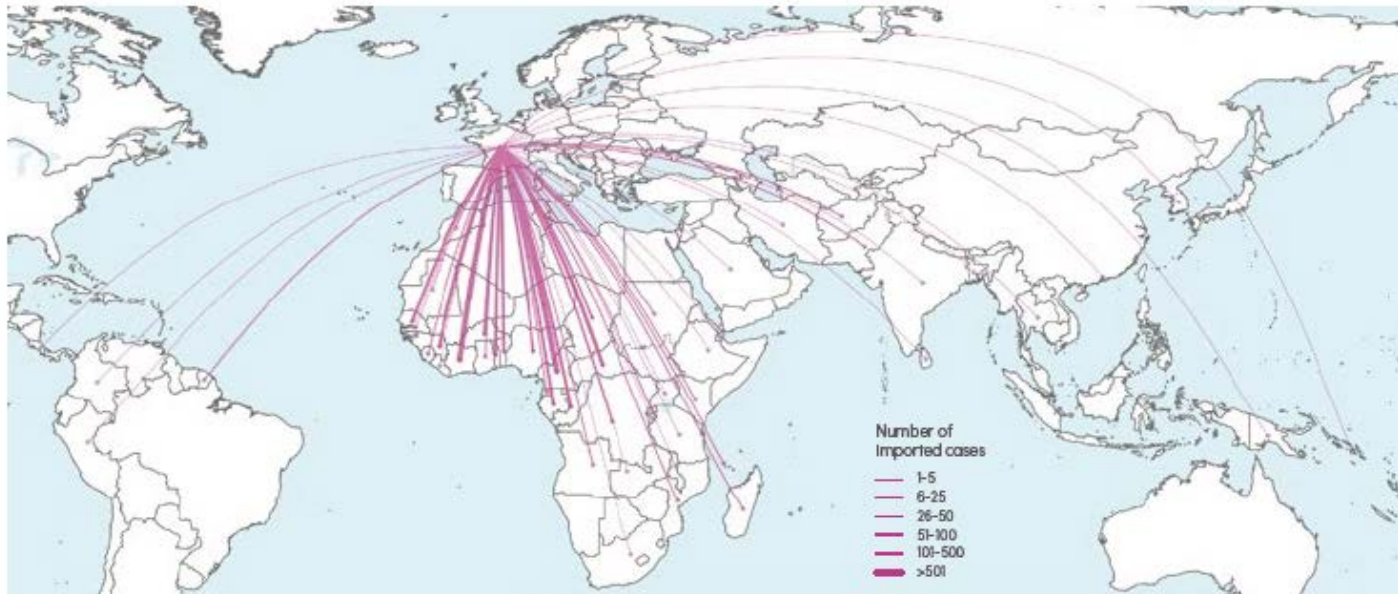
- 247mil případů (232/245/247) 234 Afrika
- 4,9mil *P. vivax*
- 619 000 úmrtí (568/625/619) 593 Afrika

World malaria report

Imports to Europe

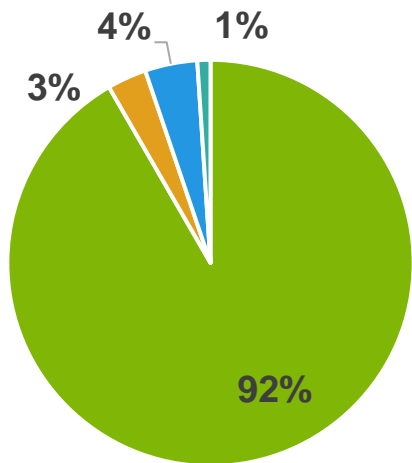
A. Origin of infection in the three European countries with highest number of imported malaria cases, 2017

1. France



Importovány do ČR z 2015-2017

2006-2014 Africa represented just 66%



- Africa
- Asia
- Melanesia
- South America

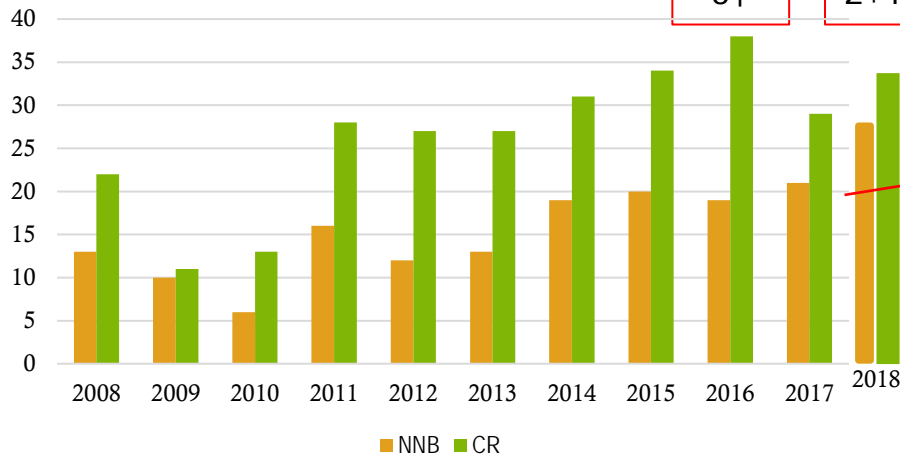




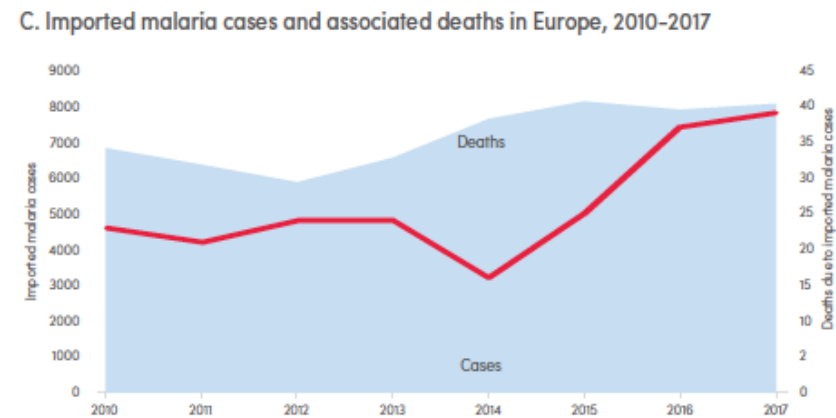
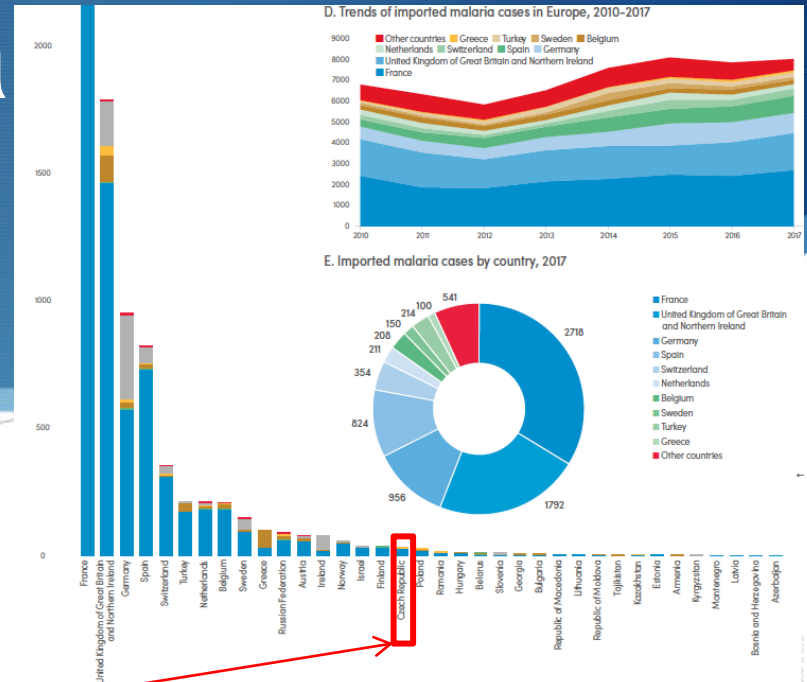
World malaria report

Malaria in Czech Republic 2008-2018

Epidat, NNB



(Epidat, SZÚ a NNB)
 2019-34
 2020-9
 2021-10
 2022-22



Malaria

- ◆ RDT antigen – *P. falciparum*/ *P.spp*
- ◆ **Microscopy** – species determination, parasitemia
- ◆ **PCR** – detection of sub microscopical parasitemia, mixed infections, damaged plasmodia

Malaria RDT

HRP – 2

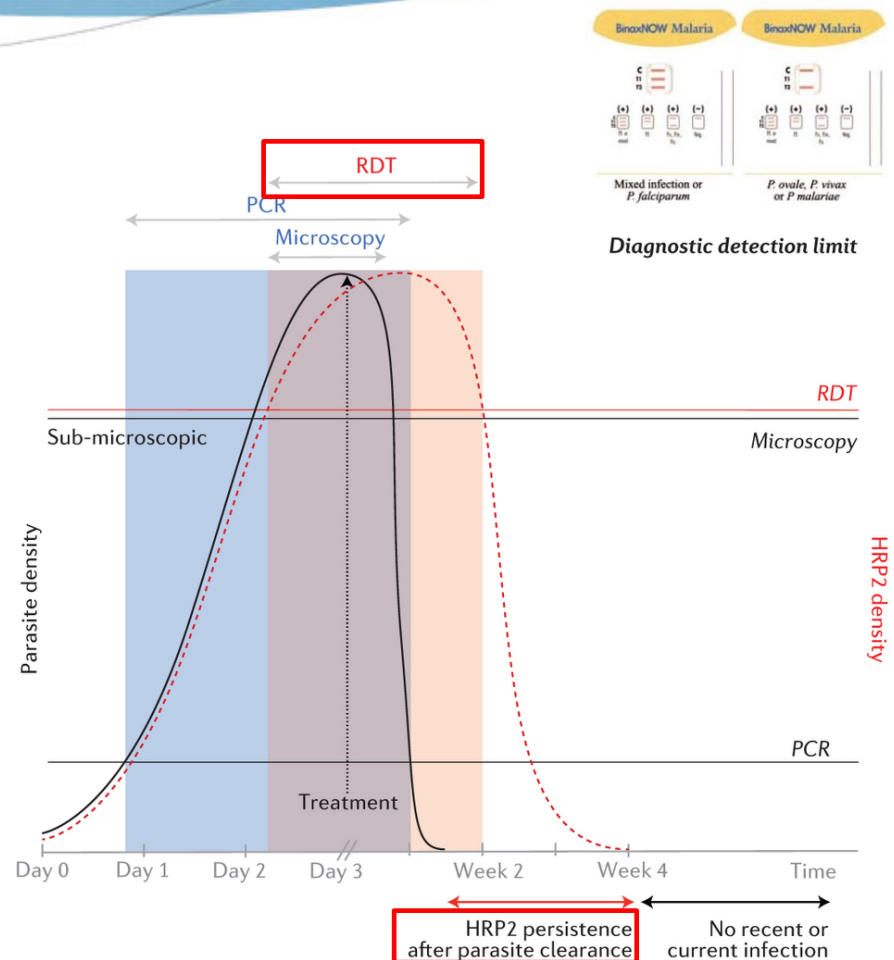
Plasmodium falciparum

Sequence polymorphism

Aldolase

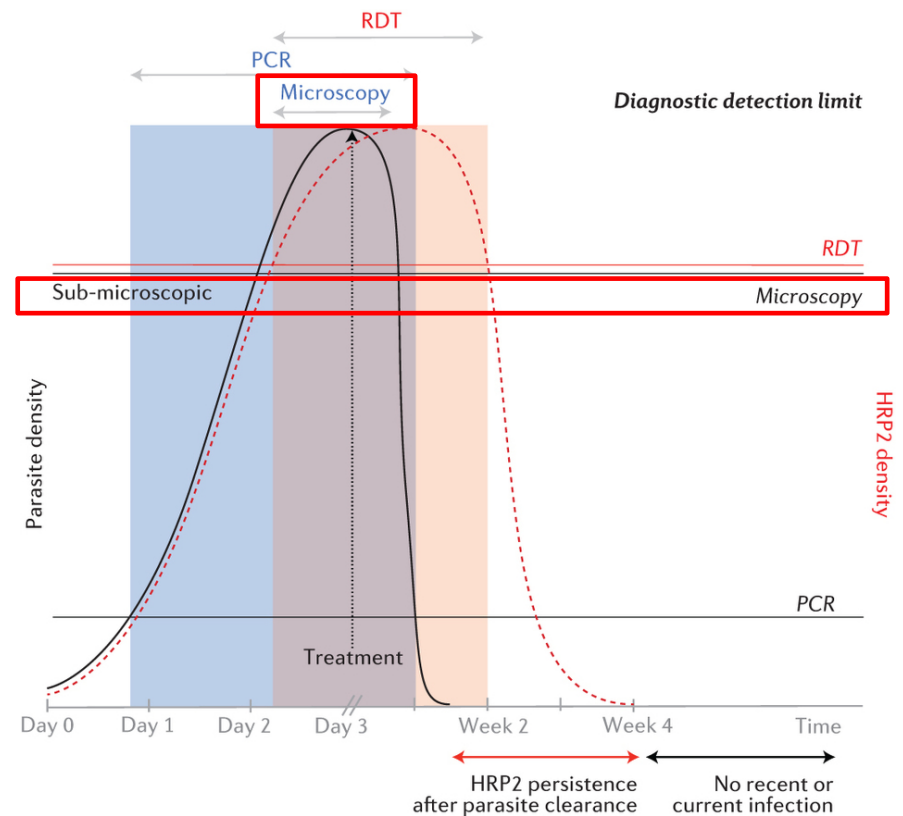
Plasmodium spp.

High false negativity *P. ovale* a *P.malariae*

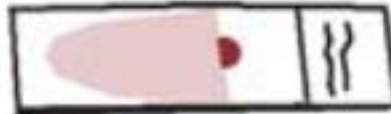
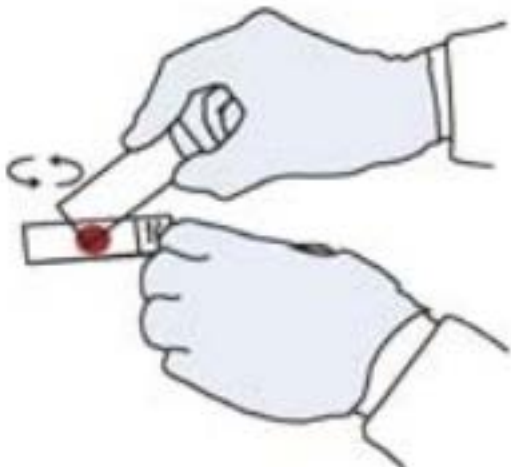
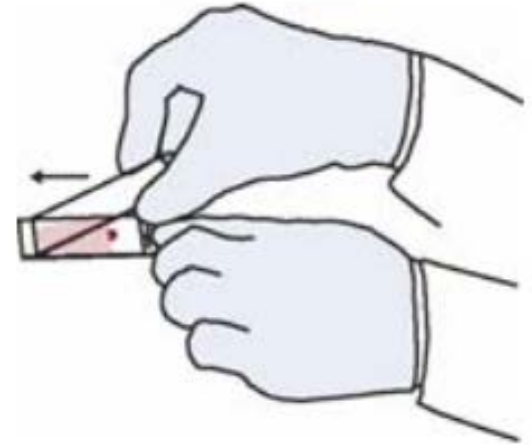
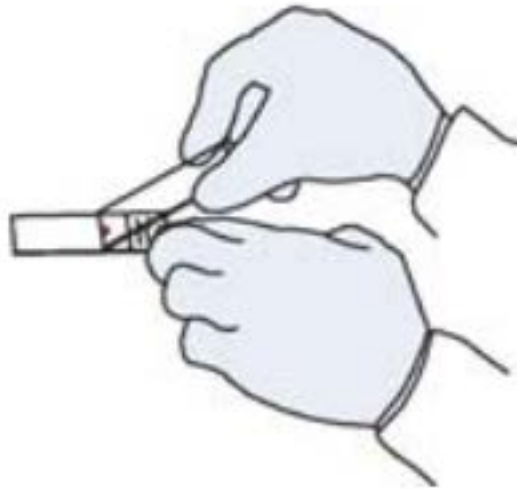
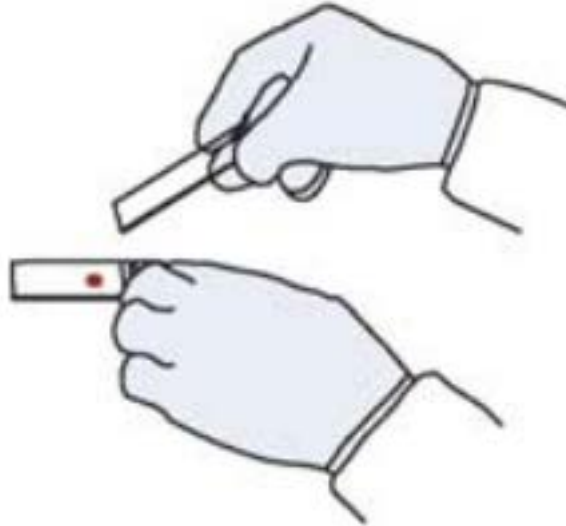


Malaria microscopy

- Essential for parasitaemia
- Detection minimum parasitaemia 0.001%
- Species identification

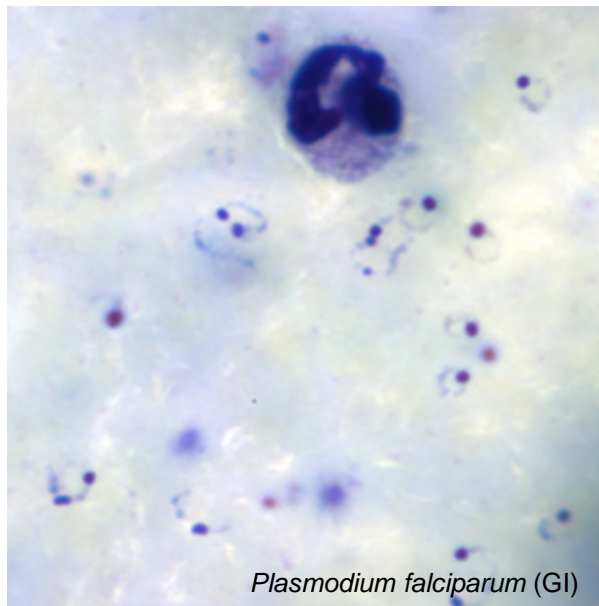


Thin and thick smear



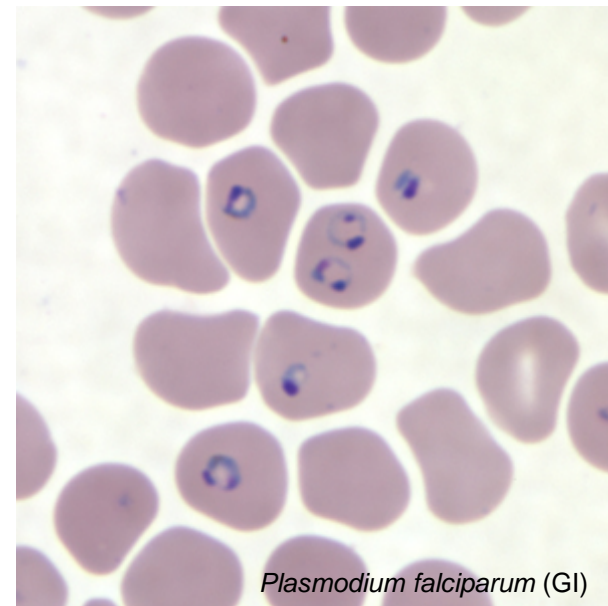
Malaria microscopy

Thick smear



10x sensitivity

Thin smear



Morfology

Thin smear

Plasmodium falciparum

Plasmodium vivax

Plasmodium falciparum Blood Stage Parasites, Thin Blood Smears

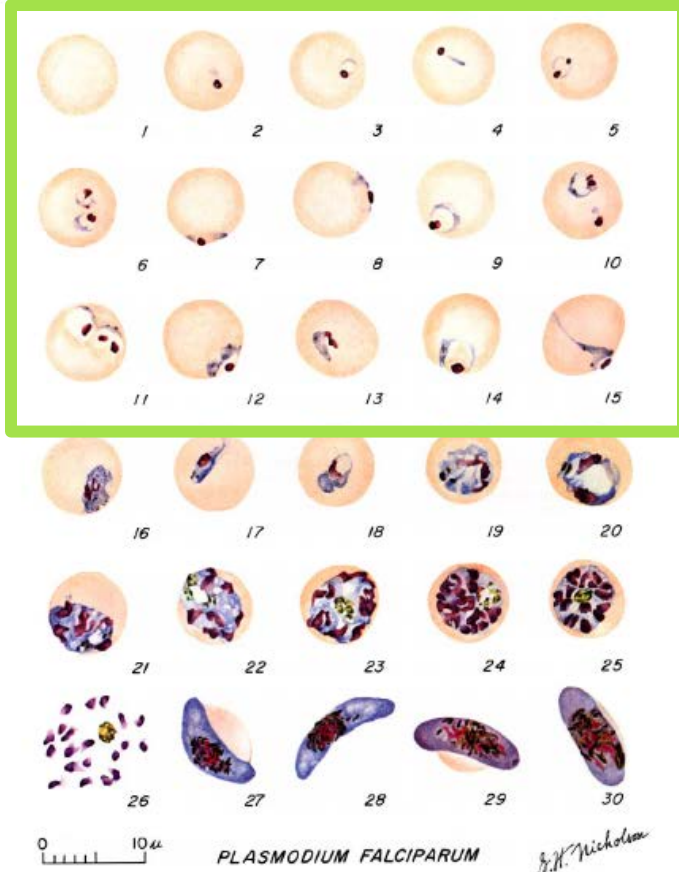


Fig. 1: Normal red cell
Figs. 2-18: Trophozoites (among these, Figs. 2-10 correspond to ring-stage trophozoites)

Figs. 19-26: Schizonts (Fig. 26 is a ruptured schizont)
Figs. 27, 28: Mature macrogametocytes (female)
Figs. 29, 30: Mature microgametocytes (male)

Illustrations from: Coakley GR, Collins WE, Warren M, Contacos PG. The Primate Malaria. U.S. Department of Health, Education and Welfare, Bethesda, 1971.

Plasmodium vivax Blood Stage Parasites, Thin Blood Smears

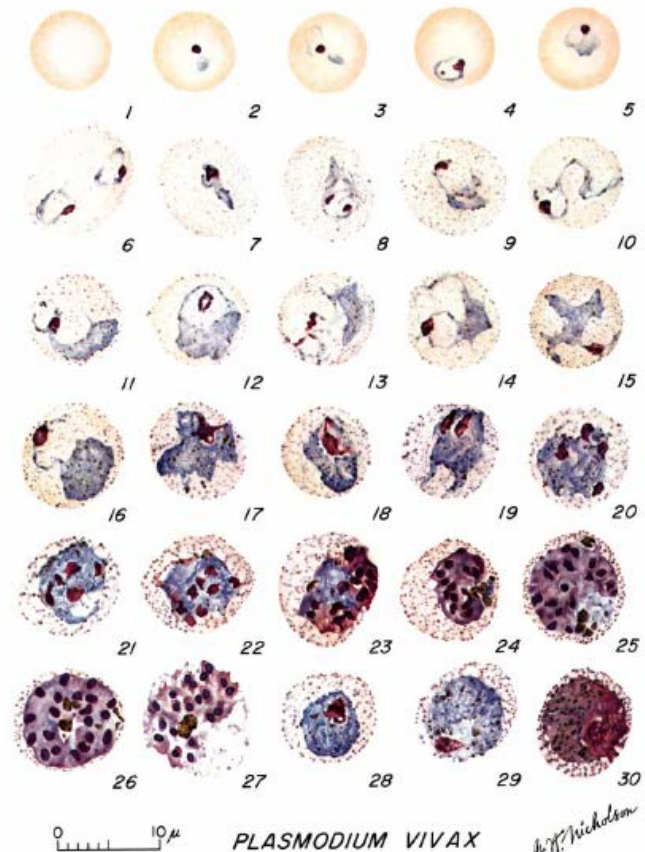


Fig. 1: Normal red cell
Figs. 2-6: Young trophozoites (ring stage parasites)
Figs. 7-18: Trophozoites

Figs. 19-27: Schizonts
Figs. 28 and 29: Macrogametocytes (female)
Fig. 30: Microgametocyte (male)

Illustrations from: Coakley GR, Collins WE, Warren M, Contacos PG. The Primate Malaria. U.S. Department of Health, Education and Welfare, Bethesda, 1971.

Malaria treatment



ACT – first line treatment



Chloroquine: 1945 - 1957

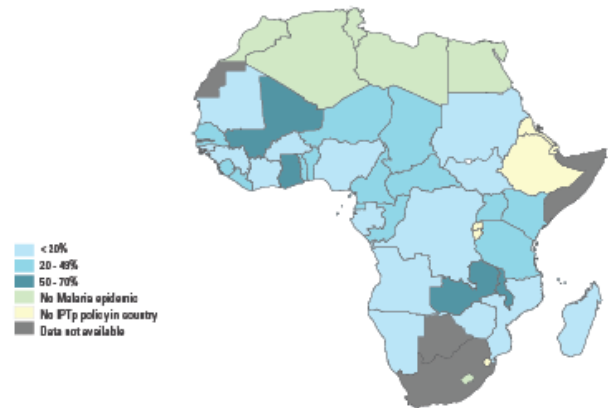
Sulfa-Pyri: 1967 - 1967

Mefloquine: 1977 - 1982

Artemisinin: 1991-?1998

Single, Subtherapeutic, Substandard, Smuggled

Intermittent preventive treatment in pregnancy (IPTp)



•2010-2015 6% - 31% increase

IPTp (2 doses sulfadoxine-pyrimethamine) female 15-49 last pregnancy

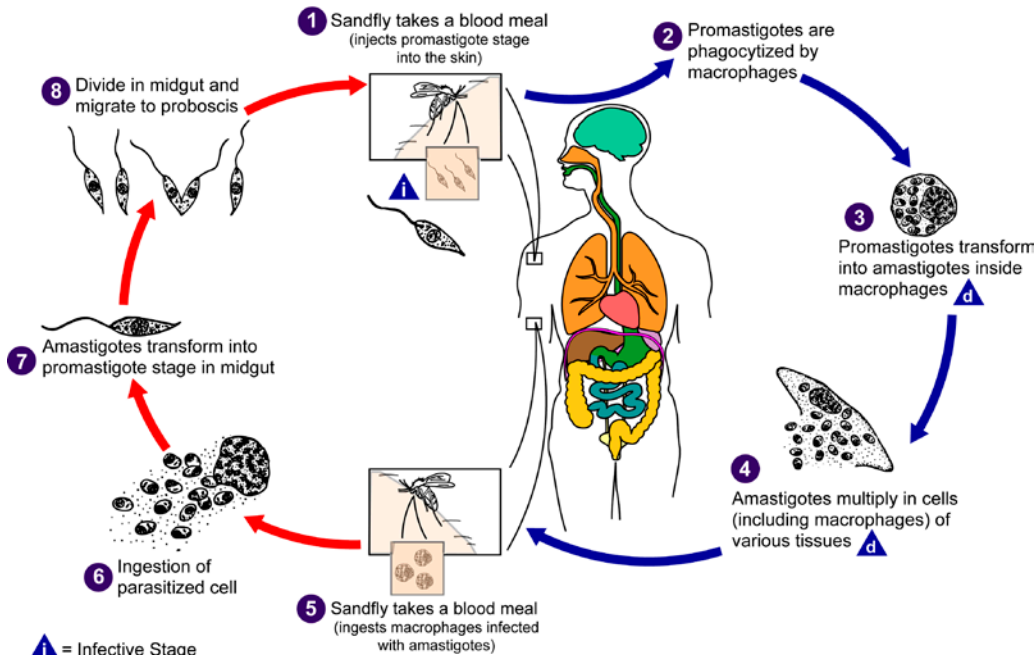
Leishmaniasis

Leishmaniasis

(*Leishmania* spp.)

Sandfly Stages

Human Stages

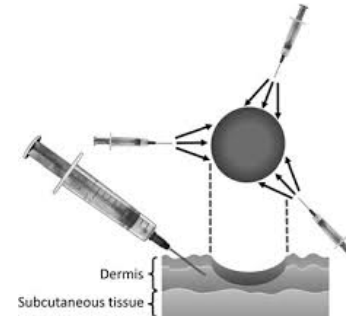
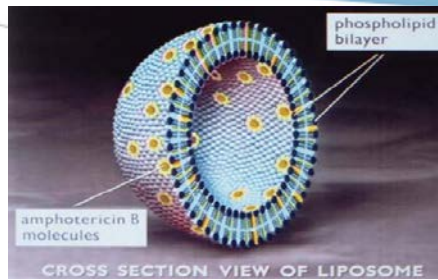
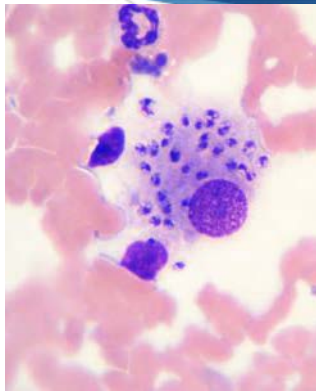


i = Infective Stage

d = Diagnostic Stage

- 700 000-1 mil cases / year
- 40 000 deaths
- Over 20 species of *Leishmania*
- 30 species of sandfly can transmit

Leishmaniasis

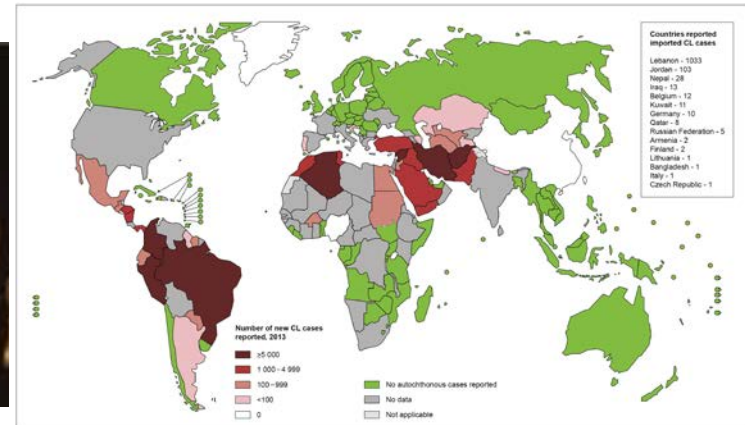
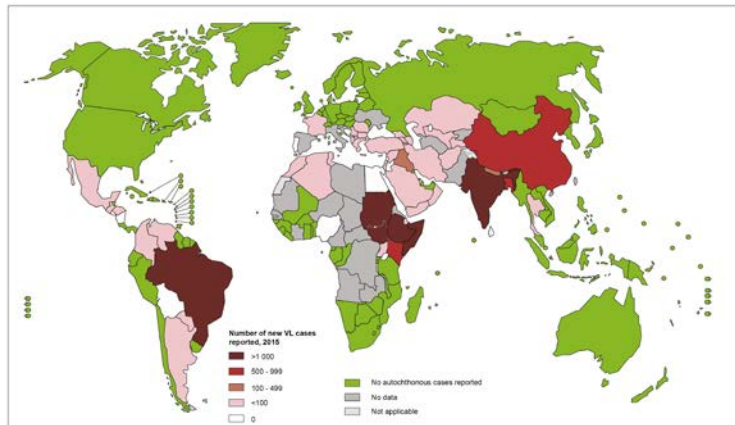


visceral

cutaneous

Status of endemicity of visceral leishmaniasis worldwide, 2015

Status of endemicity of cutaneous leishmaniasis, worldwide, 2013

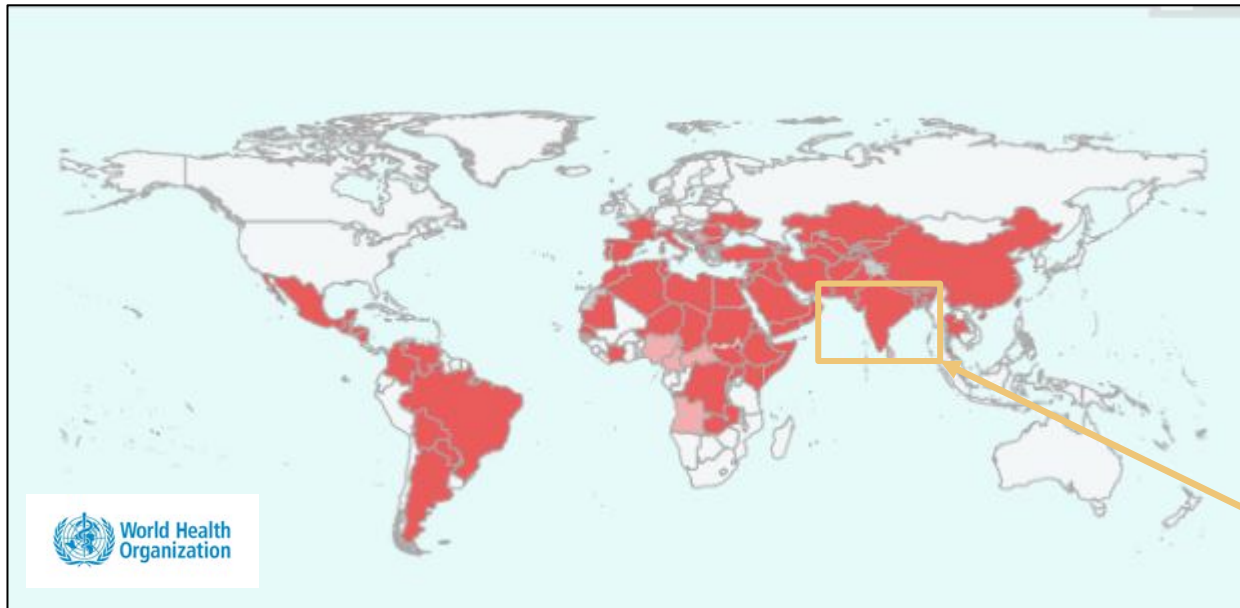
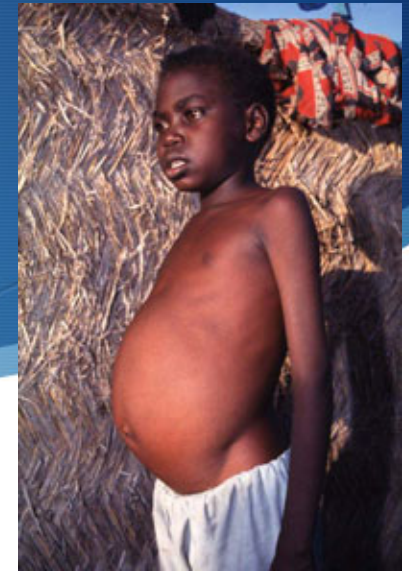
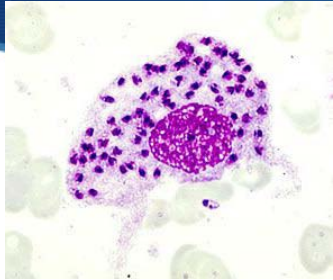


Leishmaniasis Clinical presentation

- ◆ **Cutaneous leishmaniasis** is characterized by one or more cutaneous lesions on areas where sandflies have fed.
- ◆ **sores** can be painless or painful
- ◆ Some people have swollen glands near the sores
- ◆ **Visceral leishmaniasis** usually have fever, weight loss, and an enlarged spleen and liver
- ◆ Some patients have swollen glands.
- ◆ **low blood counts**, including a low red blood cell count (anemia), low white blood cell count, and low platelet count.
- ◆ Some patients develop post kala-azar dermal leishmaniasis.



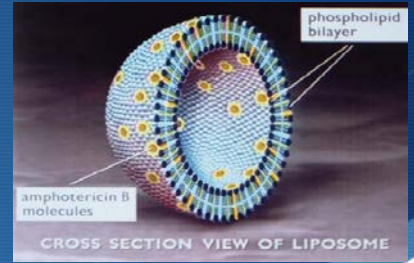
Status of endemicity of visceral leishmaniasis



Number of cases
India/ World

2005-2013 over 60 000





Acting against Kala Azar-HIV co-infection in Bihar

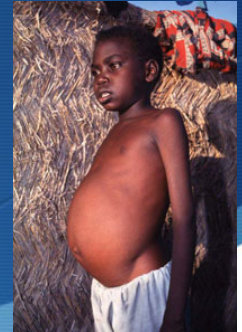


- ◆ People living with HIV are over 100 to 2,320 times more likely to develop kala azar in areas of endemicity
- ◆ Bihar has 80% of the kala azar cases reported in India
- ◆ After treating more than 13,000 patients since 2007 in Bihar's Vaishali district, MSF began focusing on the treatment of **kala azar-HIV co-infection** in partnership with the Rajendra Memorial Research Institute of Medical Sciences (RMRIMS) in Patna in 2016.

Status of endemicity of visceral leishmaniasis



World Health Organization

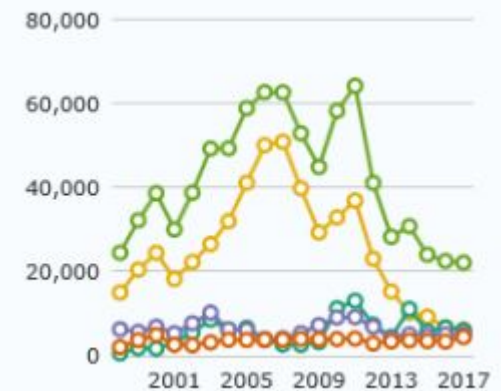


http://apps.who.int/neglected_diseases/ntddata/leishmaniasis/leishmaniasis.html

1990-2016 Brazil increase by 52,9%

Number of cases 2017

World 22 145



South-East Asia 6 176

Africa 6 050

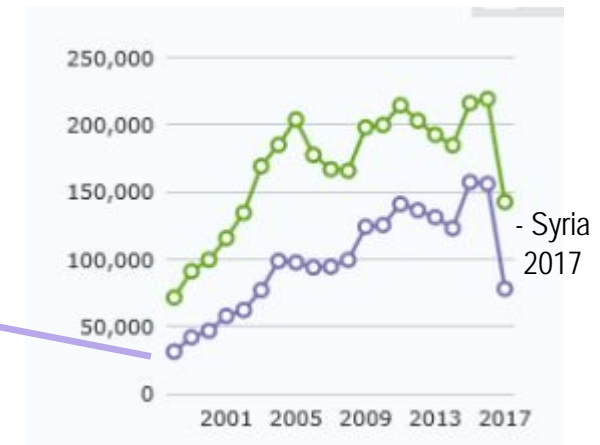
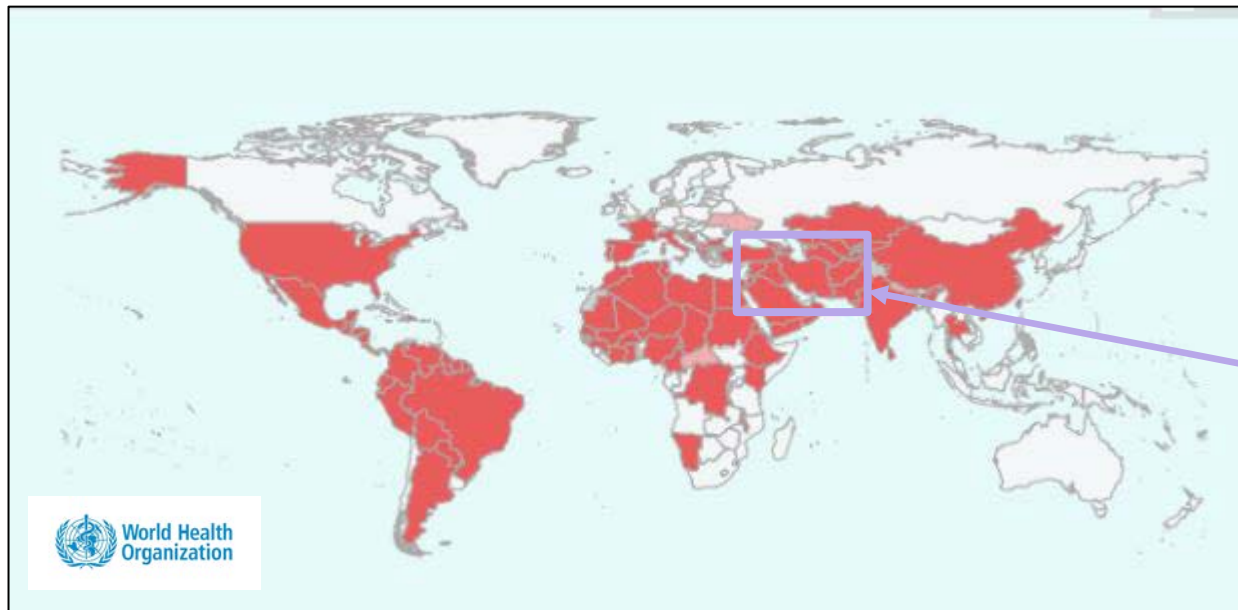
Eastern Mediterranean 5 127

Americans 4 422

Status of endemicity of cutaneous leishmaniasis



Number of cases 2016
Eastern Mediterranean/ World 219 200



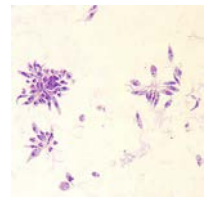
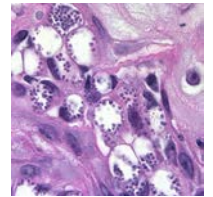
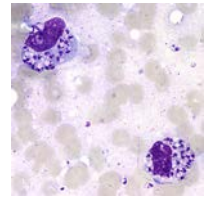
1. Syria 47 377
2. Afghanistan 35 184
3. Pakistan 27 151
4. Iraq 18 258

58%

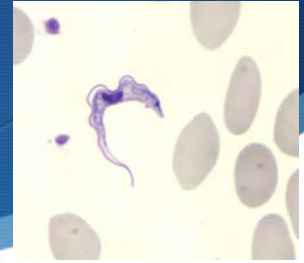
71%

Leishmaniosis - *Leishmania* spp.

- ◆ **Microscopy** – scrapings of the ulcer, bone marrow, histological slides
- ◆ **Serology** – semiquantitative haemagglutination IgG *Leishmania donovani*
- ◆ **Cultivation + Sequencing** – species determination



Sleeping sickness- *Trypanosoma gambiense*, *T. rhodesiense*

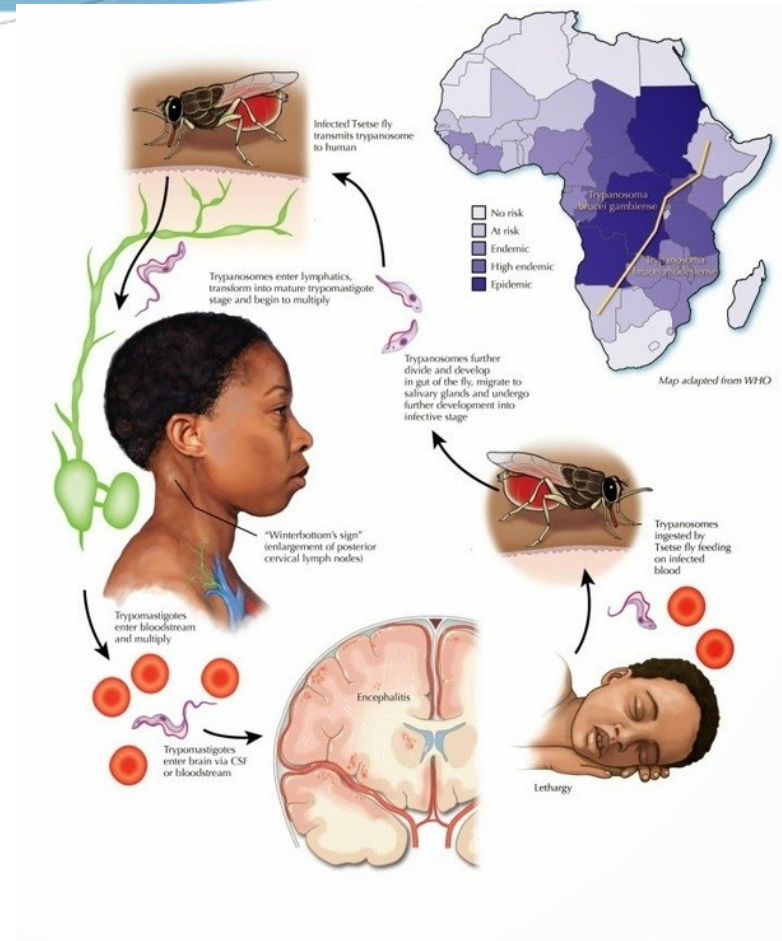
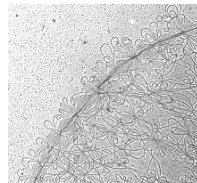


Microscopy – ulcer, aspirate from lymph nodes, blood, CSF,

PCR – kinetoplastid DNA

Serology –

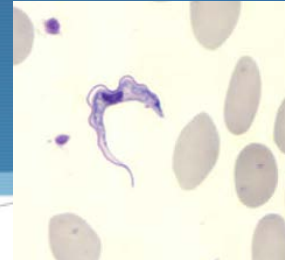
HAT Ag for *T. gambiense*



T. rhodesiense case Malawi 2019 M US 36

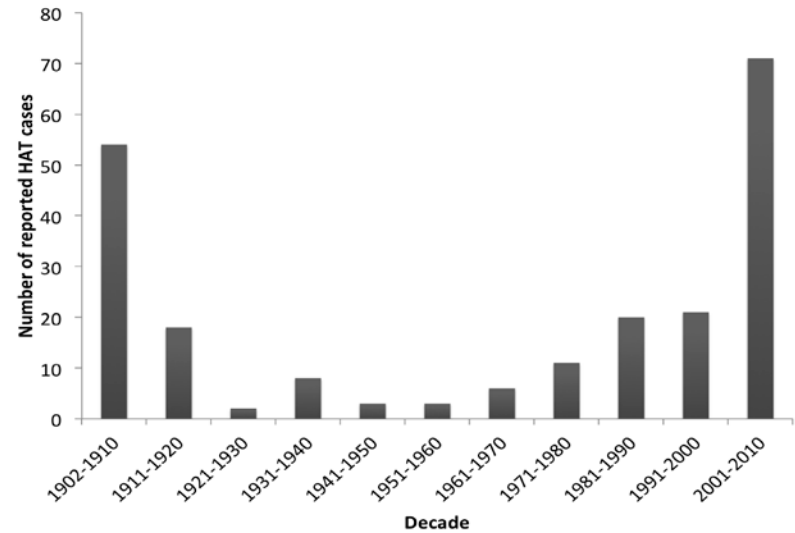
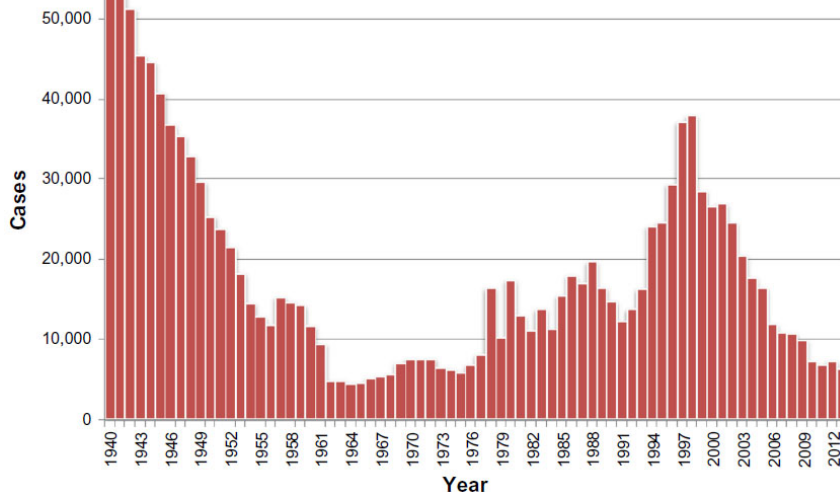
- fishing in the Nkhotakota Wildlife Reserve but did not recall seeing any tsetse flies or experiencing any tsetse bites. EAT is well documented in the reserve.
 - **Twelve days later**, he developed an acute febrile illness
- In Johannesburg EAT (**parasitaemia 5000/microL**) was confirmed.
- And the following complications have been noted: **hepatic dysfunction** with clinical jaundice, **thrombocytopenia** (platelet count $15 \times 10^9/L$) with a **petechial rash**, mild renal dysfunction, and early **ARDS** [adult respiratory distress syndrome]. There is no evidence of a **trypanosomal chancre** (**present in about 80% of patients with EAT**), his mental state was normal, and the patient was hemodynamically stable with no evidence of a myocarditis.
- Suramin (test and 1st doses) has been administered with good response. A CSF [cerebrospinal fluid] examination will be conducted once the peripheral parasitaemia has cleared and the platelet count has increased.

Sleeping sickness



Among travelers worldwide

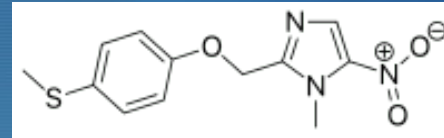
Number of new cases



Nitroimidazole derivatives - Fexinidazole

DNDi

Drugs for Neglected Diseases initiative



Fexinidazole Winthrop, a Sanofi-Aventis product developed with the DNDi, received a positive endorsement from the [European Medicines Agency](#) on November 15th, 2018, for use in non-European markets

• (metabolit=sulfoxid a sulfon) antiparazitikum s aktivitou proti

• [Trypanosoma cruzi](#)

• [Trichomonas vaginalis](#)

• [Entamoeba histolytica](#)

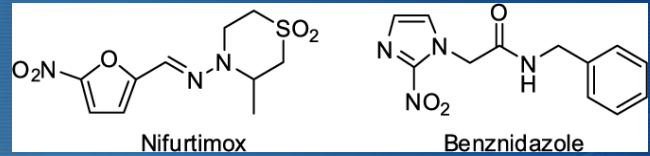
• [Trypanosoma brucei](#)

• [Leishmania donovani](#)

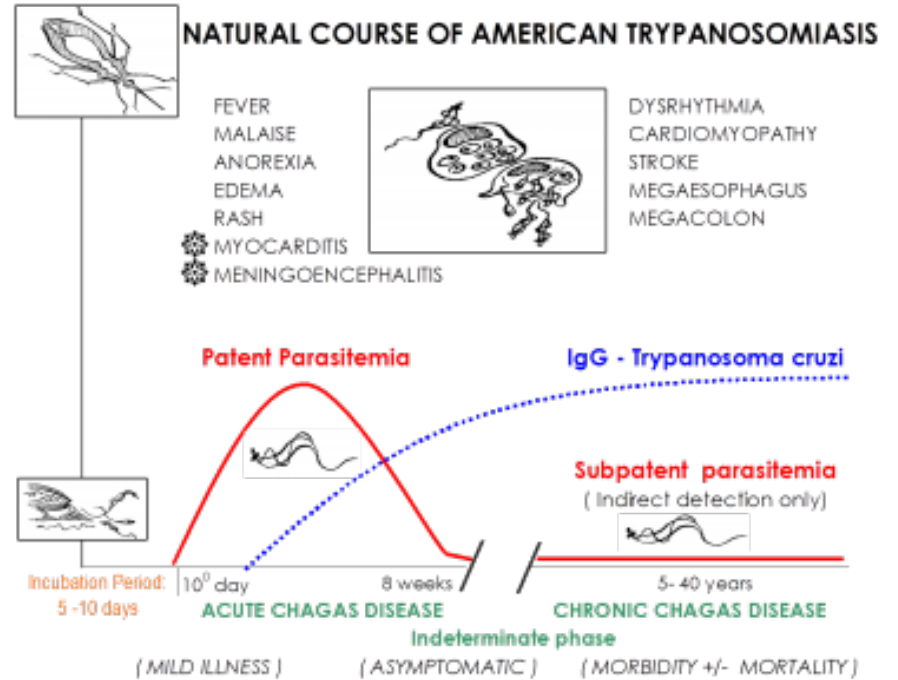
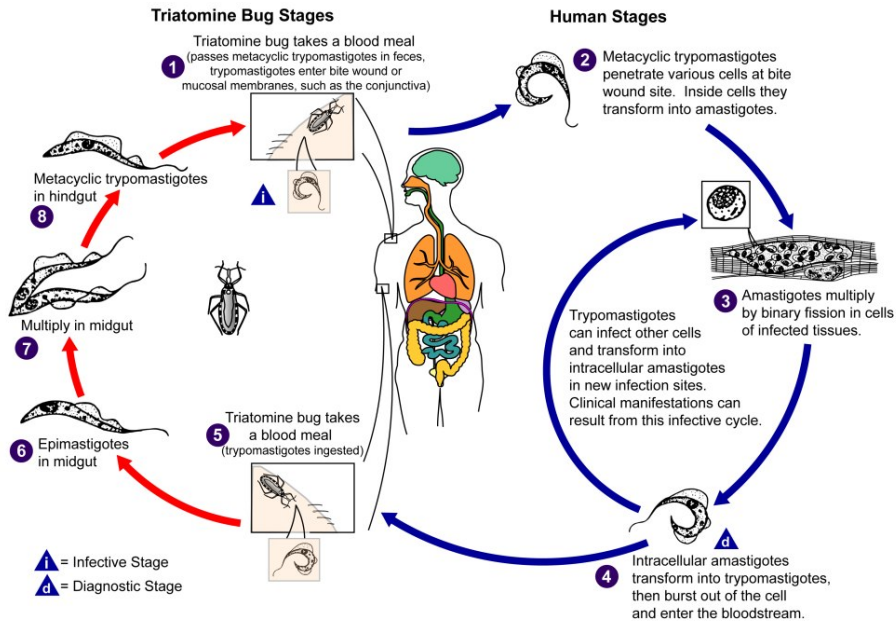
- enzyme-mediated reduction by nitroreductases to generate cytotoxic species that cause DNA, lipid and protein damage



Chagas disease



Trypanosomiasis, American (Chagas disease) *(Trypanosoma cruzi)*



Chagas disease

Trypanosoma cruzi



- ◆ **Microscopy** – acute – blood, CSF
chronic – histological slides from biopsy
- ◆ **Serology** – quantitative IgG *Trypanosoma cruzi*
- ◆ **PCR** – kinetoplastid DNA
- ◆ **Diagnostics** – kcongenital Chagas disease

Study shows dramatically shorter treatment for Chagas disease could be just as effective, and significantly safer

Barcelona/Rio de Janeiro – 14 March 2019

DNDi

Drugs for Neglected Diseases *initiative*

The results, available in early 2019, showed that all treatment arms were effective compared to placebo and the new regimens presented good safety profiles. The two-week course of treatment was particularly promising. While significantly shorter than the standard eight-week treatment, it showed 83% of efficacy and none of the patients assigned to this arm had to discontinue treatment due to side effects. The primary measure of efficacy for this study was sustained parasitological response at six months' follow-up with a final assessment at 12 months.

- Benznidazole 300mg/day 2 weeks instead of 8 weeks

- **pediatric dose** of Benznidazole added to essential drugs list by WHO



TRITON



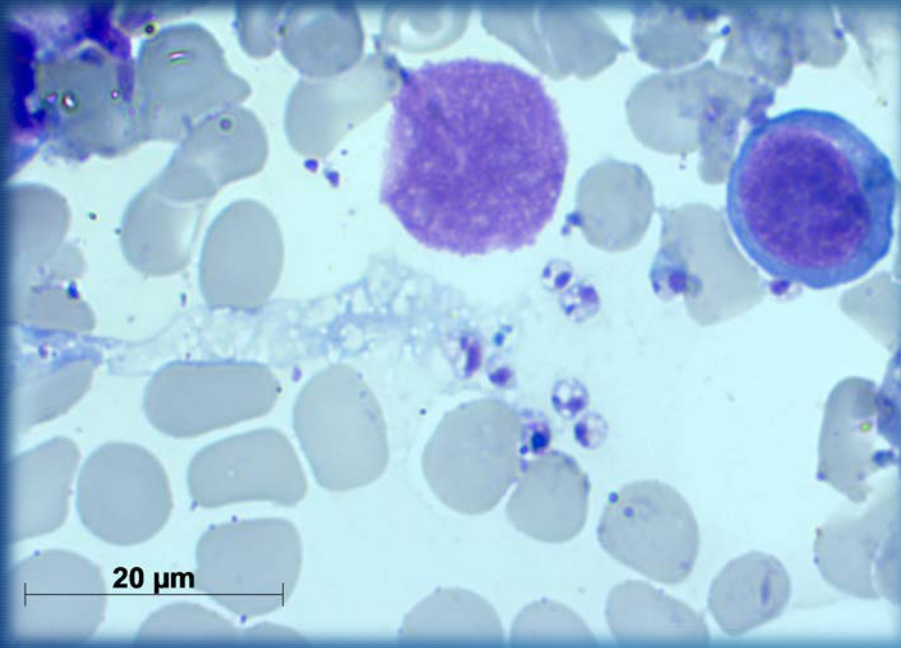
Jan Votýpka
Iva Kolářová
Petr Horák a kol.

O PARAZITECH
A LIDECH



MAGNESIA
LITERA
2019





Lenka.Richterova@bulovka.cz

<http://www.cdc.gov/dpdx/>

Tropical infectious disease 2011

https://www.cdc.gov/malaria/travelers/country_table/a.html