



Trypanosomiasis

WRAIR- GEIS 'Operational Clinical Infectious Disease' Course

UNCLASSIFIED



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Lecture Objectives

- Increase knowledge of
 - Epidemiology of African and American Trypanosomiasis
 - Disease Prevention
 - Disease Treatment



CLASS
Kinetoplastida

ORDER
Trypanosomatida

FAMILY
Trypanosomatid

GENERA
Trypanosoma

Other Genera
(*Leishmania*, *Crithidia*)

↓
Trypanosoma
cruzi

↓
Trypanosoma
brucei



African Trypanosomiasis

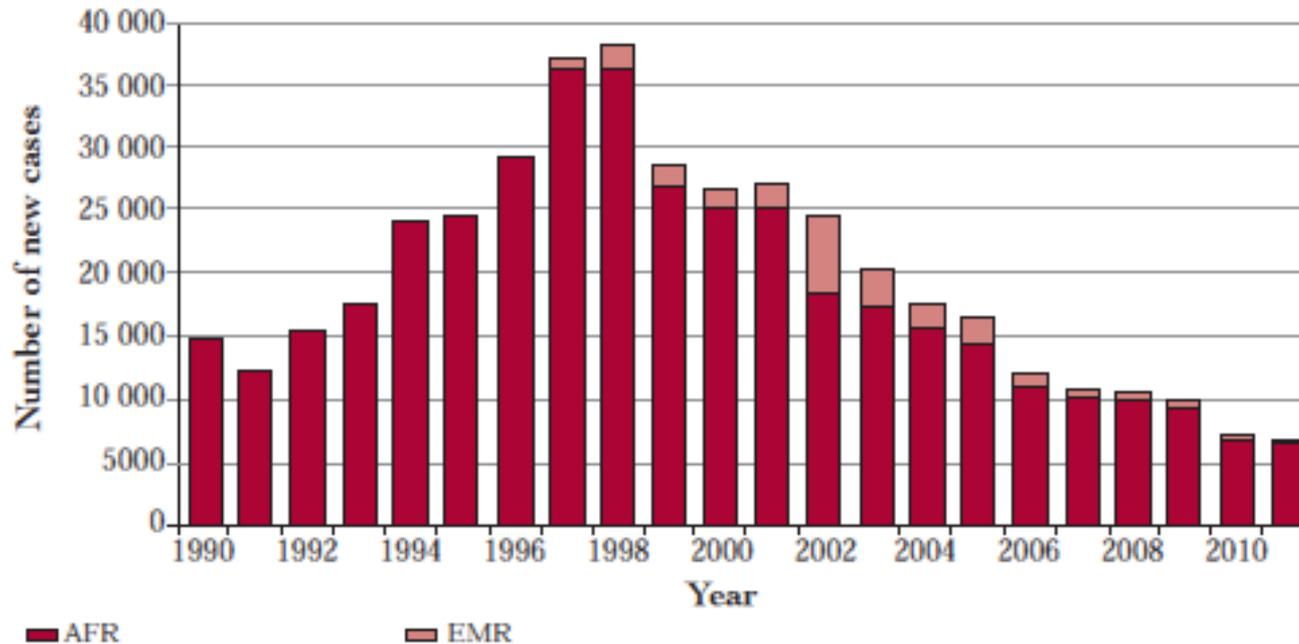
Introduction

- 3 subspecies
 - *Trypanosoma brucei brucei* (causes animal disease only)
 - *T. b. gambiense*
 - *T. b. rhodesiense*
- *T. b. gambiense* accounts for 98% of reported cases and is endemic in 24 countries
- *T. b. rhodesiense* is endemic in 13 countries and accounts for 2% of all reported cases
- All vectored by the tsetse fly (*Glossina* sp)
- Always fatal without treatment



Introduction

Fig. 3.8.3 Global number of new cases of human African trypanosomiasis reported to WHO, 1990–2011

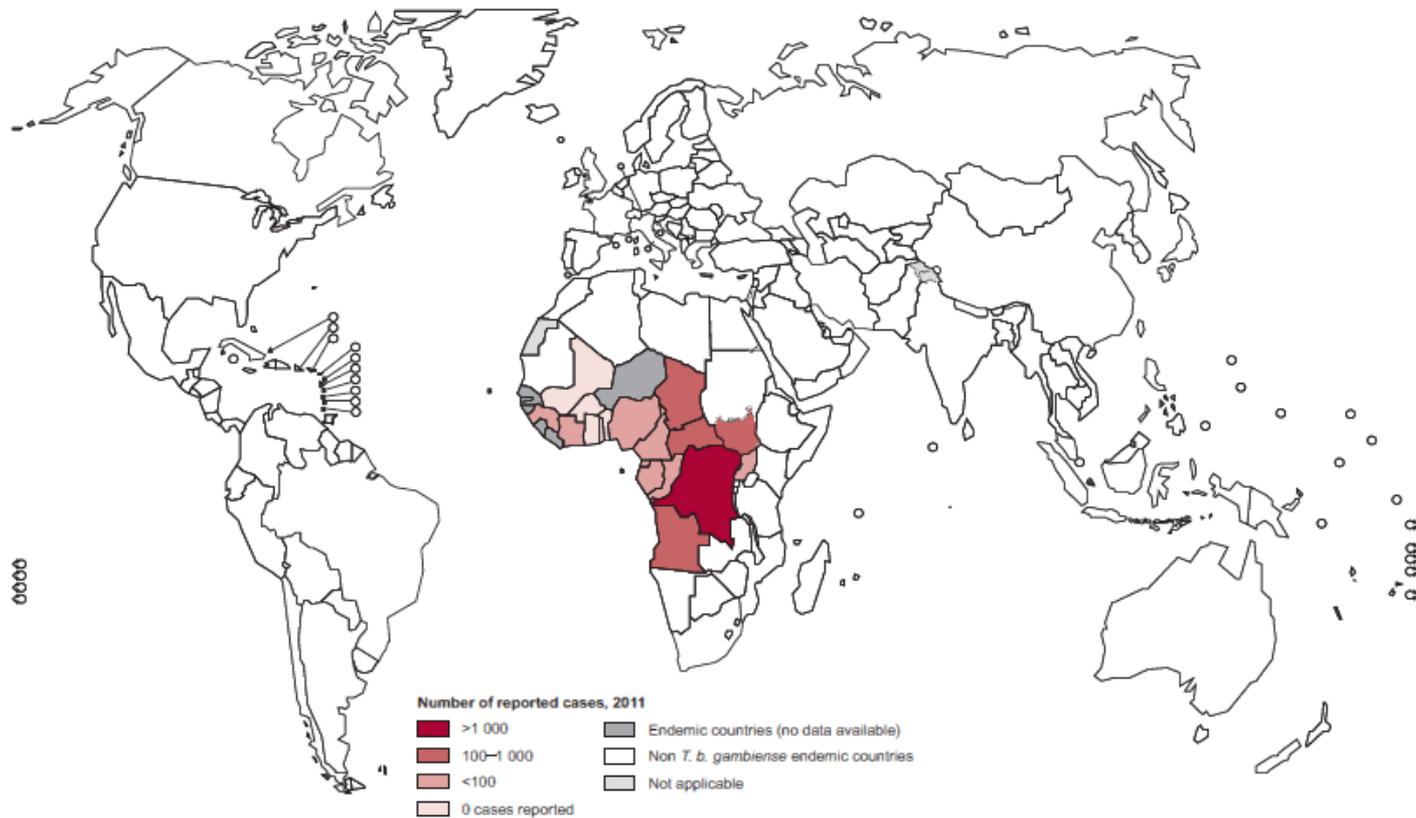


AFR – African Region / EMR–Eastern Mediterranean Region

World Health Organization. *Sustaining the drive to overcome the global impact of neglected tropical diseases: second WHO report on neglected diseases*. World Health Organization, 2013.



Fig. 3.8.1 Global distribution of human African trypanosomiasis (caused by *Trypanosoma brucei gambiense*), 2011



World Health Organization. *Sustaining the drive to overcome the global impact of neglected tropical diseases: second WHO report on neglected diseases*. World Health Organization, 2013.



Fig. 3.8.2 Global distribution of human African trypanosomiasis (caused by *Trypanosoma brucei rhodesiense*), 2011

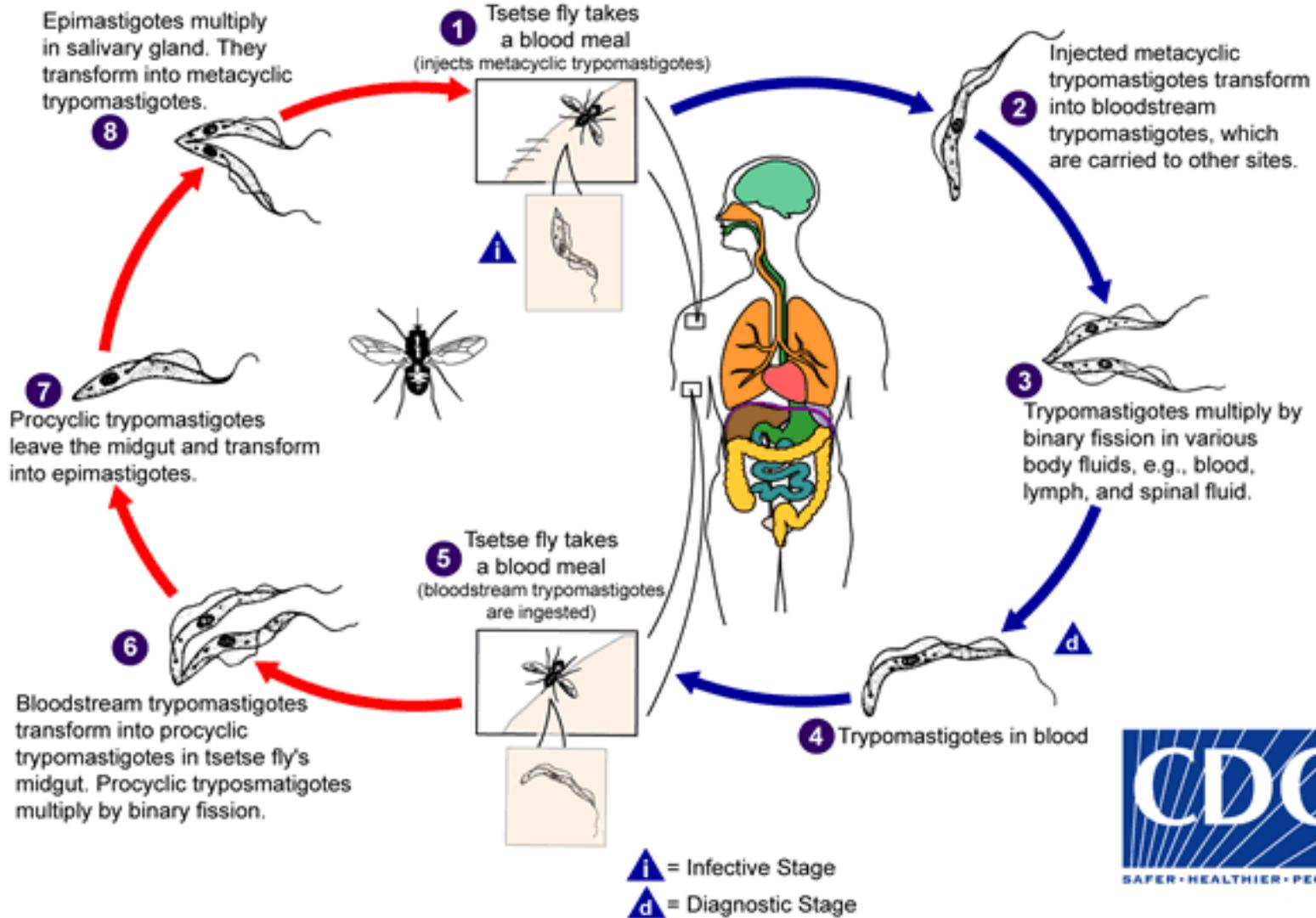


World Health Organization. *Sustaining the drive to overcome the global impact of neglected tropical diseases: second WHO report on neglected diseases*. World Health Organization, 2013.



Tsetse fly Stages

Human Stages



The Vector (Tsetse Fly)



- Resemble house flies
- 29 to 31 total species and subspecies but only 6 are recognized as vectors for human disease vectors
 - *Glossina palpalis*, *G. tachinoides*, *G. fuscipes*, *G. morsitans*, *G. swynnertoni*, *G. pallidipes*
- Transmit by mechanical and biological transmission
- Long term control of the vector has been fleeting
 - Slaughter of wild animals
 - Land Clearing (prefer tree trunks for resting)
 - Sterile Insect Technique
 - Pesticide Campaigns



Blood Stage Infection

- Occurs while the disease is located in peripheral circulation
- Painless sick chancre appearing 5-15 days post bite (less commonly seen in *T. b. gambiense* infection)
- Intermittent fever, malaise, arthralgias, headache
- Rash
- Generalized or regional lymphadenopathy
 - Winterbottom sign characteristic *T. b. gambiense*



Winterbottom's Sign



Chancre



Photos courtesy of <http://legacy.earlham.edu/~martilu/trypanosomiasispathology.htm>



Late Stage Infection

- Occurs when the parasite crosses the blood-brain barrier
 - Weeks for *T. b. rhodesiense*
 - 1 to 2 years for *T. b. gambiense*
- Sleep cycle disturbances
- Personality changes
- CNS infection progresses causing seizures, coma and organ failure
- Death
 - Months for *T. b. rhodesiense*
 - Up to 7 years for *T. b. gambiense*



Late Stage Infection



Photos courtesy of <http://legacy.earlham.edu/~martilu/trypanosomiasispathology.htm>



Differential Diagnosis

Blood Stage Fever

- Malaria, HIV infection, Borreliosis, Brucellosis, Typhoid Fever, enteric fevers

Blood Stage Lymphadenopathy

- Tuberculosis lymphadenitis, HIV infection, Cancer

Neurologic Stage Mental Status Changes

- TB, meningitis, HIV-related opportunistic infections

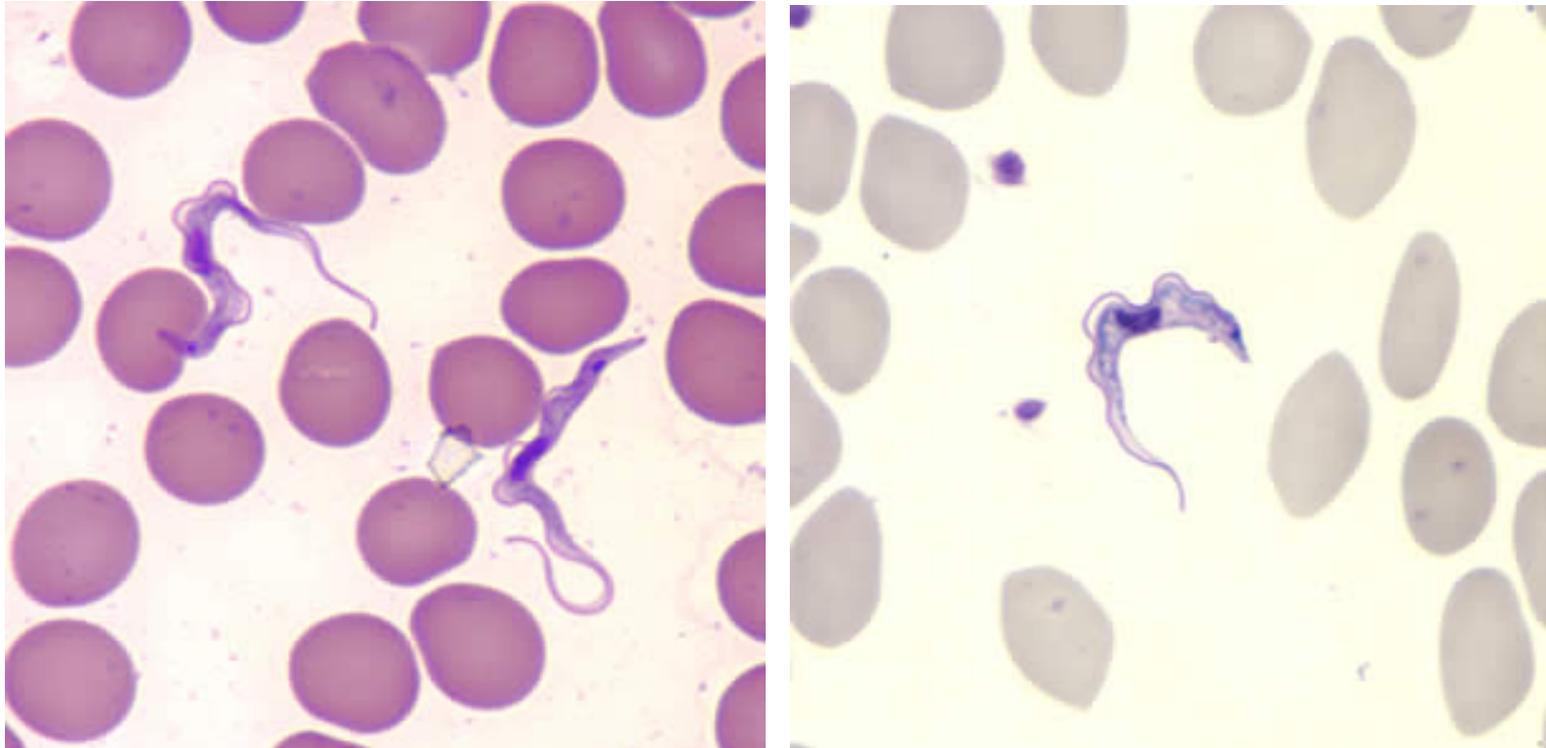


Diagnosis

Technique	Test	Sensitivity	Specificity
Parasite Demonstration	Quantitative Buffy Coat (QBC) Capillary tube centrifrification (CTC) Wet blood films Thick blood films Lymph node aspirate examination	44.8% to 91%	~100%
Parasite DNA detection	Polymerase chain reaction (PCR) Reverse transcriptase PCR Loop mediated isothermal amplification (LAMP)	~95%	~100%
Serology	Card agglutination test (CATT) (The standard screening test for <i>T. brucei gambiense</i>)	68%-99.5% (regional differences)	83.5%-98.4%



Microscopy



Courtesy of the CDC Public Health Image Library



Treatment

Species	Drug of Choice	Adult Dosage
T. b. rhodesiense, hemolymphatic stage	Suramin	1 gm IV on days 1,3,5,14, and 21
T. b. rhodesiense, CNS involvement	Melarsoprol	2-3.6 mg/kg/day IV x 3 days. After 7 days, 3.6 mg/kg/day x 3 days. Give a 3rd series of 3.6 mg/kg/d after 7 days.
T. b. gambiense, Hemolymphatic stage	Pentamidine	4 mg/kg/day IM or IV x 7-10 days
T. b. gambiense, CNS involvement	Eflornithine	400 mg/kg/day in 4 doses x 14 days



Treatment

- Choice of therapy is dependent on the infecting subspecies and disease stage
- 1st stage disease drugs
 - Pentamidine for *T. b. gambiense*
 - Suramin for *T. b. rhodesiense*
 - Effective against *T. b. gambiense* but causes severe reaction in those infected with *Onchocerca*
- 2nd stage disease drugs
 - Eflornithine for *T. b. gambiense*
 - Melarsoprol for *T. b. rhodesiense*
 - Adverse reactions can be severe and life threatening

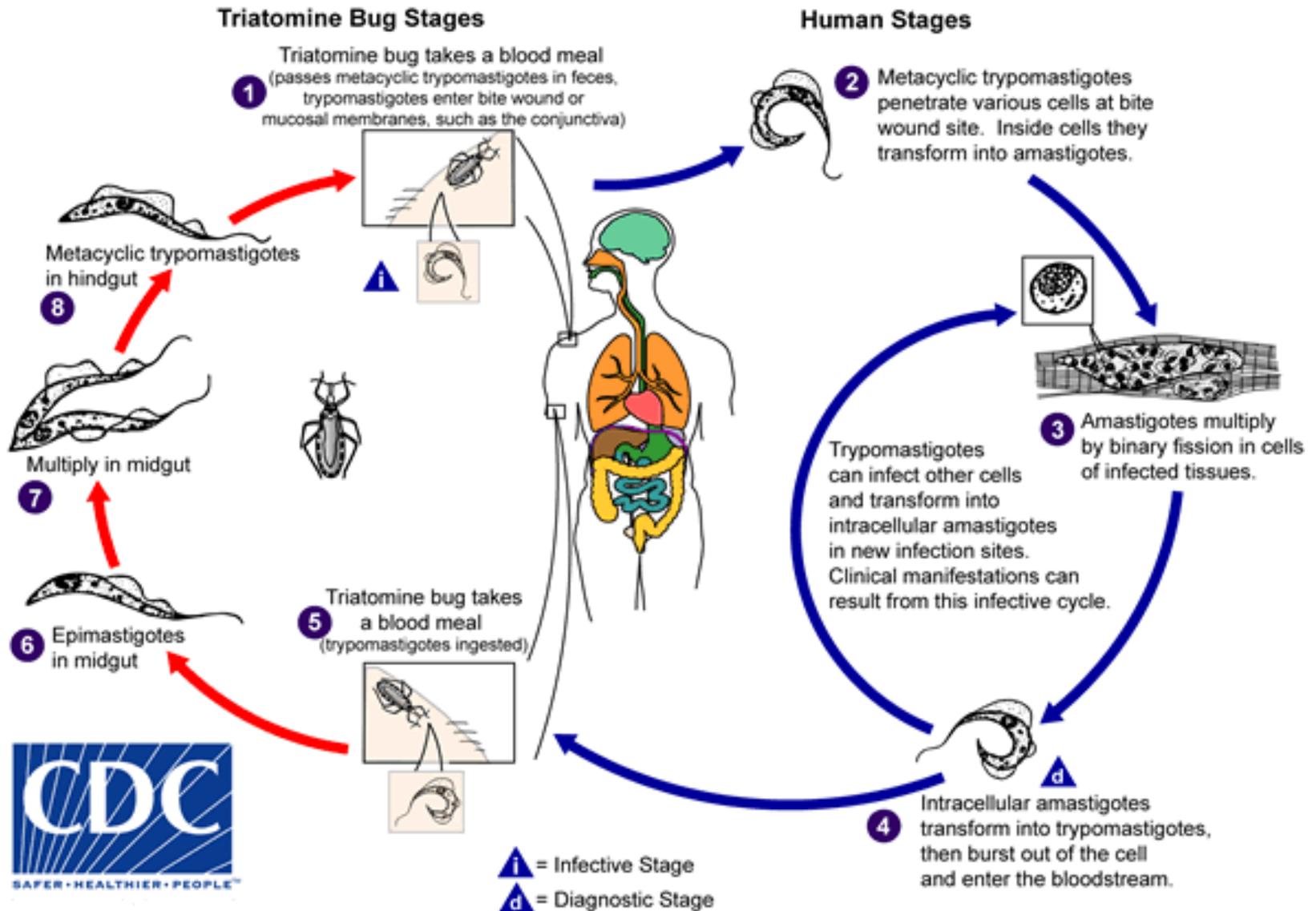


American Trypanosomiasis (Chagas Disease)

- Transmitted by the feces of an infected triatomine bug
- Infection also occurs from
 - mother-to-baby (congenital)
 - contaminated blood products (transfusions)
 - infected donated organs
 - laboratory accident
 - contaminated food or drink



Life Cycle





Ribeiro, Antonio L., et al. "Diagnosis and management of Chagas disease and cardiomyopathy." *Nature Reviews*



The Vector (Triatomine Bug)

- Called “Kissing Bugs” or “Cone-nosed Bug”
- Parasite is in the feces not saliva
- All stages and genders blood feed
- Species can be domestic, peridomestic, or sylvatic
- 138 species all potentially able to transmit *T. cruzi*
 - *Triatoma infestans*, *T. dimidiata*, *T. brasiliensis*, *Rhodnius prolixus*, and *Panstrongylus megistus*



Acute Symptoms

- Asymptomatic
- Mild febrile illness
- Eyelid swelling (Romana's sign) or swelling at bite site

- Rare symptoms
 - Myocarditis
 - Heart Failure
 - Meningo-encephalitis



Romaña's sign



Courtesy of WHO/TDR

Chronic Symptoms

- Mostly asymptomatic
- 20 to 30% develop symptoms
 - Heart failure
 - Arrhythmias
 - Megaesophagus
 - Megacolon

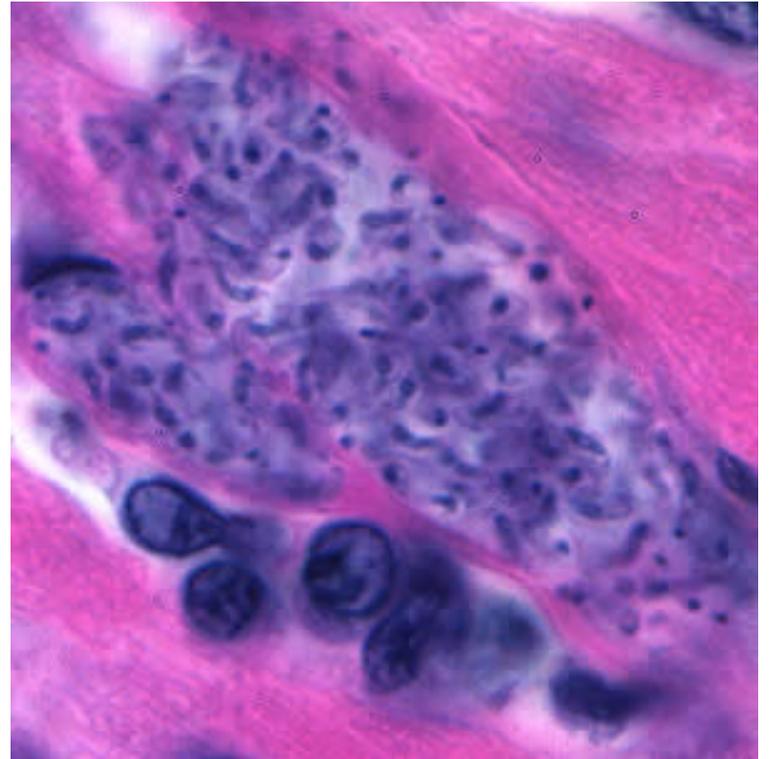


Diagnosis

- Parasitological Tests
 - Only useful in the acute phase when parasitemia is high
 - Blood Smears, Buffy Coat Analysis, Blood Culturing, Xenodiagnosis
- Serological Tests
 - Detect specific antibodies to *T. cruzi*
 - IFAT, ELISA, IHA
- Immunochromatographic Tests (rapid tests)
- Molecular Tests
 - Polymerase Chain Reaction (PCR)
 - Detects the minicircle DNA present in *T. cruzi*



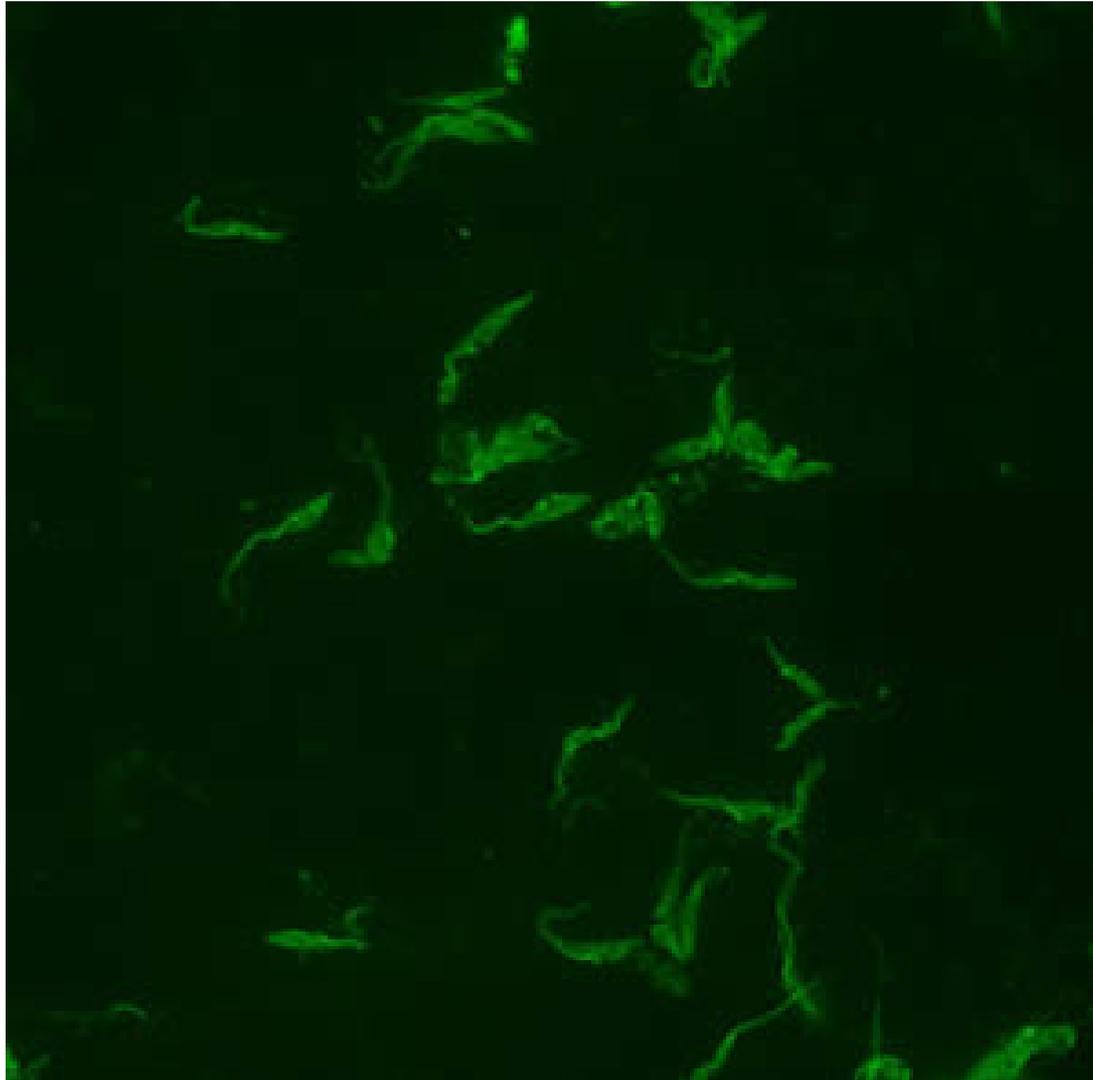
Microscopy



Courtesy of the CDC Public Health Image Library



Serologic Test (IFAT)



Courtesy of the CDC Public Health Image Library



Treatment

Benznidazole and Nifurtimox are the only two treatments

60 to 85% cure rate in acute cases

Less effective in chronic cases

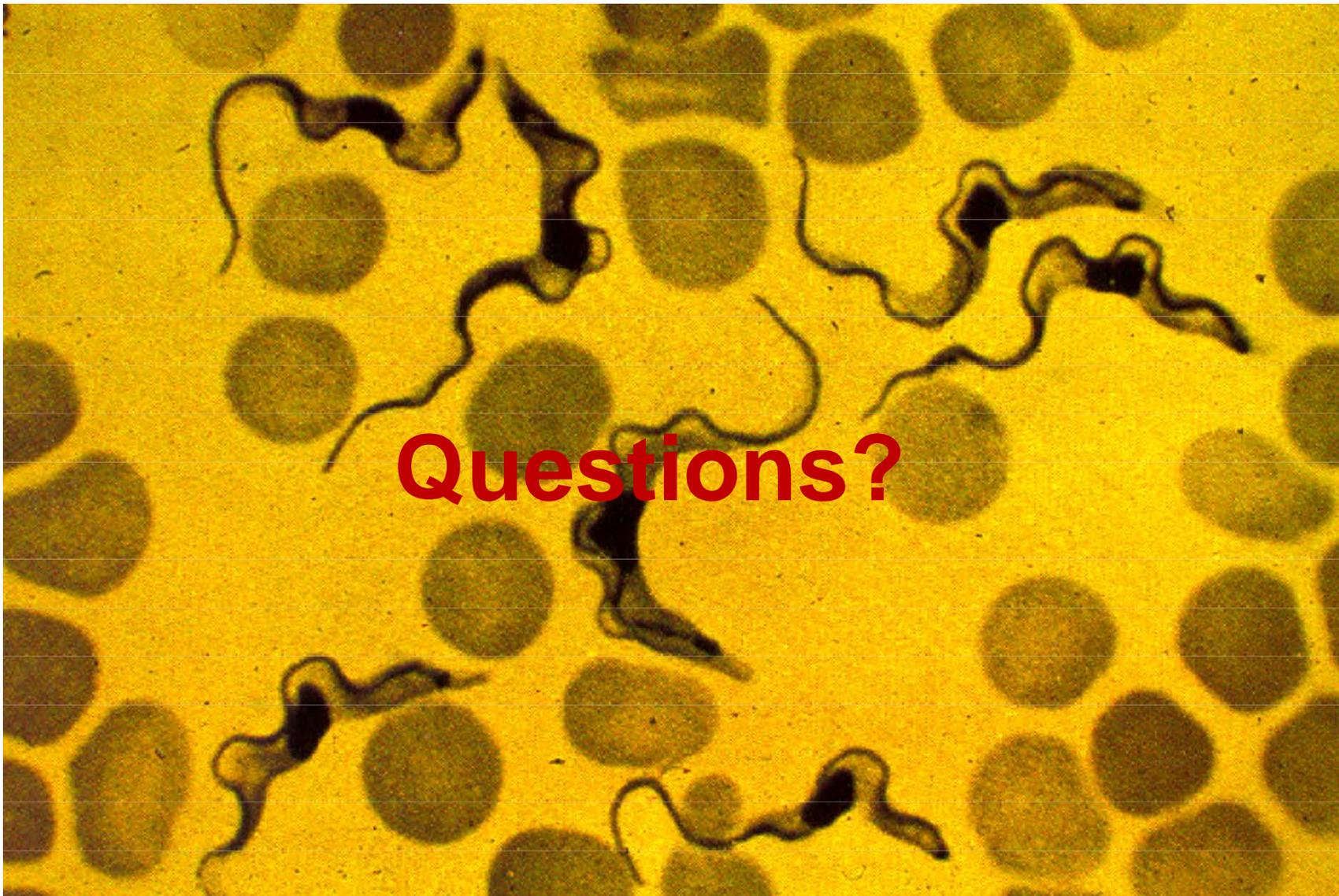
New therapies are needed



Prevention

- 4 main public health strategies
 - Elimination of domestic vectors
 - Screening of blood and organ donors
 - Maternal screening and treatment of infected newborns
 - Active case finding and treatment of school age children





Questions?

