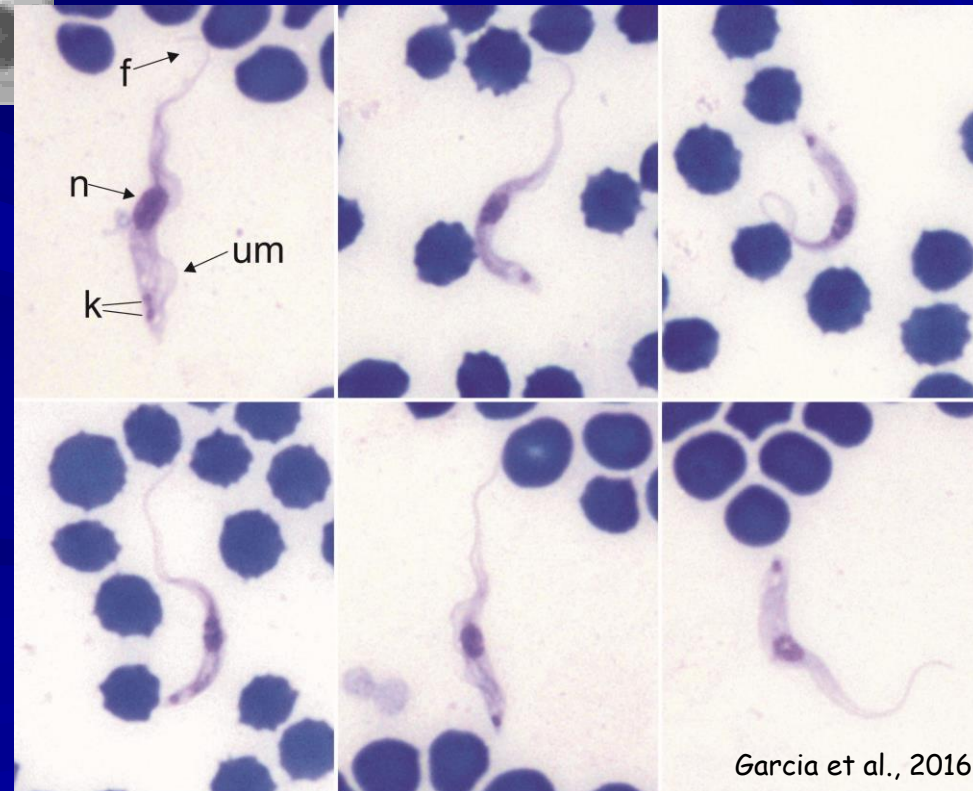
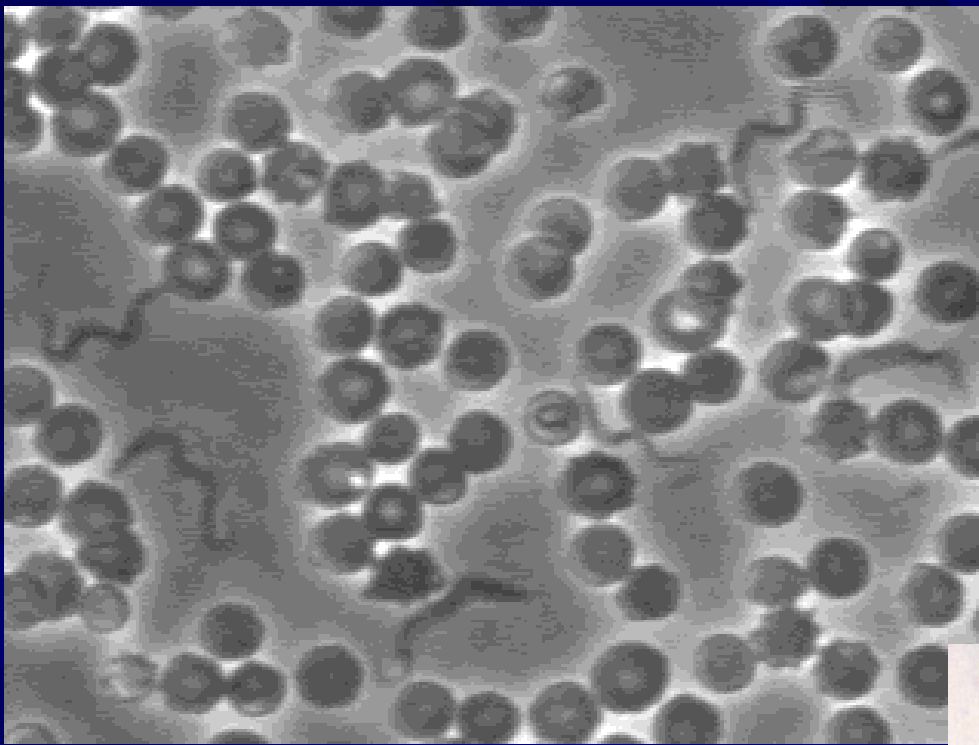


Tripanossomas de origem
Africana de importância
Médico veterinária e humana

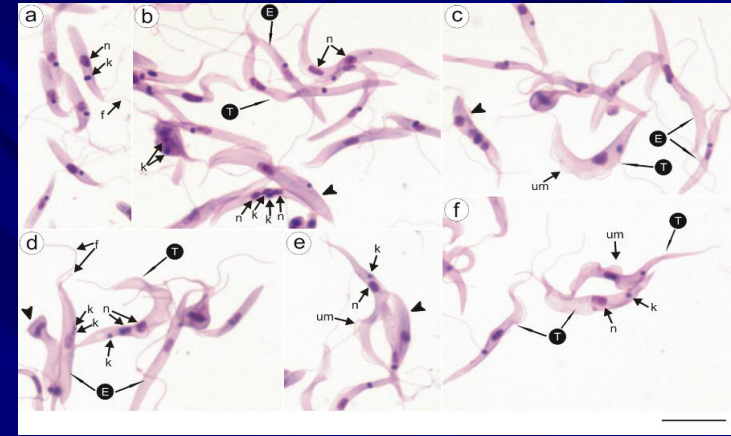


Herakles A. García P.
Pesquisador Colaborador
Depto. Parasitologia
ICB II USP São Paulo
heraklesantonio@gmail.com

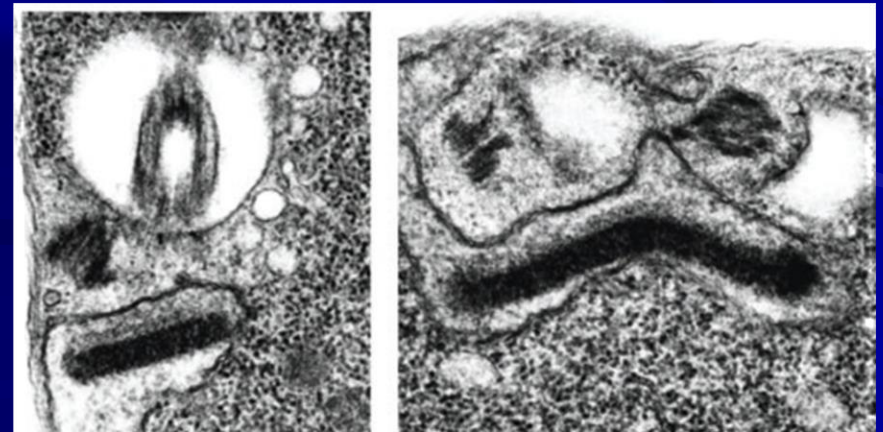
Filo Euglenozoa
Classe Kinetoplastea

Família Trypanosomatidae

presença do cinetoplasto, uma região especializada da mitocôndria constituída por moléculas de DNA circulares concatenadas



Cinetoplasto



Tripanossomatídeos



uniflagelados
unicelulares

grande distribuição
geográfica

- Invertebrados
- Plantas
- Todas as ordens de vertebrados

monoxênicos de insetos:

(~15 gêneros)

heteroxênicos (5 gêneros)

Phytomonas (**insetos e plantas**)

Leishmania, *Trypanosoma*, *Endotrypanum* e *Porcisia*

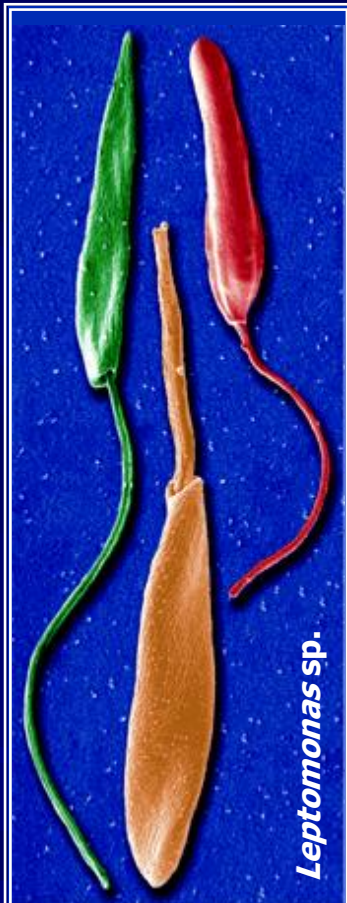
(**insetos e vertebrados**)

Quando patogênicos, estes organismos são responsáveis por doenças de grande importância médica humana e veterinária.

- **Tripanossomíases Africana**

- **Doença de Chagas**

- **Leishmanioses**



Leptomonas sp.

False-colour scanning
electron micrographs
Images courtesy Prof.
J. Lukeš and D. Maslov



Glossina sp.



África

Tripanossomatídeos

Estruturas características

Trypanosoma

o cinetoplasto – ligado a sua longa mitocôndria e contendo um DNA (kDNA).

De suas proximidades parte um flagelo curto ou longo.

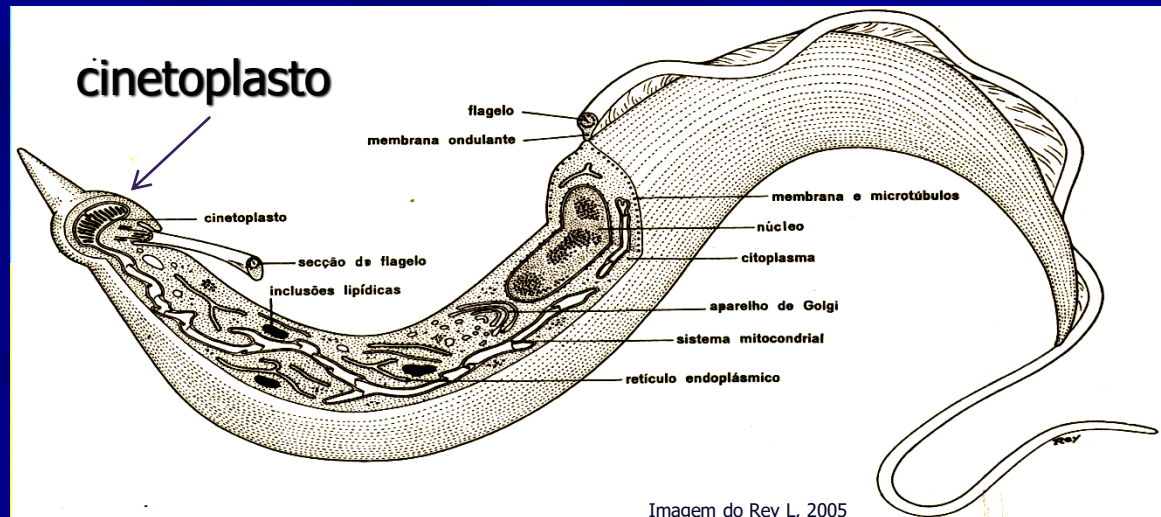
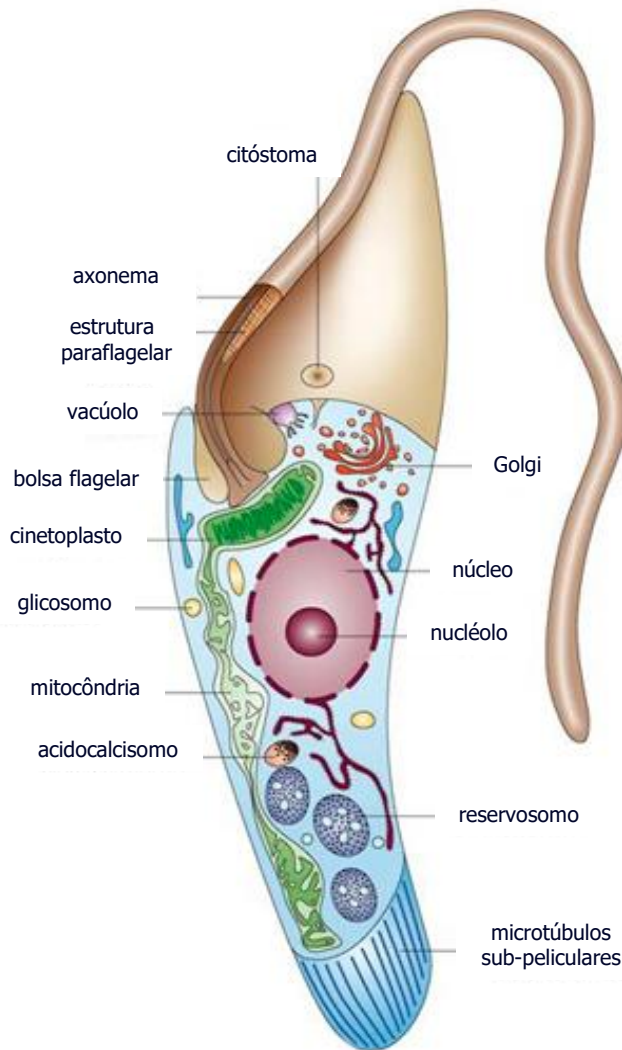
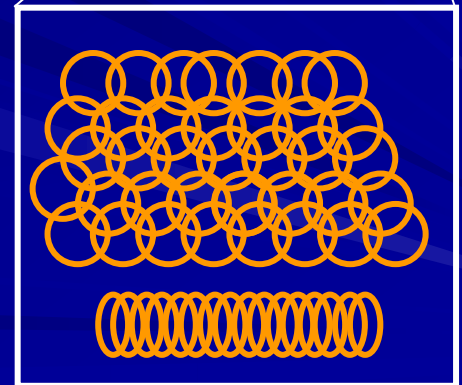
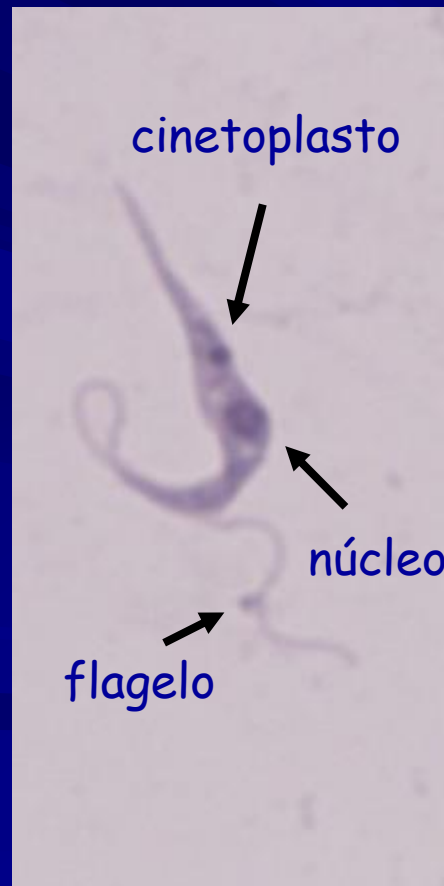
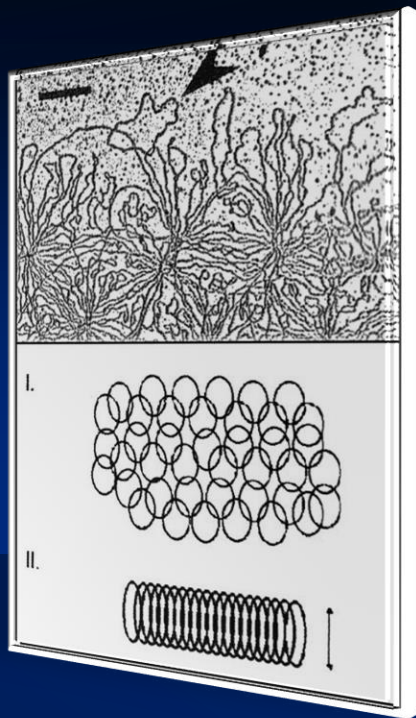


Imagem do Rey L, 2005

Cinetoplasto: uma região especializada da mitocôndria constituída por moléculas de DNA circulares (maxicírculos e minicírculos) concatenadas.

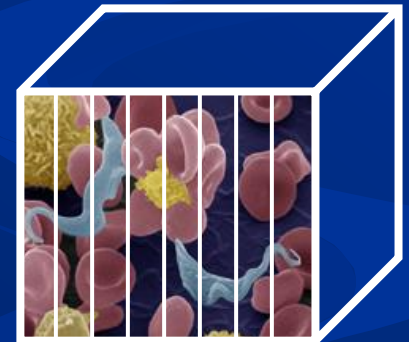




O cinetoplasto (mitocôndria) contém DNA circular em duas formas: **minicírculos** e **maxicírculos**.

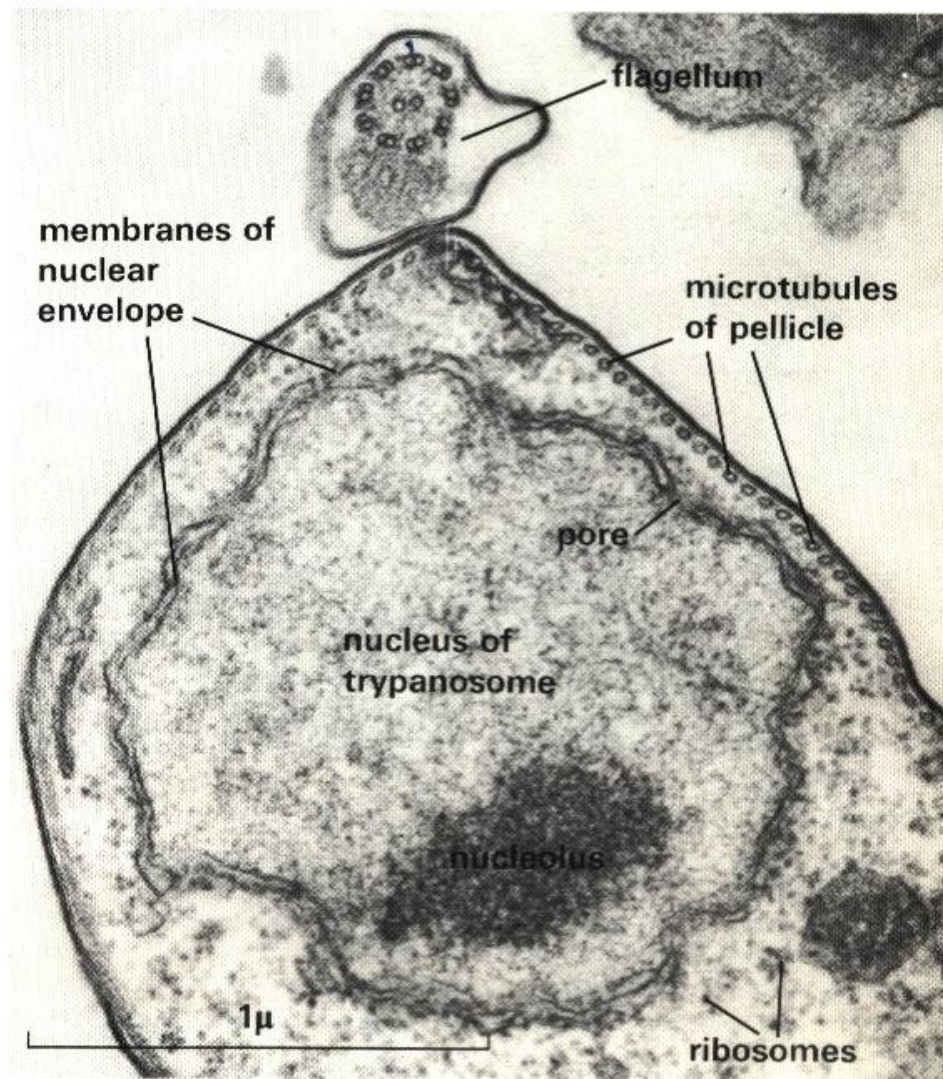
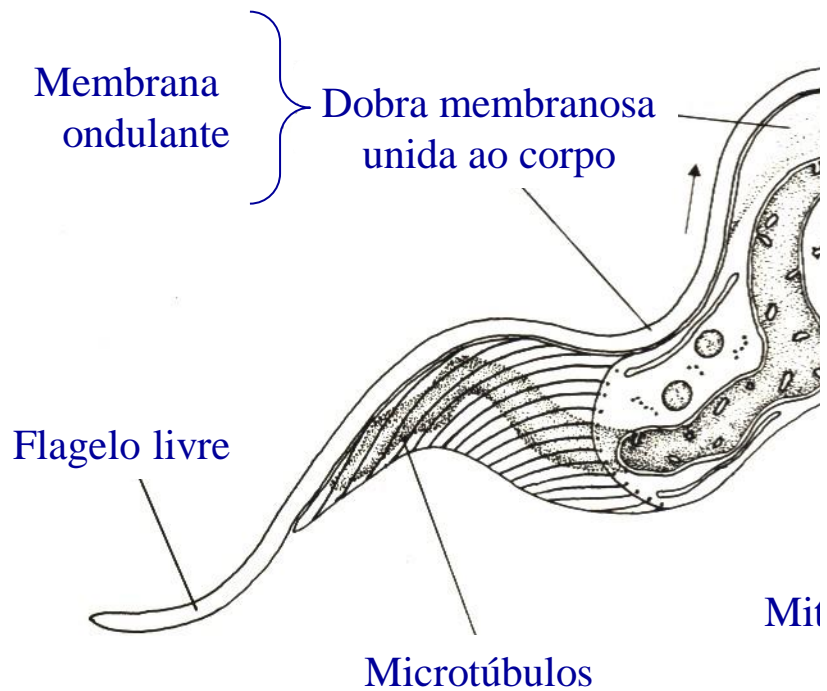
Os **minicírculos** produzem RNA guia (gRNA) para decodificar as informações do maxicírculo por inserção ou deleção de resíduos de uridina (RNA editing).

Perda de kDNA	parcial (discinetoplastia Dk)
	total (acinetoplastia Ak)



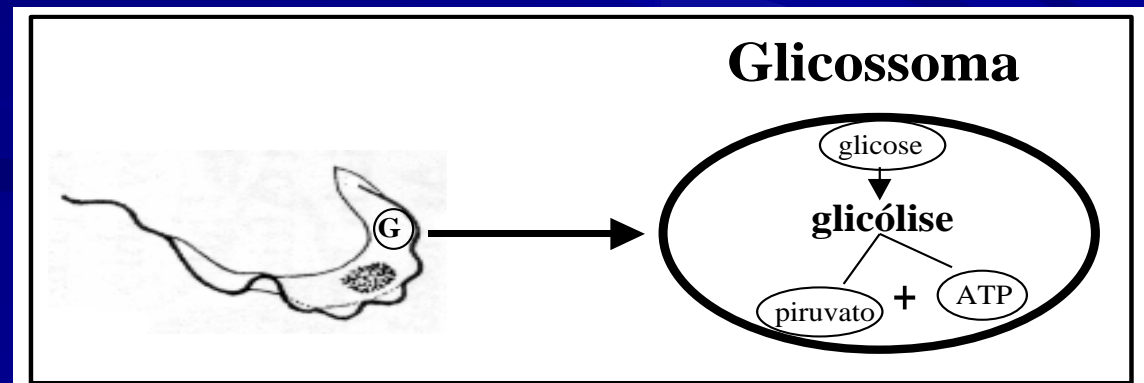
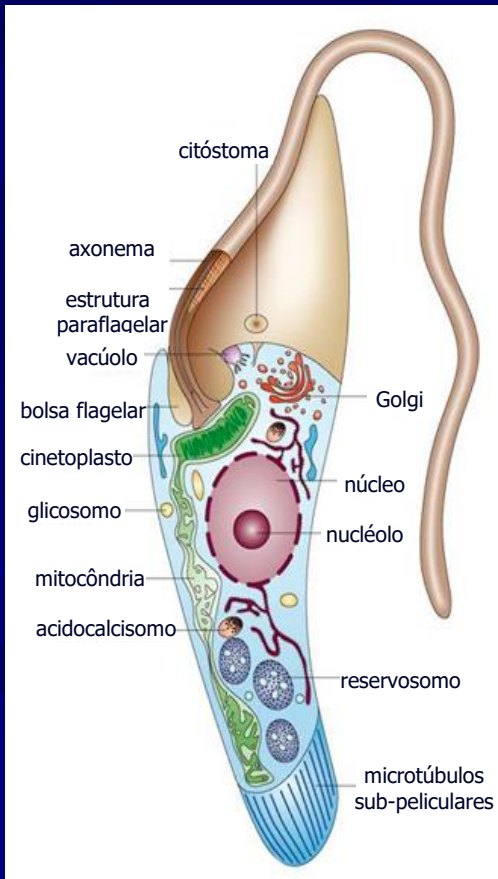
Tsé-tsé: proliferação do parasita depende de glicólise e de uma mitocôndria funcional

Locomoção e organelas envolvidas



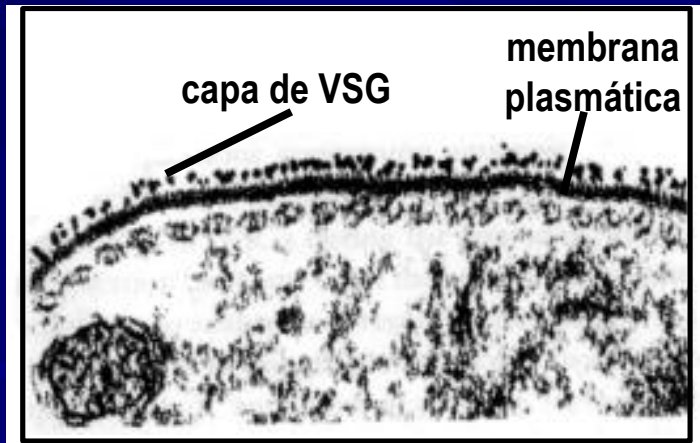
Glicossomo

– Organela que contém enzimas da **via glicolítica**. Permite que as formas sanguíneas dos tripanossomas se multipliquem intensamente no sangue.

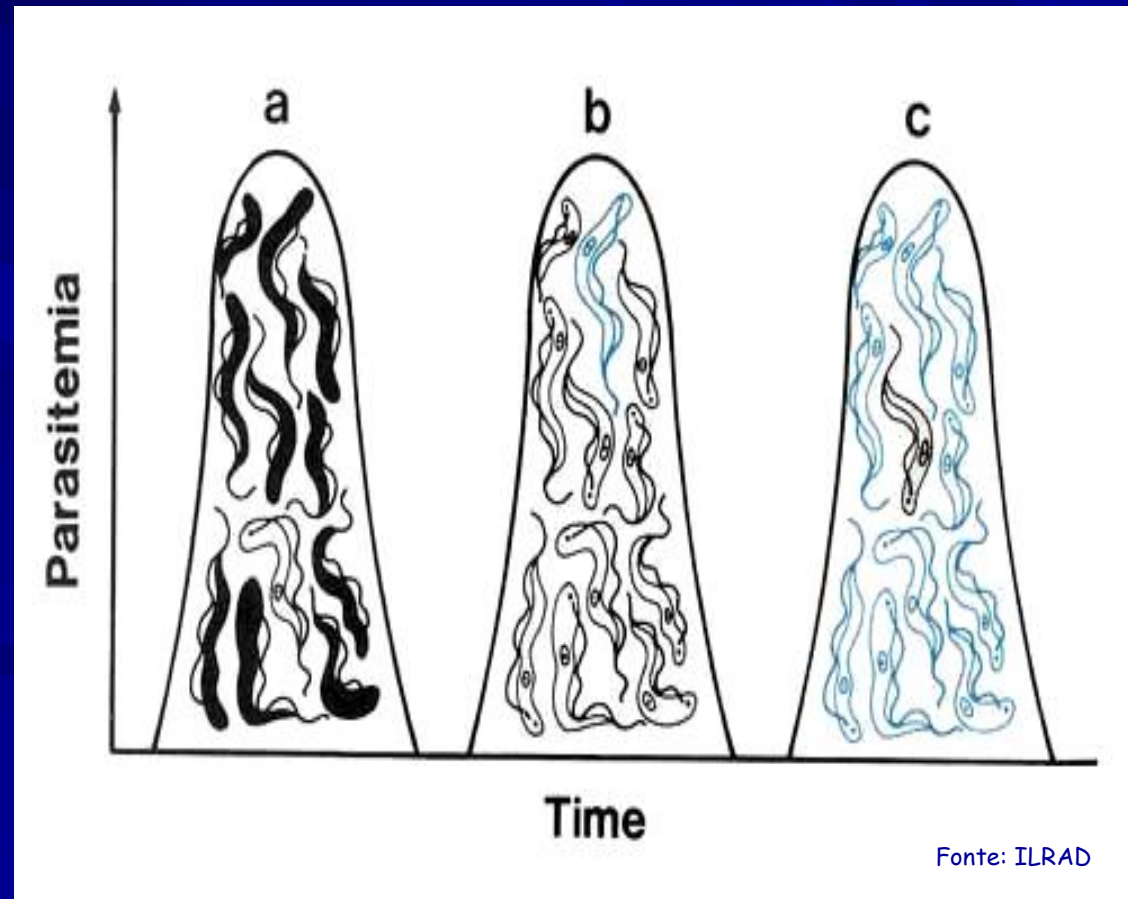


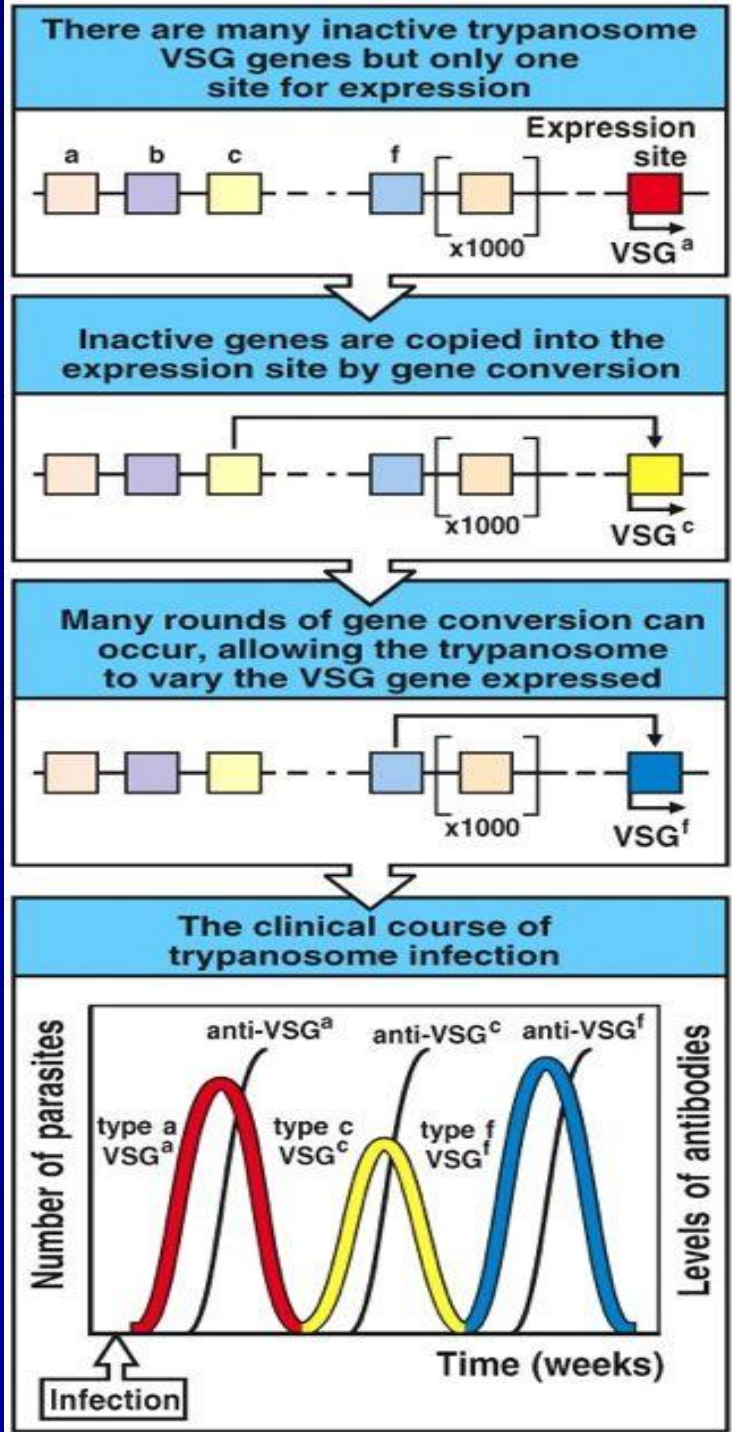
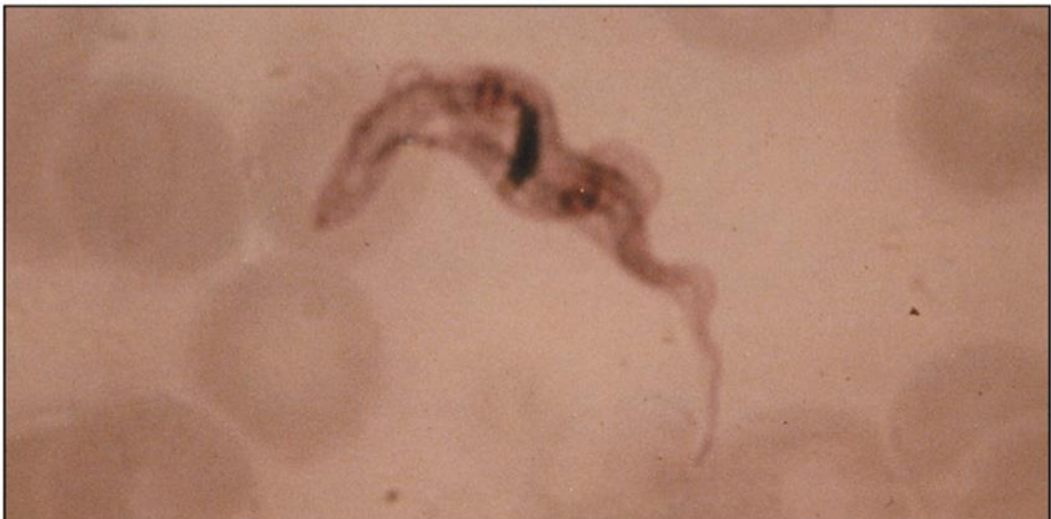
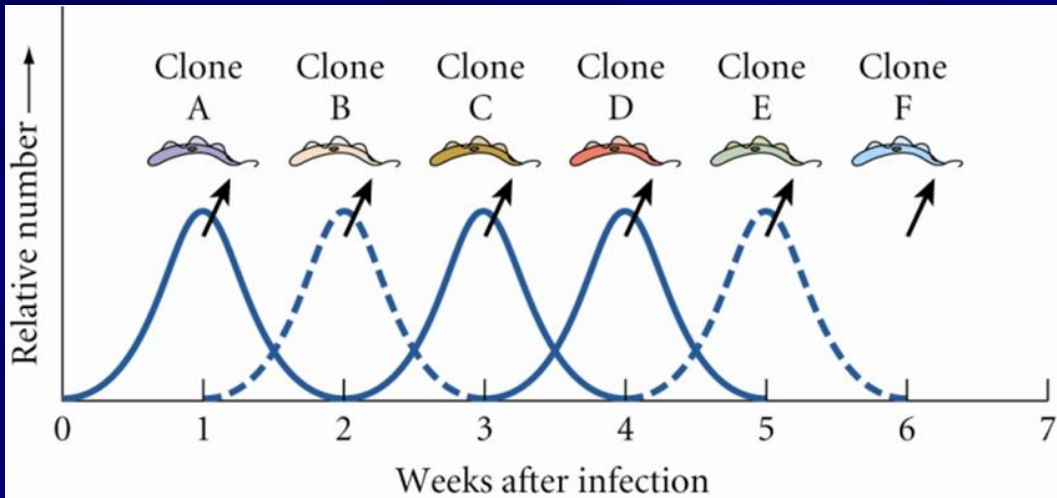
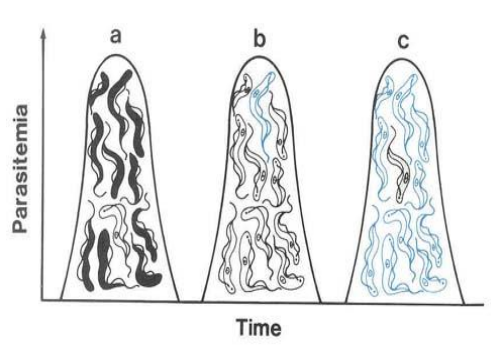
VSGs e variação antigênica

- mecanismo de escape da resposta imune do hospedeiro, usado pelos tripanossomas Africanos – capa de glicoproteínas variantes (Variant surface glycoprotein – VSG)

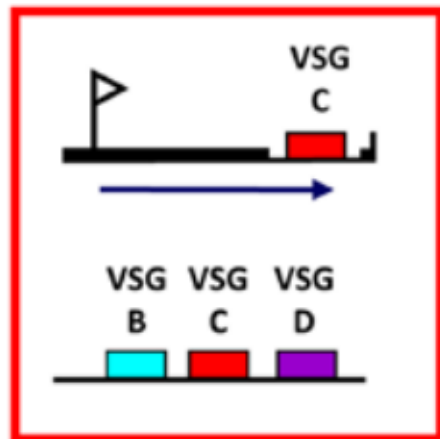
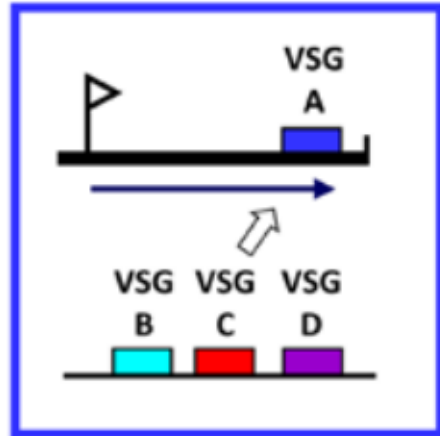


Infecções crônicas

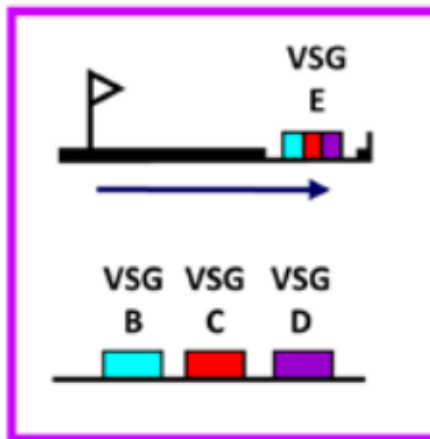
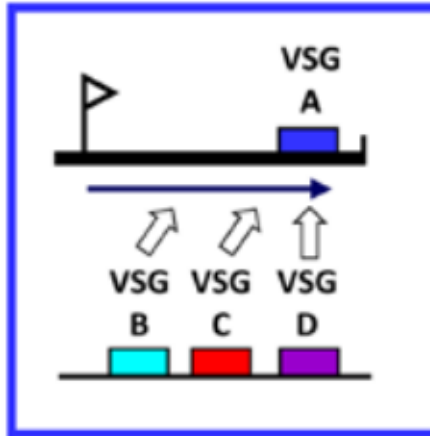




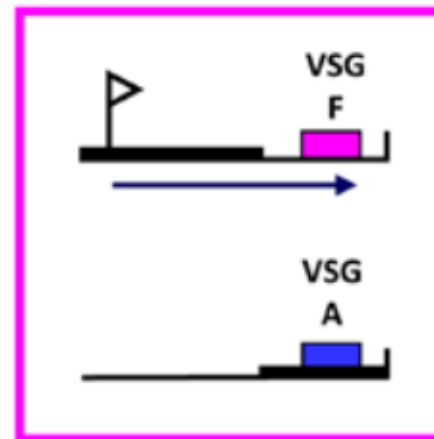
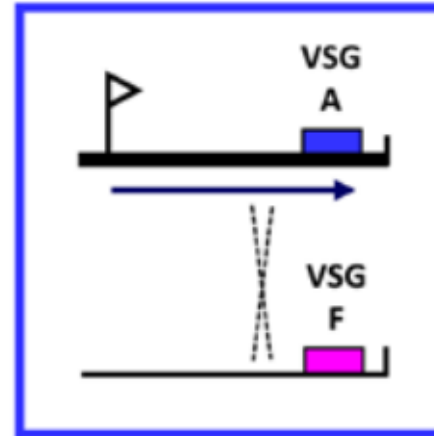
A Duplicative gene conversion



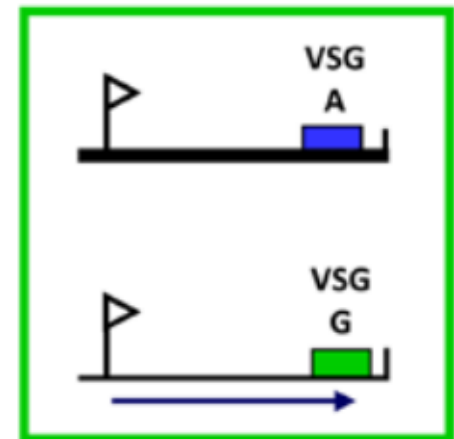
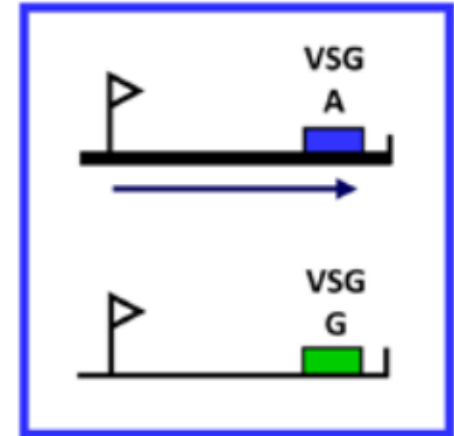
B Segmental gene conversion



C Telomere exchange



D ES switch



Gênero *Trypanosoma*

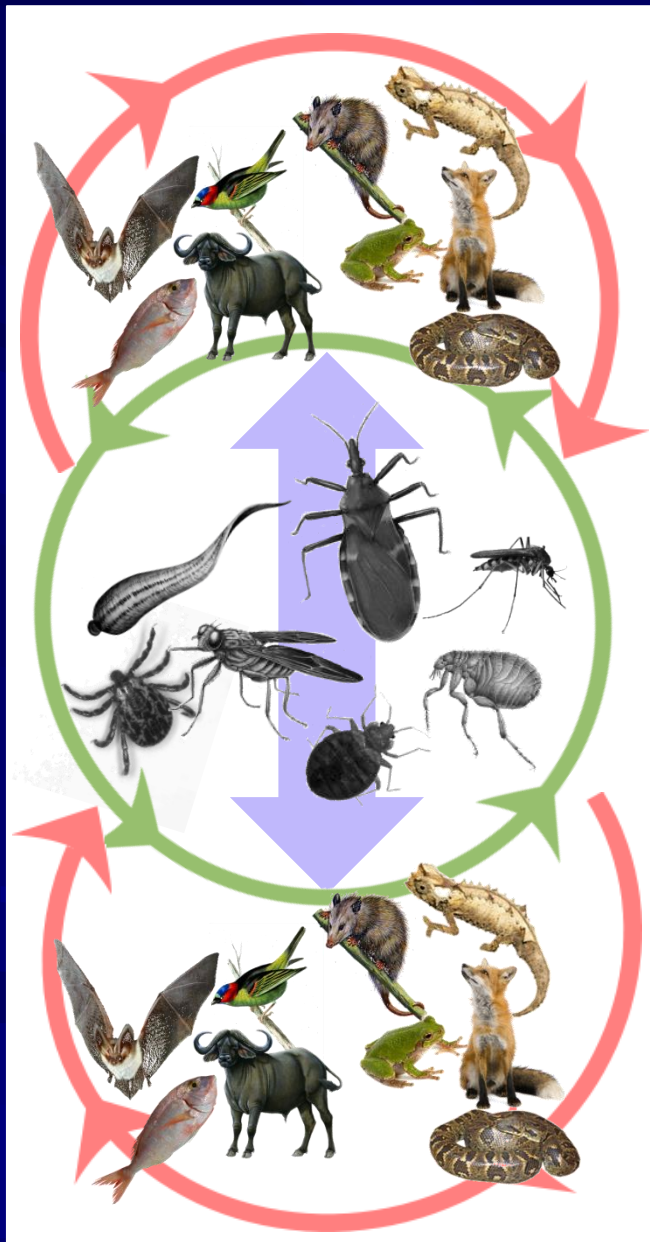
Parasitas heteroxênicos

Vertebrado x Invertebrado

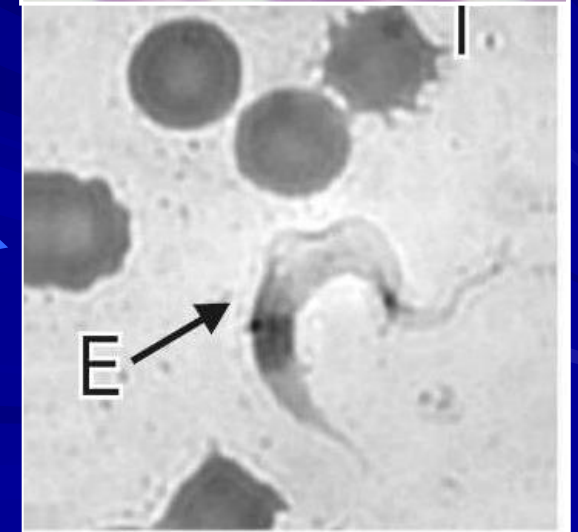
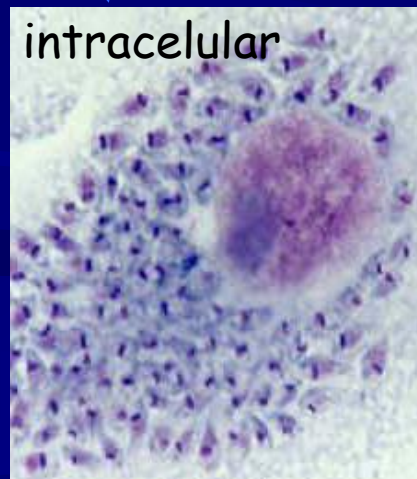
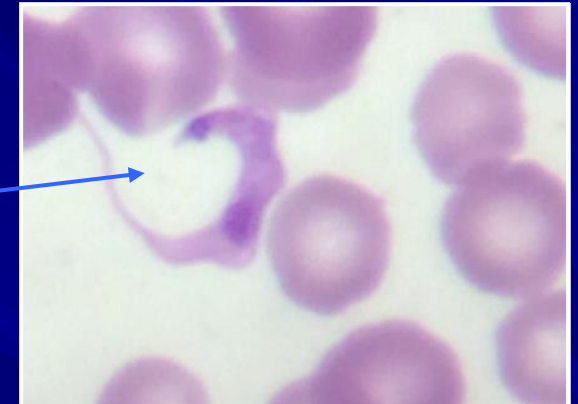
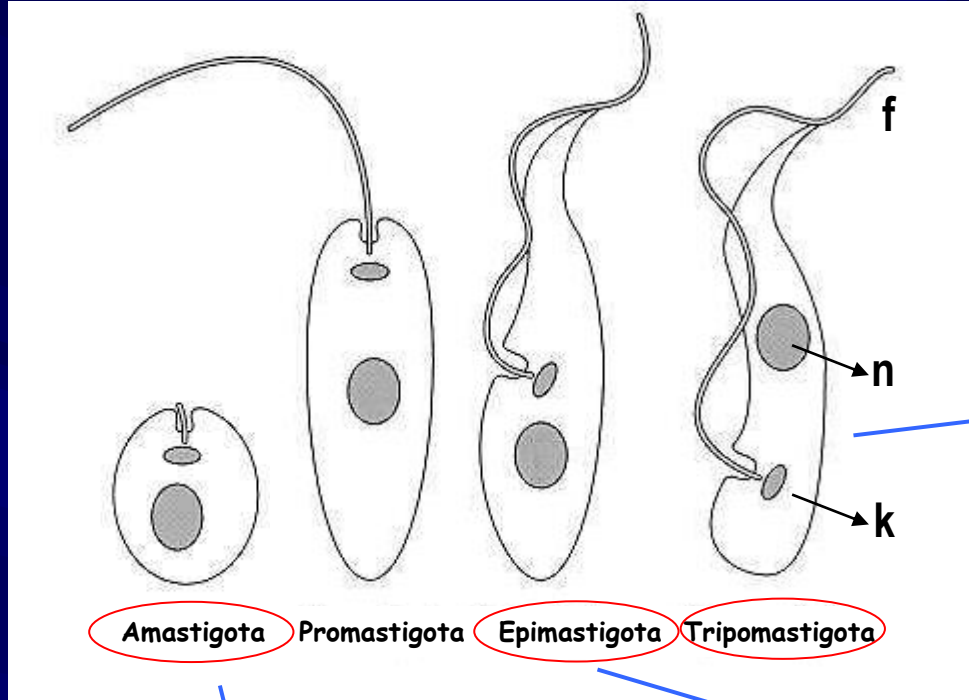
- **MAMÍFEROS**
- **aves**
- **peixes**
- **répteis**
- **anfíbios**
- **Moscas hematófagas**
- **pulgas**
- **carrapatos**
- **hemípteros**
- **mosquitos**
- **sanguessugas**

Ampla diversidade morfológica e de ciclo de vida

Das centenas de espécies em todo o mundo, maioria não é considerada patogênica

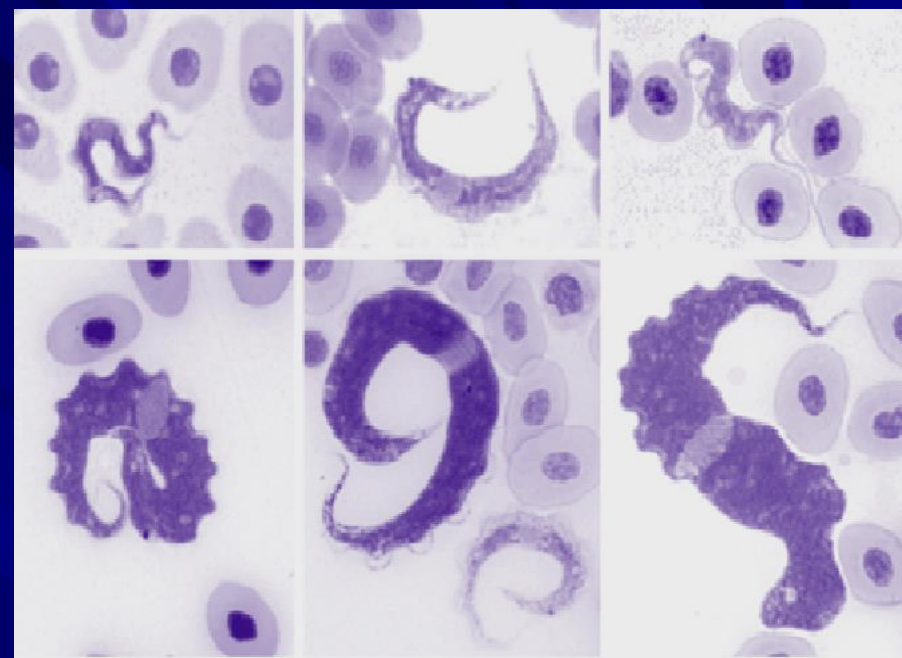


Morfologia dos tripanossomas



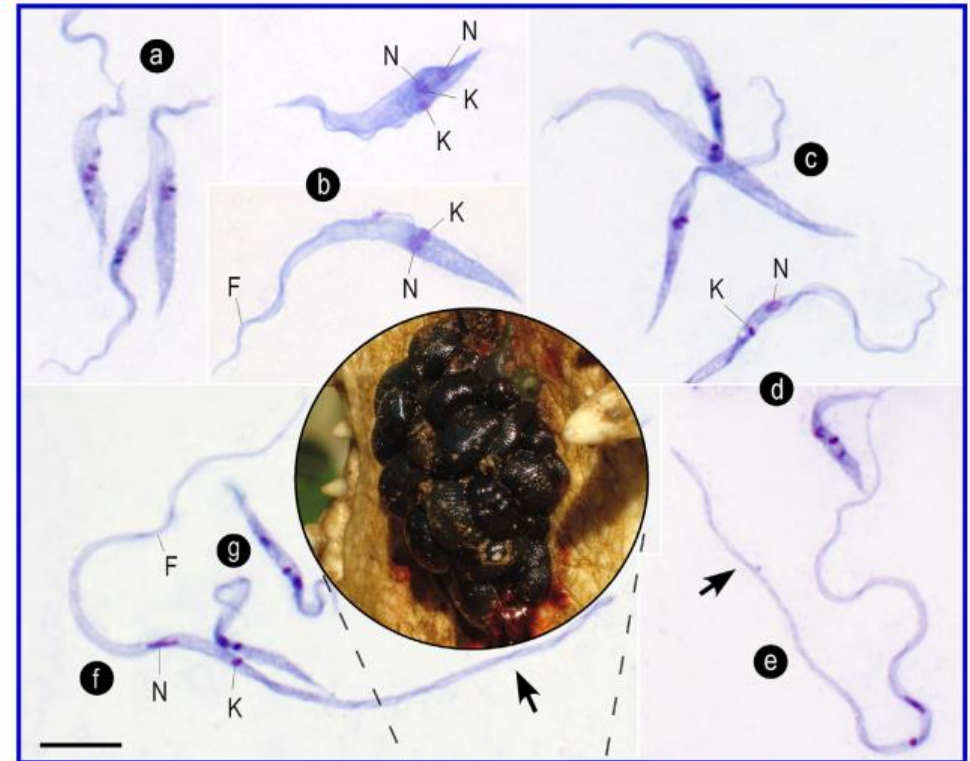
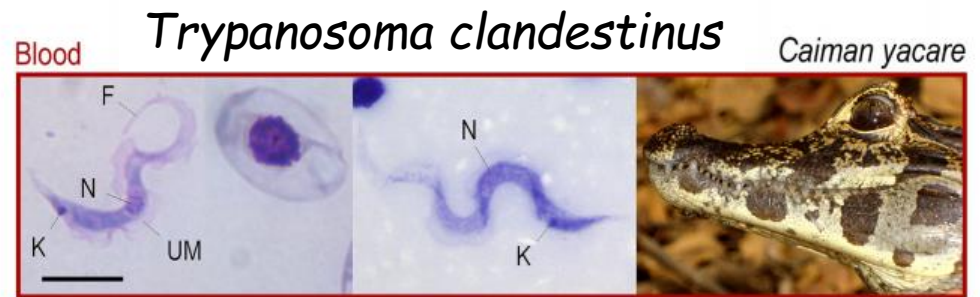
Tripanossomas de peixes

transmitidos
por sanguessugas



Tripanossomas de répteis

transmitidos por sanguessugas



Leech

Haementeria sp.

Caiman yacare

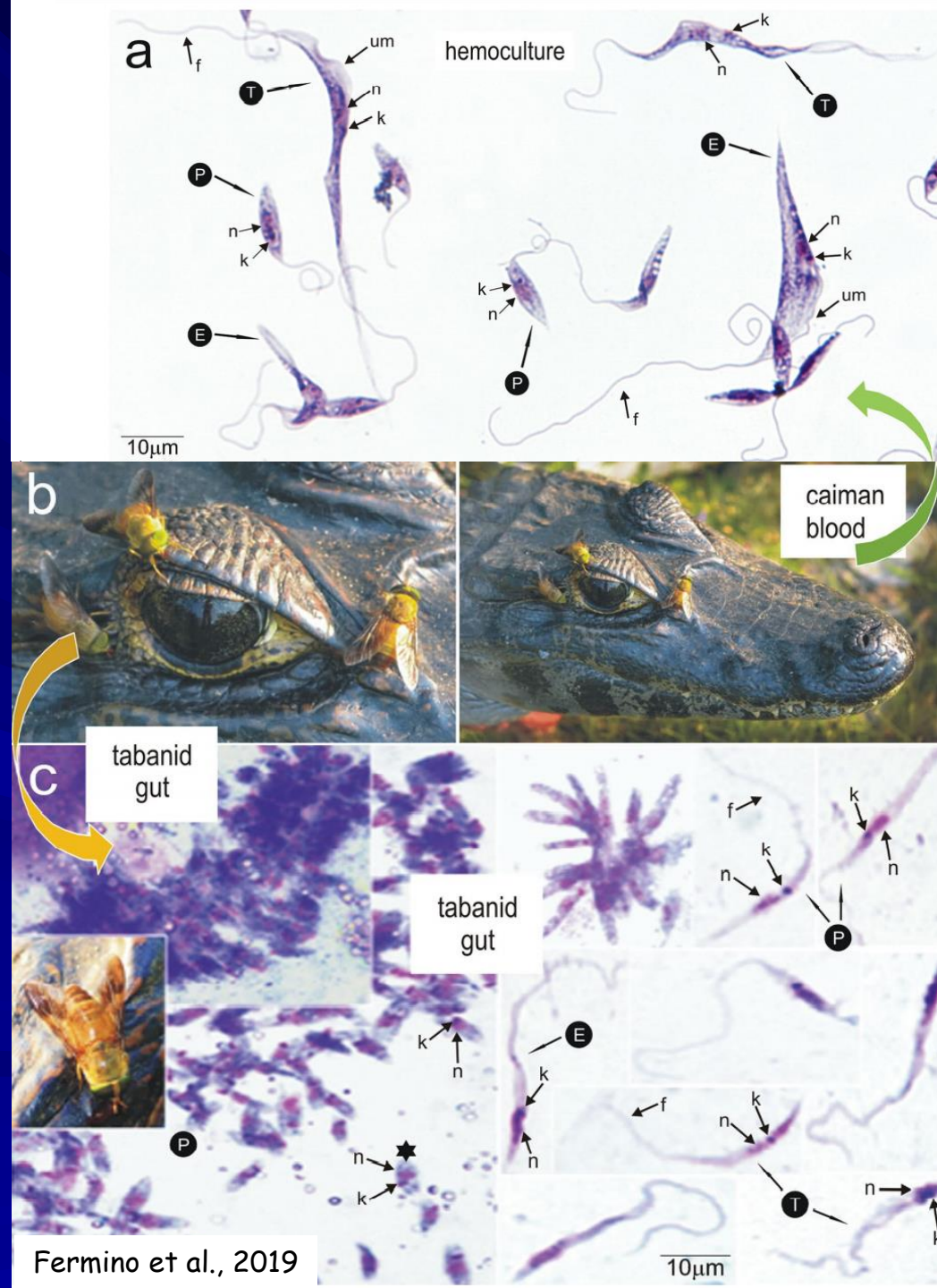
Leech

Fermino et al., 2015

Tripanossomas de répteis

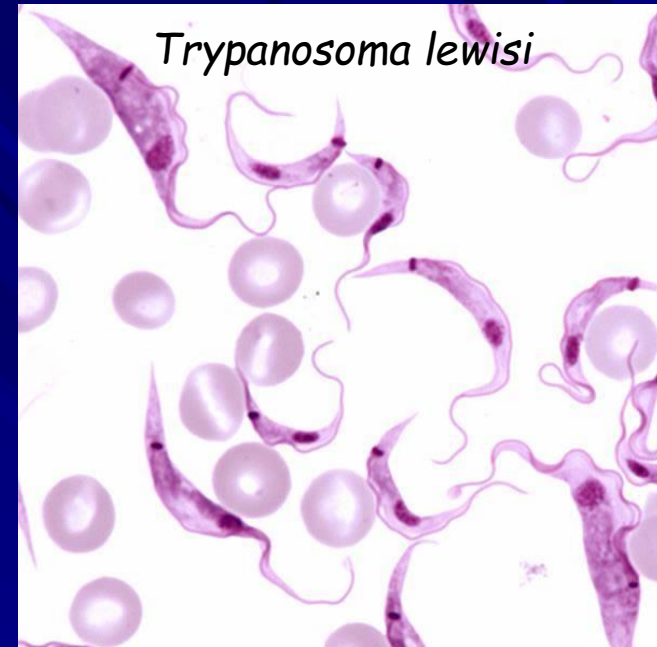
transmitidos por tabanídeos

Trypanosoma kaiowa n. sp.
Ciclo biológico previsto



Tripanossomas de *Rattus* sp.

transmitidos
por pulgas



Tripanossomas de cervídeos (hipoboscídeos)

Trypomastigotes

A

Odocoileus virginianus
White-tailed deer

B

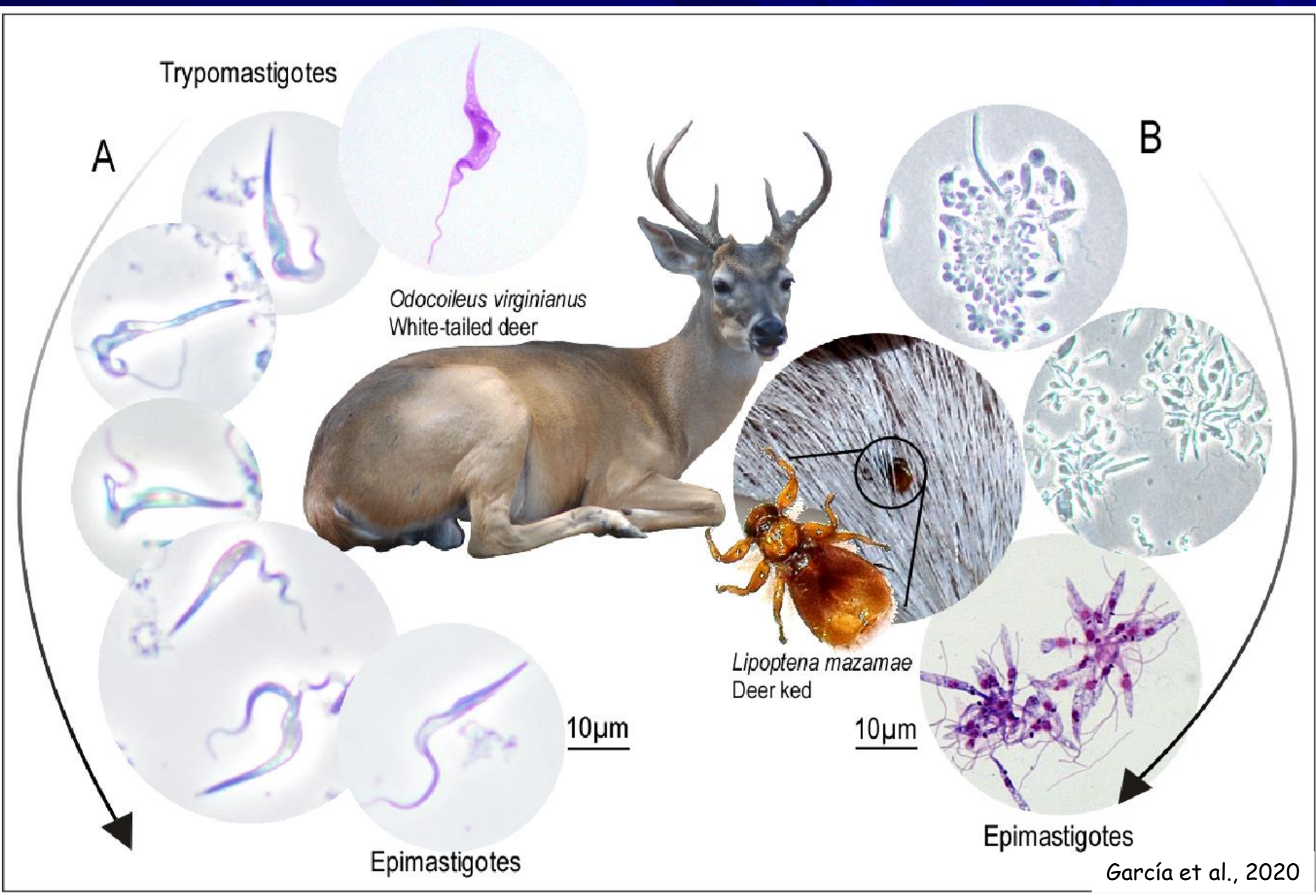
Lipoptena mazamae
Deer ked

10µm

10µm

Epimastigotes

Epimastigotes



Tripanossomas africanos
(moscas tsé-tsé)



Trypanosoma cruzi
(barbeiros)

TRIPANOSSOMAS AFRICANOS DE INTERESSE HUMANO E MÉDICO VETERINÁRIO



Gênero *Trypanosoma*

Tripanossomas de mamíferos

(Hoare, 1964)

Stercoraria

contaminativa



Secções

Transmissão

Subgênero

Salivaria

inoculativa



insetos vetores

Schizotrypanum *T. cruzi*

Herpetosoma *T. lewisi*

Megatrypanum *T. theileri*

Pycnomonas *T. suis*

Duttonella *T. vivax*

Trypanozoon *T. brucei brucei*

T. b. gambiense

T. b. rhodesiense

T. evansi

T. equiperdum

Nannomonas *T. congolense*

(savannah, forest, kilifi)

T. simiae

T. simiae Tsavo

T. godfreyi

Mamíferos
(áreas)

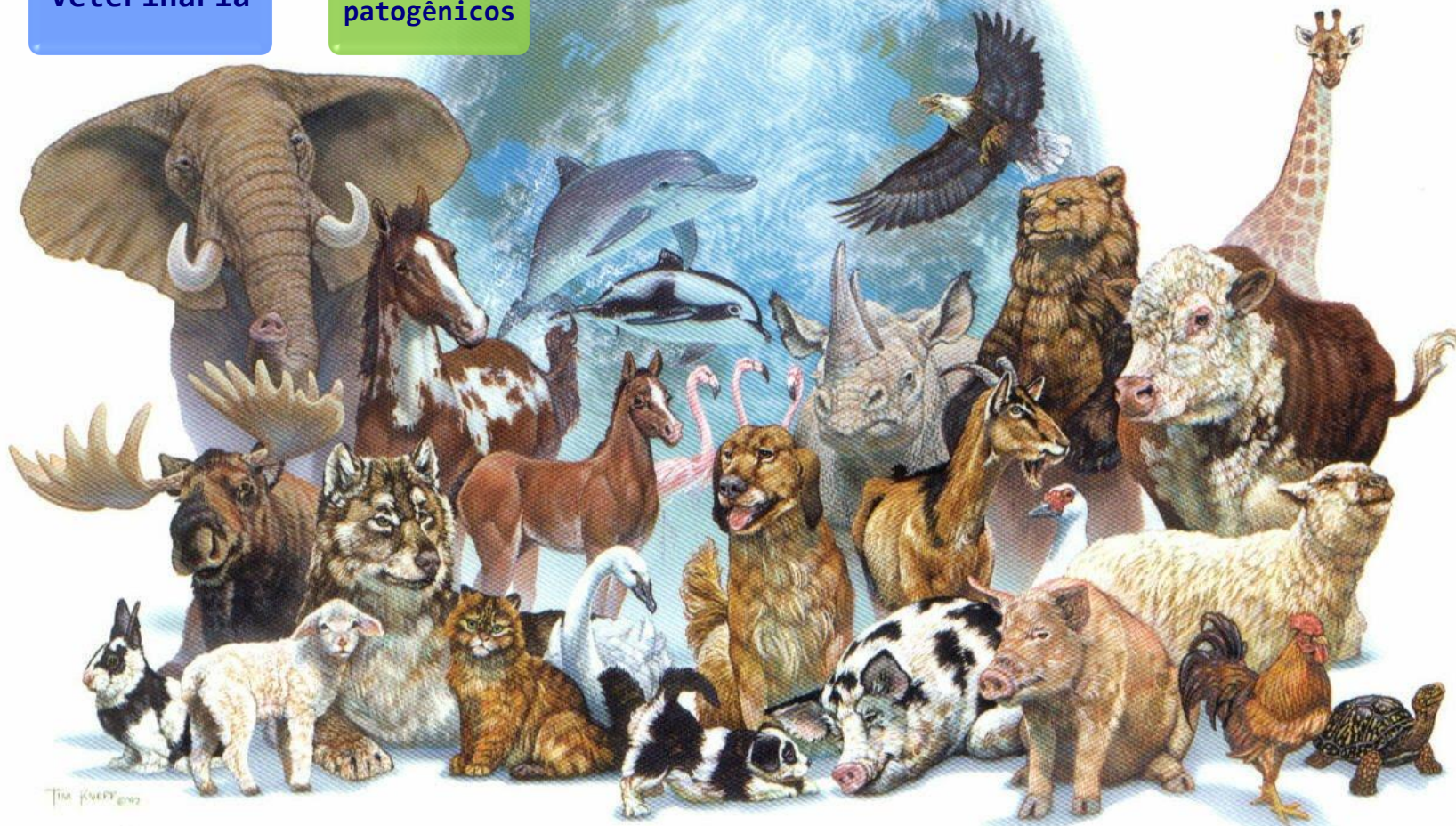
Humana

Veterinária

Tripanossomas

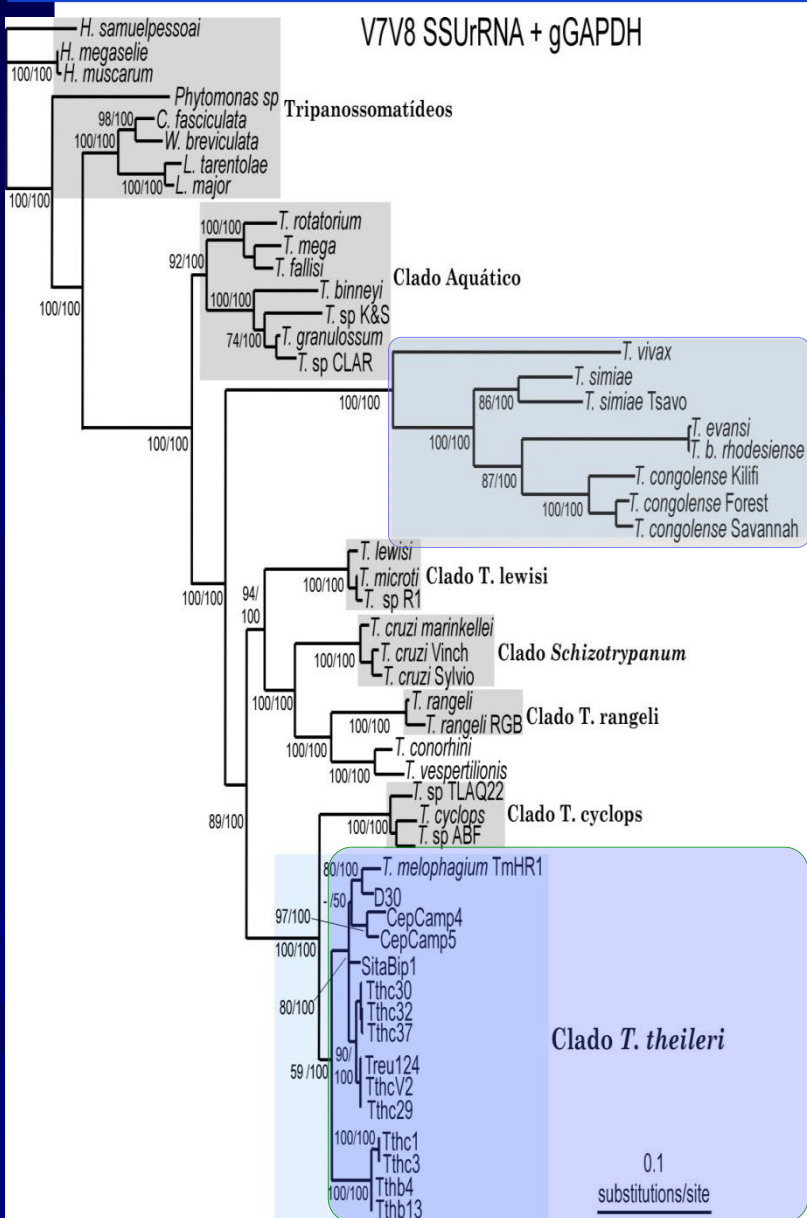
Patogênicos 

Não
patogênicos



Análises filogenéticas

V7V8 SSUrRNA + gGAPDH



Clado *T. brucei*
 Trypanosomas africanos
 (patogênicos)

- *Duttonella*
- *Trypanozoon*
- *Pycnomonas*
- *Nannomonas*

Clado *T. theileri*
 (não - patogênicos)

- *Megatrypanum*



T. congolense

T. simiae

Trypanozoon

T. simiae Tsavo



***Glossina* sp.**

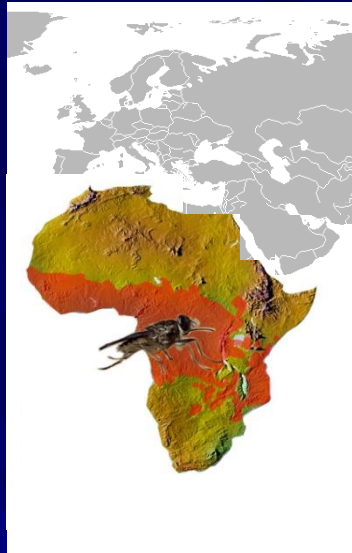
T. godfreyi

T. suis



T. vivax

Tripanossomas patogênicos de origem Africana



T. brucei spp.
T. vivax
T. congolense
T. simiae
T. evansi
T. equiperdum

(*Glossina* spp.
inoculativa)

Tabanídeos
Sexual

Bovinos, bufalinos, ovinos, caprinos, equinos, suínos, humanos

Tripanossomas africanos



vetores



reservatórios

ungulados/
humanos

hospedeiros naturais



Tripanossomas Africanos

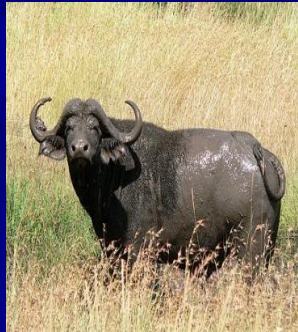
Mamíferos

AHT - Humanos



AAT - Animais

Artiodactyla



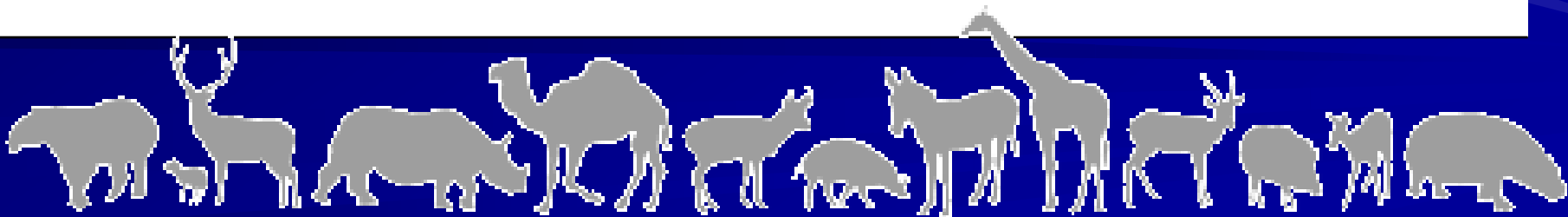
Perissodactyla



Tripanossomas de interesse para animais domésticos

Tripanossomas africanos

Subgênero	espécie	boi	cabra	ovelha	porco	cavalo	jumento
<i>Trypanozoon</i>	<i>T. brucei</i>	+	+	+	+	+	+
	<i>T. evansi</i>	+	+	+	+	+++	++
	<i>T. equiperdum</i>	-	-	-	-	+++	++
<i>Nannomonas</i>	<i>T. congolense</i>	+++	+++	+++	+	++	++
	<i>T. simiae</i>	-	-	-	+++	-	-
<i>Duttonella</i>	<i>T. vivax</i>	++	++	++	-	+	+



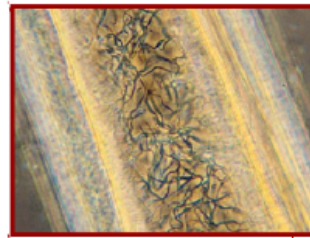


Mosca tsé-tsé
Glossina spp.

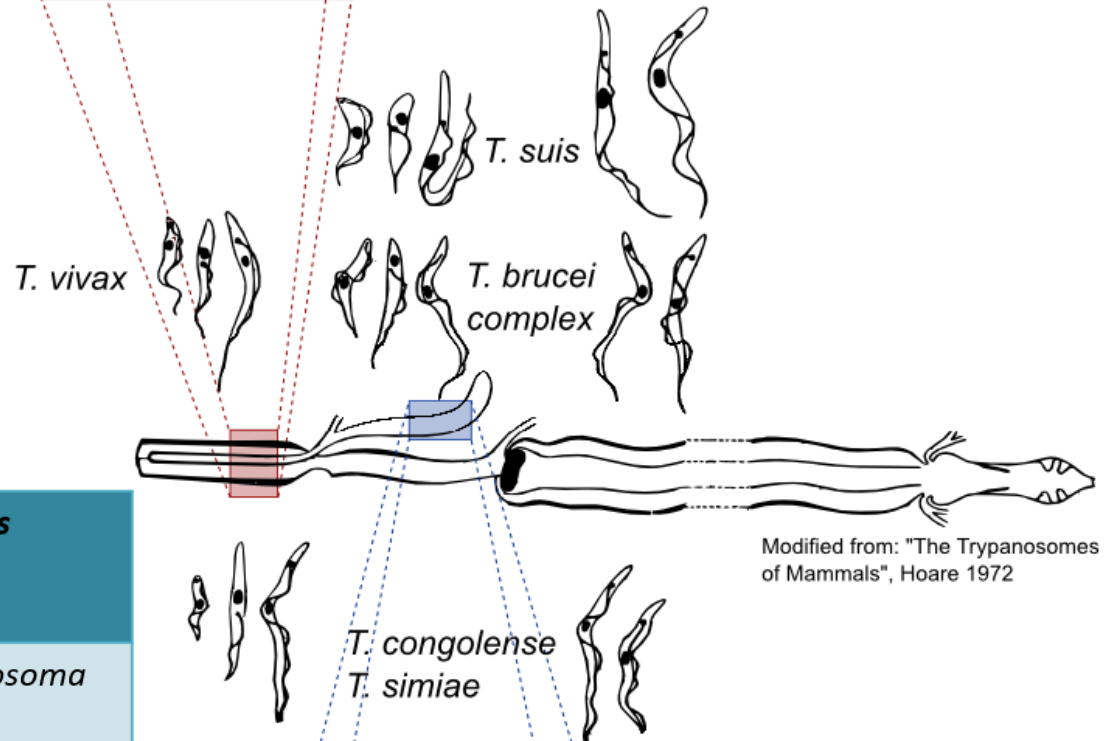
ÁFRICA



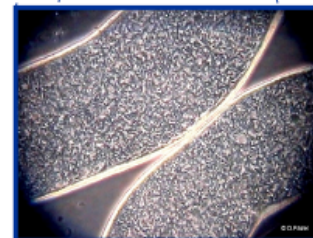
Localização nas tsé-tsé



Trypanosoma congolense epimastigotes in a tsetse proboscis (labrum)
(Steven Mihok 1999 - 2009)



Modified from: "The Trypanosomes of Mammals", Hoare 1972



Salivary glands from glossina infected with the S12/9/5 Trypanosoma brucei gambiense isolate (Raveel et al., 2006)

Subgênero	Local de desenvolvimento na tsetse	Espécies
Trypanozoon	Intestino médio e Glândula salivar	Trypanosoma brucei
Nannomonas	Intestino médio e Probóscide	<i>T. congolense</i> , <i>T. simiae</i>
Duttonella	Probóscide e bomba cibarial	<i>T. vivax</i> , <i>T. uniforme</i>
Pycnomonas	Intestino médio, Glândula salivar e Probóscide	<i>T. suis</i>

Tripanossomas africanos

Transmissão

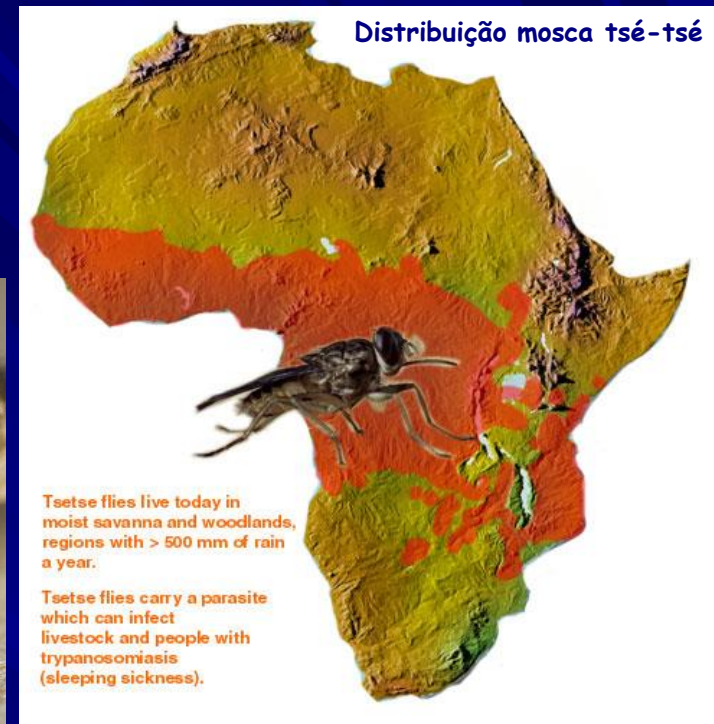
Vetorial – África

Restrita à mosca tsé-tsé

T. brucei ssp., *T. congolense* (genótipos) e *T. simiae*

T. vivax - vetorial e *mecânica*

T. evansi - *exclusivamente mecânica*



Transmissão nas Américas:

T. vivax e *T. evansi*

exclusivamente mecânica

Tripanossomíases Africana

DOENÇA	ESPÉCIE	VETOR	VIA TRANSMISSÃO
Nagana	<i>T. b. brucei</i>	tsé-tsé	inoculativa
	<i>T. congolense</i>	tsé-tsé	inoculativa
	<i>T. vivax</i>	tsé-tsé	inoculativa mecânica
Doença do Sono - Humana	<i>T. b. gambiense</i>	tsé-tsé	inoculativa
	<i>T. b. rhodesiense</i>		
Surra ou Mal de Cadeiras	<i>T. evansi</i>	Tabanídeos	mecânica
Dorina	<i>T. equiperdum</i>	-	coito

Tripanossomas africanos



***T. brucei* ssp., *T. congolense* e *T. simiae* – África**

***T. vivax* - África**

- Américas do Sul e Central

- Sudoeste da Ásia - Iraque, Iran (2020-2022)

***T. evansi* - África, Américas do Sul e Central, Ásia,
Surtos Europa**

***T. equiperdum* - África, Ásia, Américas**

Distribution of tsetse-transmitted animal trypanosomes



Desquesnes et al. Parasites & Vectors (2022) 15:64



T. vivax, *T. congolense* & *T. b. brucei*

Fig. 1 Geographical distribution of the "Nagana" disease complex (*Trypanosoma congolense*, *T. vivax* and *T. brucei*) [32–36]

Distribution of *Trypanosoma vivax*

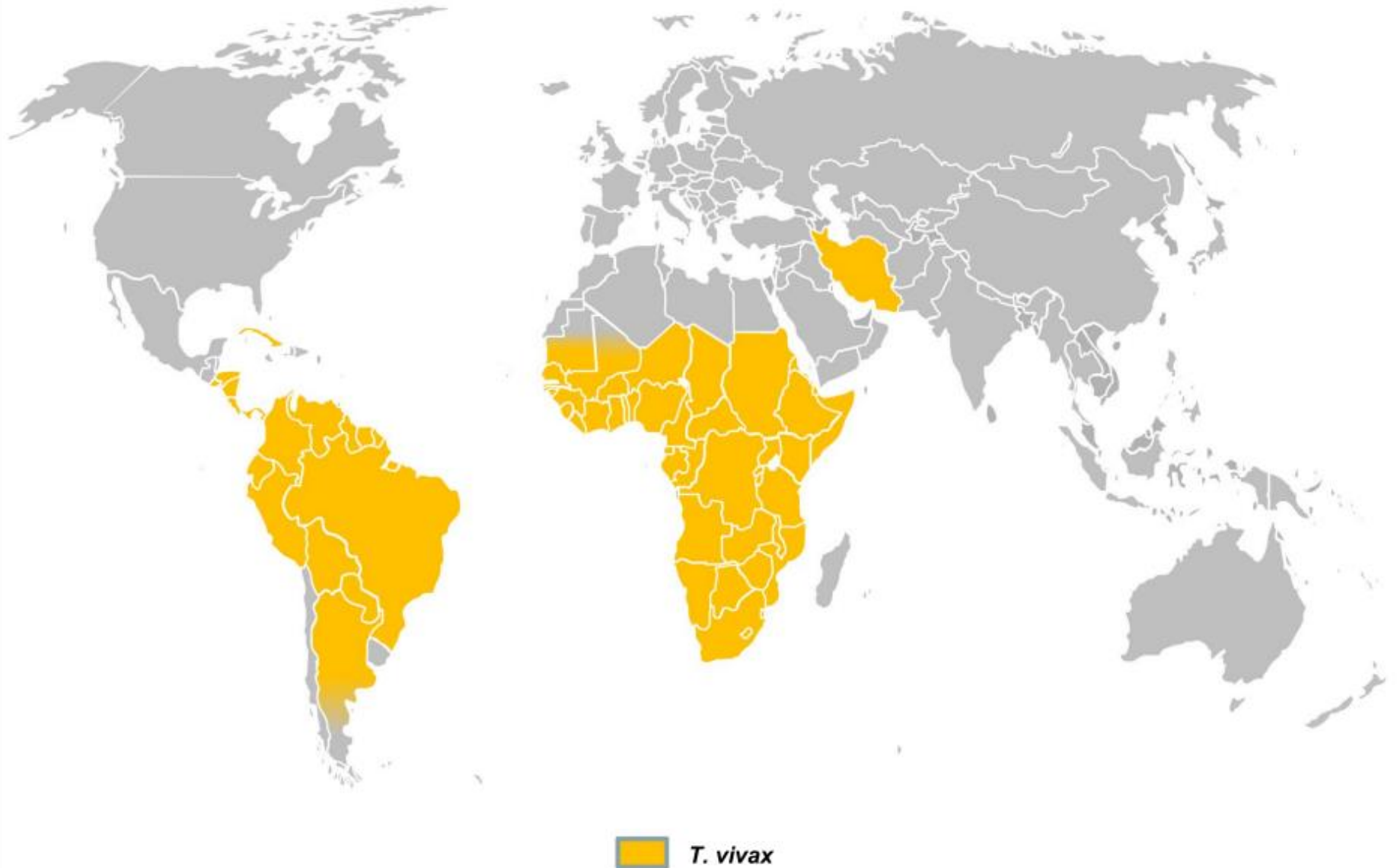


Fig. 2 Geographical distribution of *Trypanosoma vivax* [6, 32–34, 36, 42]

Distribution of *Trypanosoma evansi*

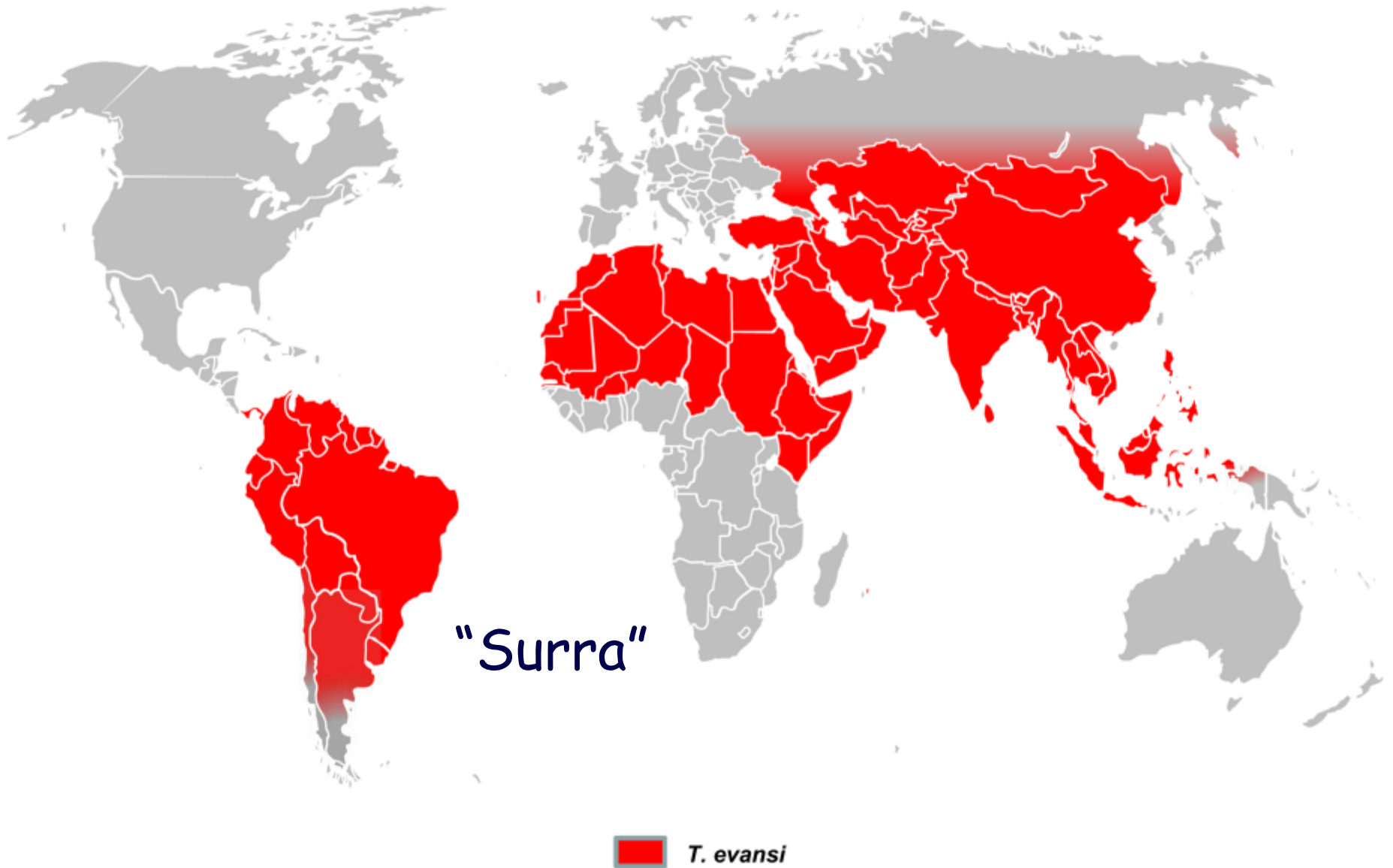
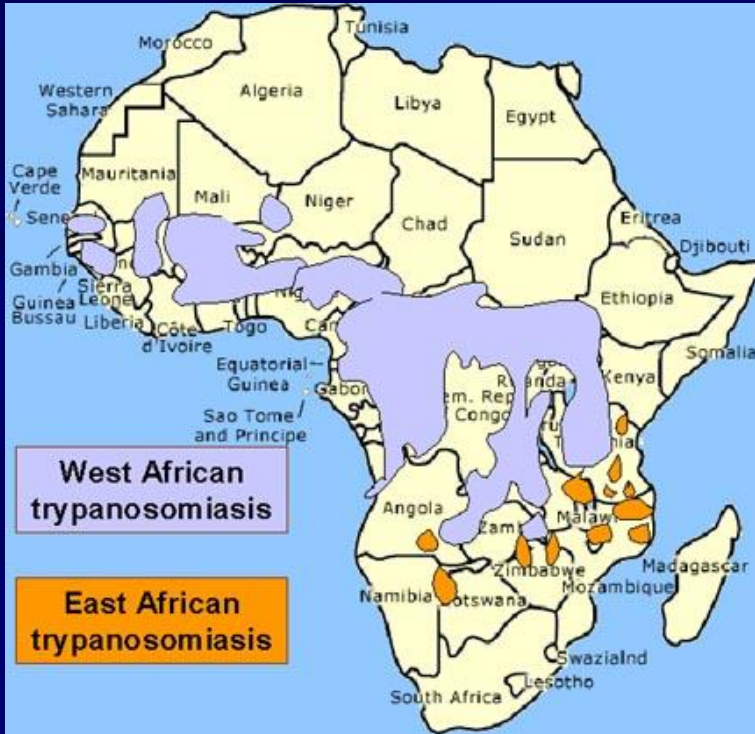


Fig. 3 Geographical distribution of *Trypanosoma evansi* ("Surra") [6, 33, 43, 50]

Doença do sono. Tripanossomíases Africana Humana (HAT)



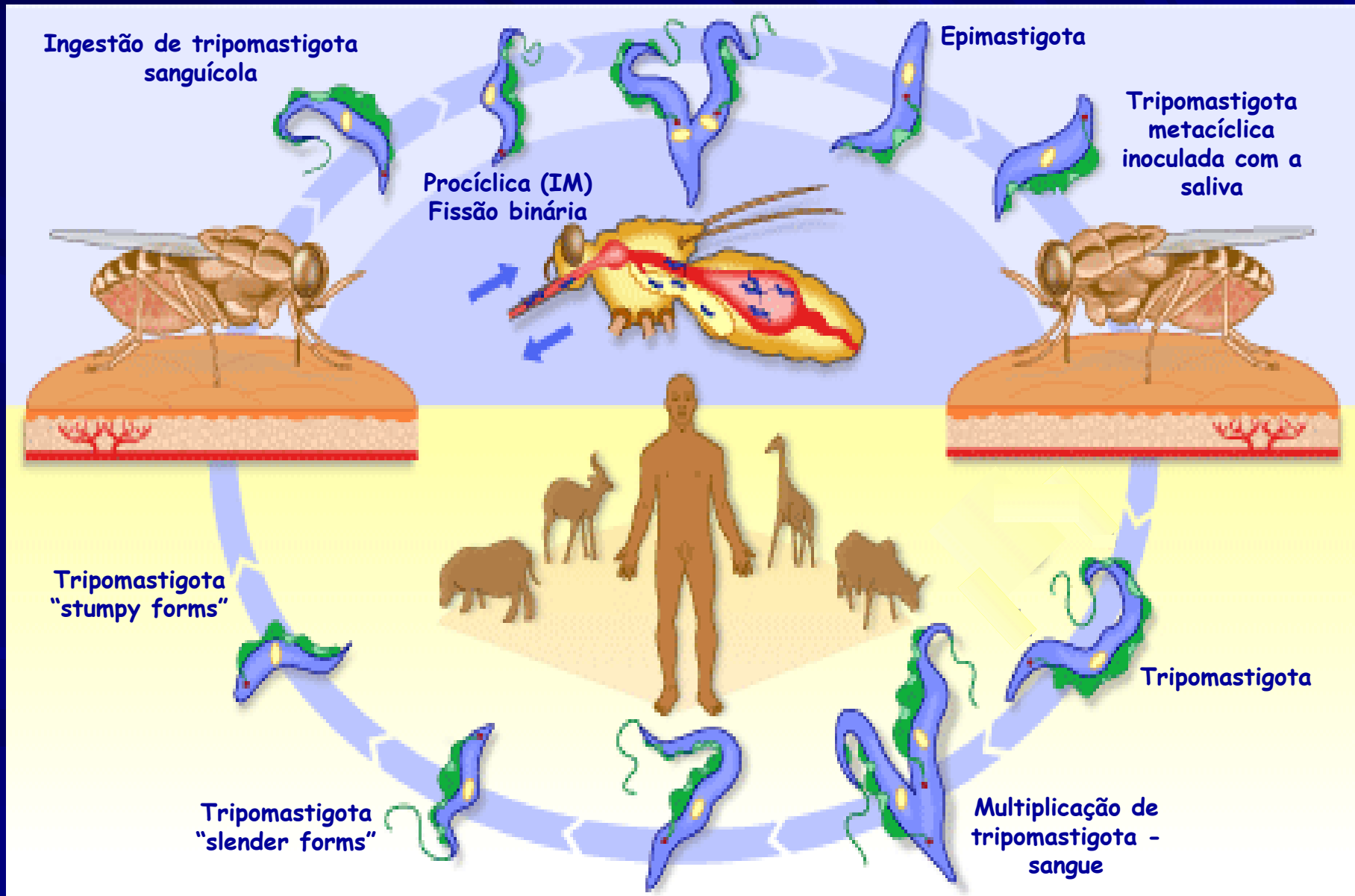
T. brucei gambiense (95 - 97%)
T. brucei rhodesiense



SNC

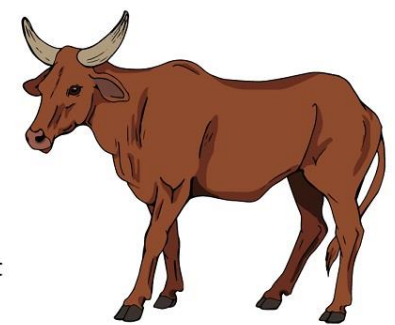
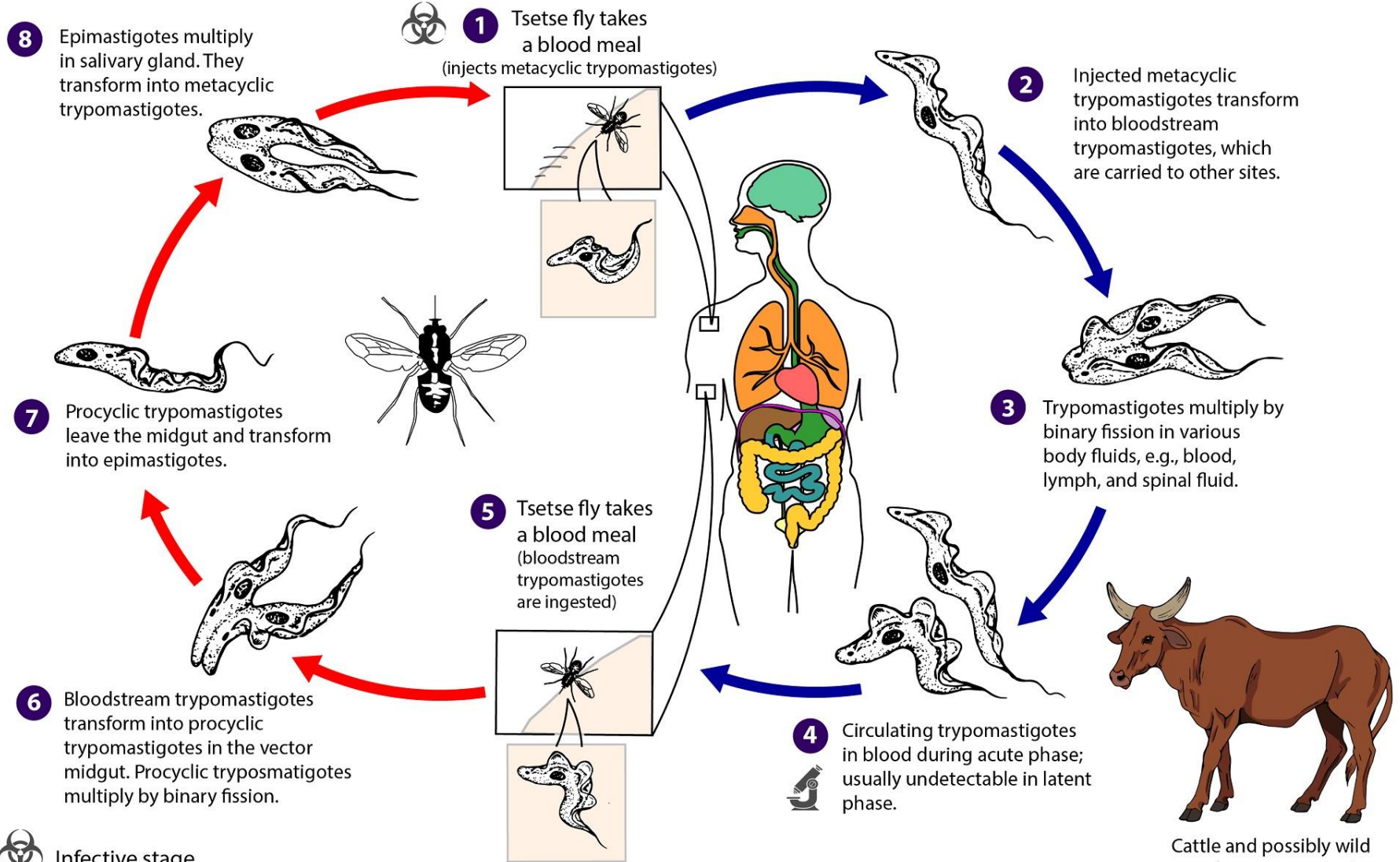
Sonolência

Ciclo biológico – *Trypanosoma b. gambiense*



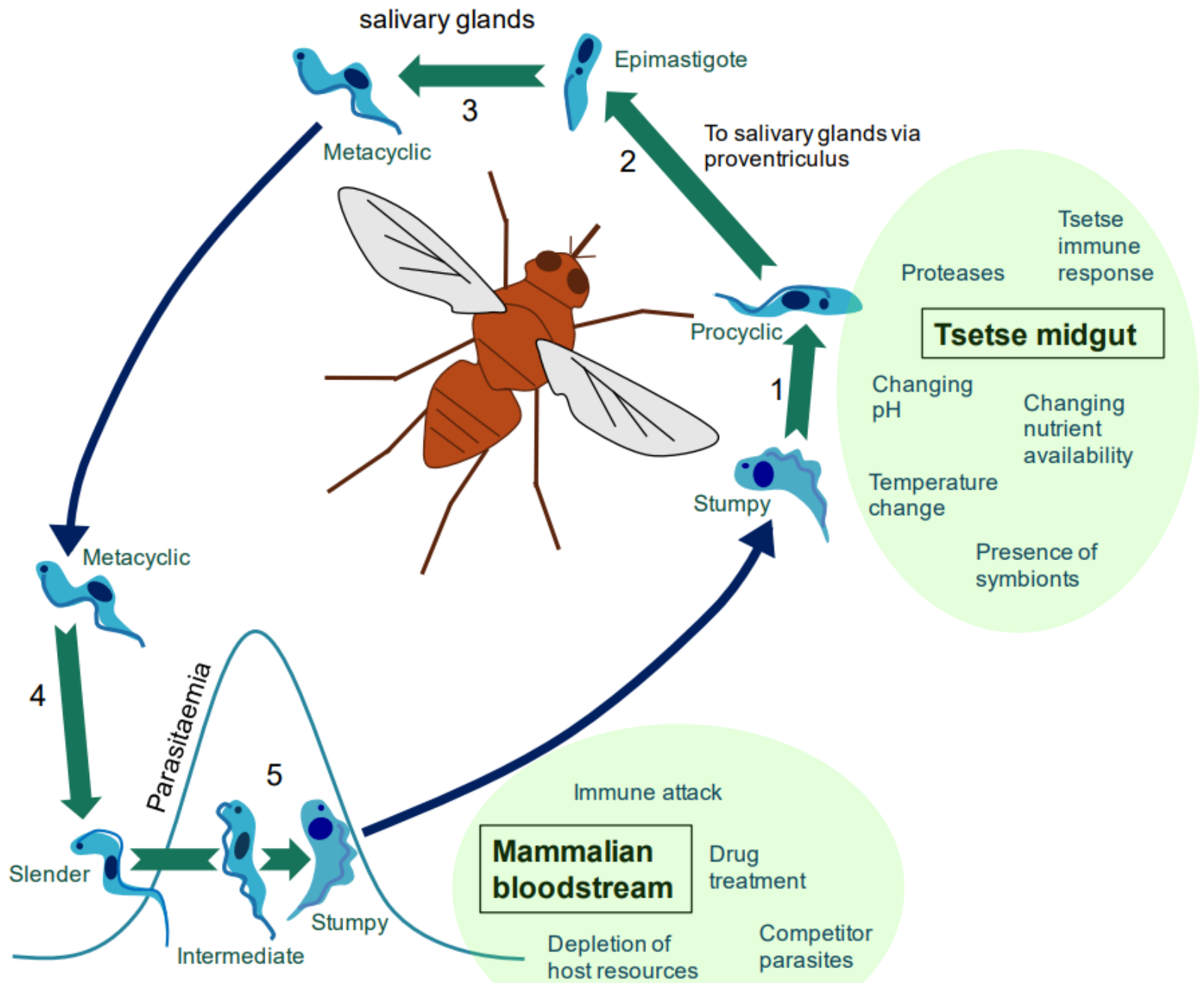
Tsetse Fly Stages

Mammalian Stages



Cattle and possibly wild ungulates are reservoirs for *T. b. rhodesiense*.

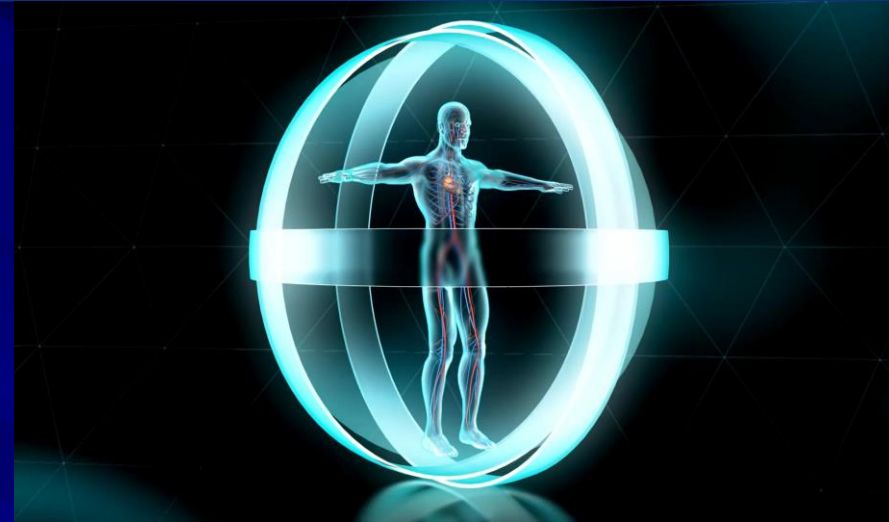
- Infective stage
- Diagnostic stage



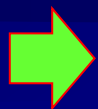
Mecanismos de defesa dos hospedeiros aos tripanossomas Africanos

Defesa humana inata (HS)

- Apolipoproteína A1 (APOA1)
- Apolipoproteína L1 (APOL1)
- Haptoglobin related protein (HPR)



Dentro de 2 complexos de proteínas do soro
-Factor lítico de tripanossomas 1 e 2 (TLF-1 & TLF-2)

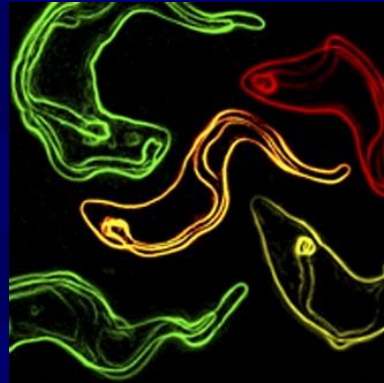


LISE DOS TRIPANOSSOMAS NO SANGUE
NHS

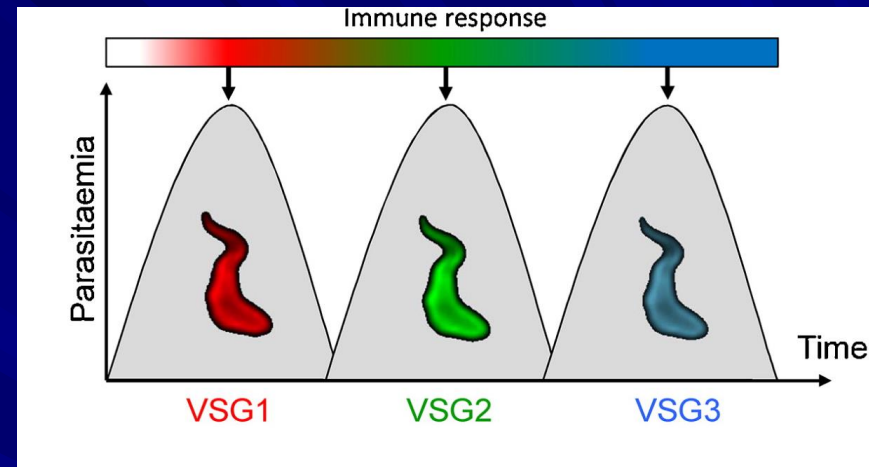


Mecanismos de escape da resposta imune dos tripanossomas Africanos

VSGs e variação antigênica



Capa de Glicoproteínas Variantes
(Variant surface glycoprotein – VSG)



T. brucei rhodesiense

Serum resistance associated
gene (SRA SRP)
liga e inibe TLF

T. brucei gambiense

Não possui o SRA-gene
TgsGP (VSG mutação)
Cisteíno proteases - (APOL1)
Redução da sensibilidade do
receptor TLF do parasita

HAT - Sintomas de Fase I - Hematolinfática

Inoculação do parasita

Sinais não específicos e compartilhados com outras doenças endêmicas. Início 1-3s picadura)

Cancro (>Tbr 2d-2w)

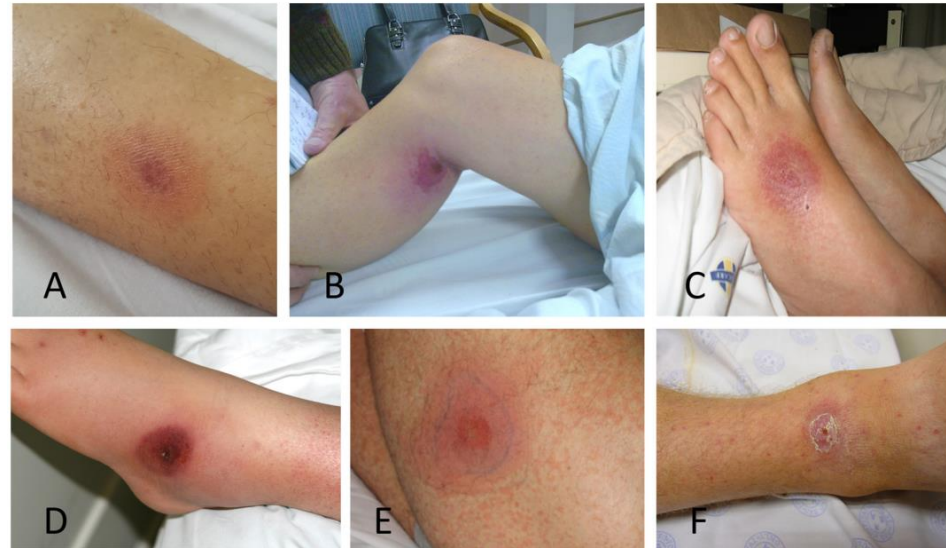
Febre, Mal-estar geral, Indisposição

Dor articular (artralgia), Dor de cabeça

Disseminação

Linfadenopatia (cervical posterior = Sinal de **Winterbottom** > Tbg, ou axilar, inguinal ou epitrocLEAR)

Hepatomegalia, esplenomegalia, perda de peso e febre intermitente



Frean et al., 2018. Aparência variável de cancros Tbr-HAT



Gómez-Junyent et al., 2017



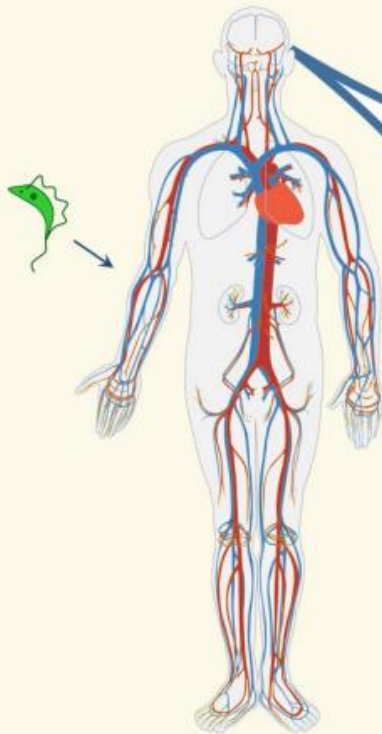
McGovern DermatologyAdvisor
<https://www.dermatologyadvisor.com>



The trypanosomiasis. The Lancet.
Barrett et al., 2003

**Early-stage infection
(haemolympathic)**

**Late-stage infection
(meningoencephalitic)**



3. PARENCHYMAL VASCULATURE
Vasculature; tight junctions

- post capillary venules
- **Brain microvascular endothelial cells; tight junctions**
- **Endothelial basement membrane**
- **Parenchymal basement membrane**

1. CHOROID PLEXUS
Vasculature; fenestrated

- vasculature
- stroma choroid plexus
- **Choroid plexus epithelium, tight junctions, BCSFB**
- **ventricular CSF**
- sub-arachnoid space

2. CIRCUMVENTRICULAR ORGANS
Vasculature; fenestrated

- Vasculature or ventricular CSF
- Parenchyma of CVOs
- **tanycyte barrier, tight junctions**

NEUROINFLAMMATORY RESPONSE

- Astrocyte activation
- Inflammatory cell infiltration
 - macrophages
 - T-cells
 - B-cells
 - Plasma cells
 - Mott cells
- BBB dysfunction
 - Contrast enhanced MRI
 - Fluorescent dye penetration

CLINICAL SIGNS

- Lymph node enlargement
- Hepatomegaly / splenomegaly
- Febrile episodes
- Pruritus
- Systemic inflammation
 - Cytokine / chemokine production
 - Lymphocyte activation

HAT - Sintomas de Fase II - Meningoencefálica

Os parasitas atravessam a barreira hematoencefálica

★ *Inicia em média: Tbr 21-60d / Tbg 300-500d*

Patogênese



Inflamação neurológica,
ativação de astrócitos,
meningoencefalite,
manguito perivascular
(células Mott),
Disfunção da BBB



Alterações do CSF
(> 5 leucócitos / μ L,
proteínas 370mg/L,
tripanossomas)

Neuropsiquiátricas

Alteração do ciclo do sono (insônia noturno e sonolência no dia "sleeping sickness"), vontade repentina de dormir

Mentais

Alucinações, delírio, ansiedade, labilidade emocional, déficit de atenção, apatia, agressividade, confusão

HAT - Sintomas de Fase II - Meningoencefálica

Deterioração progressiva da barreira cefalorraquidiana conduzindo ao agravamento das manifestações neurológicas

Motoras

Fraqueza motora, tônus anormal, distúrbio da marcha, ataxia, tremor, distúrbios da fala

Sensoriais

Parestesia, hiperestesia, anestesia, prurido, problemas visuais

Neurológicos

Reflexos anormais, convulsões, Rebaixamento dos níveis de consciência, coma, morte.

SYMPOSIUM

Human African Trypanosomiasis in a Spanish traveler returning from Tanzania

Joan Gómez-Junyent^{1*}, María Jesús Pinazo¹, Pedro Castro², Sara Fernández², Jordi Mas¹, Cristian Chaguaceda³, Martina Pellicé², Joaquim Gascón¹, José Muñoz¹

1 ISGlobal, Barcelona Ctr. Int. Health Res. (CRESIB), Hospital Clínic - Universitat de Barcelona, Barcelona, Spain, 2 Medical Intensive Care Unit, Hospital Clínic, IDIPABS, Universitat de Barcelona, Barcelona, Spain, 3 Pharmacy Department, Hospital Clínic, IDIBAPS, Universitat de Barcelona, Barcelona, Spain

* gjunyent@hotmail.com

Saharan African trypanosomiasis: a new diagnosis of a 2017 disease in

Human African trypanosomiasis is endemic to parts of sub-Saharan Africa. The most common form of the disease is caused by *T. brucei*.

¹These authors

persist. We report a recent case of stage 2 trypanosomiasis



administered patient was

imported man who had been diagnosed by blood smear. The second patient traveled to Tanzania and was diagnosed after re-molecular

CASE REPORT

Open Access



Trypanosoma brucei rhodesiense infection in a Chinese traveler returning from the Serengeti National Park in Tanzania

Qin Liu¹, Xiao-Ling Chen², Mu-Xin Chen¹, Han-Guo Xie³, Qing Liu^{2*}, Zhu-Yun Chen³, Yao-Ying Lin³, Hua Zheng², Jia-Xu Chen¹, Yi Zhang¹ and Xiao-Nong Zhou^{1*}



Fig. 2 Chancre due to *Trypanosoma brucei rhodesiense* infection in a Chinese traveler returning from Serengeti, Tanzania and Masai Mara Kenya, August 2017

Tbr representa ~70% dos casos de HAT em viajantes a África: Pesca, caça, safaris, visita aos parques de caça africanos.

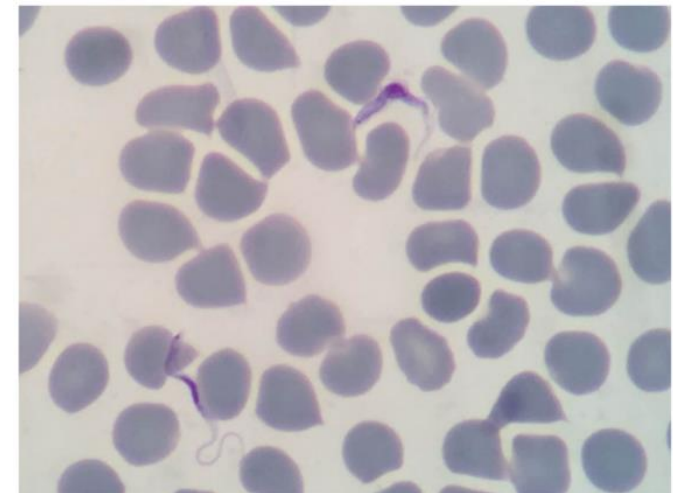


Fig. 3 *Trypanosoma* species confirmed in a Giemsa-stained thin blood film from a Chinese traveler returning from Serengeti, Tanzania and Masai Mara Kenya, August 2017



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journal homepage: www.elsevier.com/locate/ijid



INTERNATIONAL
SOCIETY
FOR INFECTIOUS
DISEASES

Case Report

Human African trypanosomiasis caused by *Trypanosoma brucei gambiense*: The first case report in China

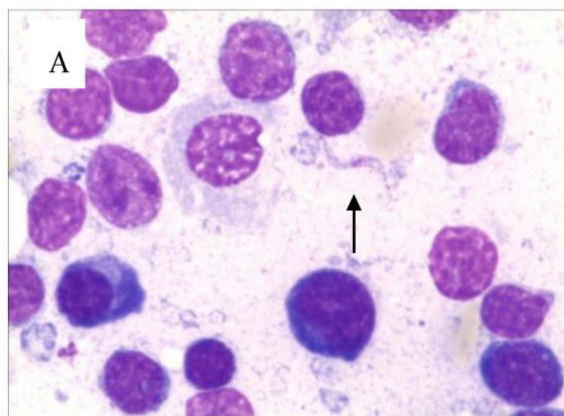


Nian Chen^a, Ke Jin^a, Jingjing Xu^b, Jianfu Zhang^c, Yali Weng^{a,*}

^a Department of Infectious Diseases, The First Affiliated Hospital of Nanjing Medical University, Jiangsu Province Hospital, 210029, China

^b Department of Respiration, Wuxi Xishan People's Hospital, Wuxi, 214011, China

^c Department of Hematology Laboratory, The First Affiliated Hospital of Nanjing Medical University, Jiangsu Province Hospital, 210029, China



ABSTRACT

We report the first imported case in China of human African trypanosomiasis (HAT), caused by *Trypanosoma brucei gambiense*, in a sailor returning from Gabon in 2014. The diagnosis was delayed and relapse led to death, despite treatment with eflornithine, as recommended by the World Health Organization for late-stage HAT. This case shows that early diagnosis of HAT and close follow-up with proper retreatment are critical.

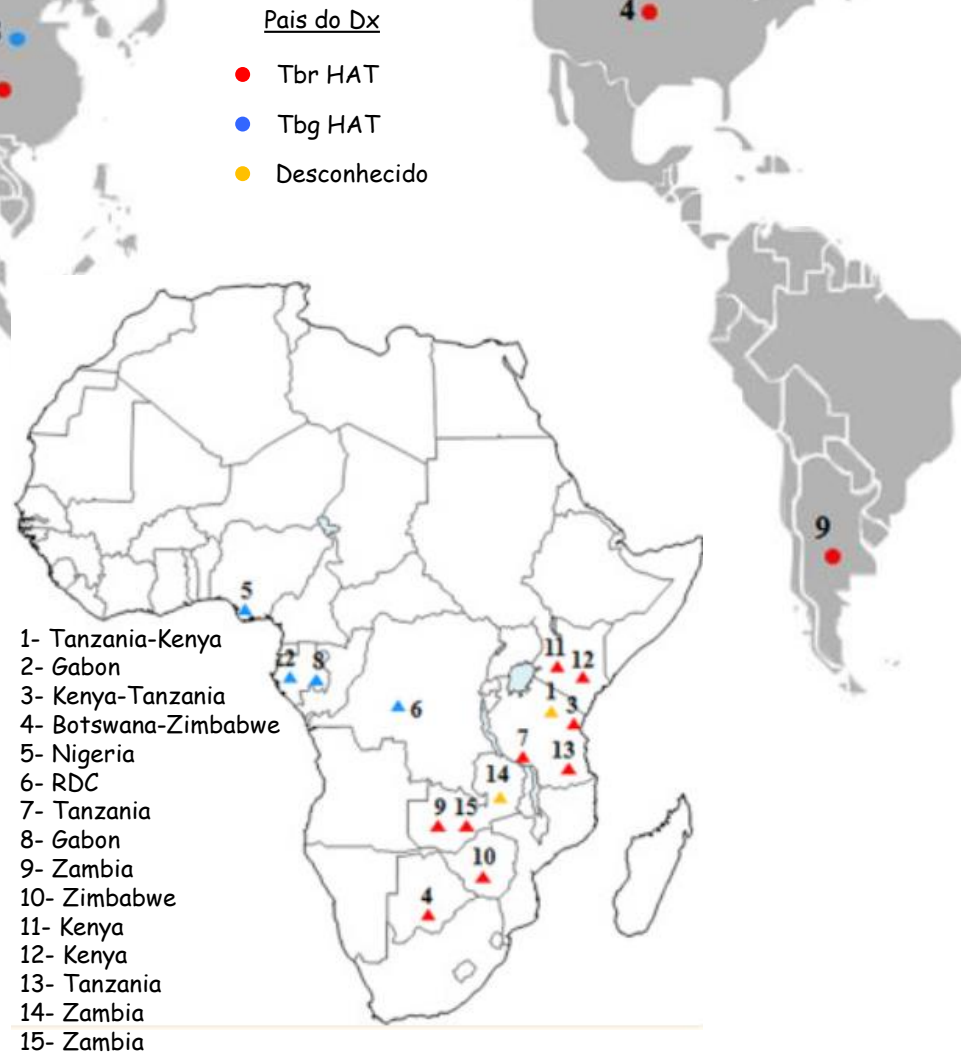
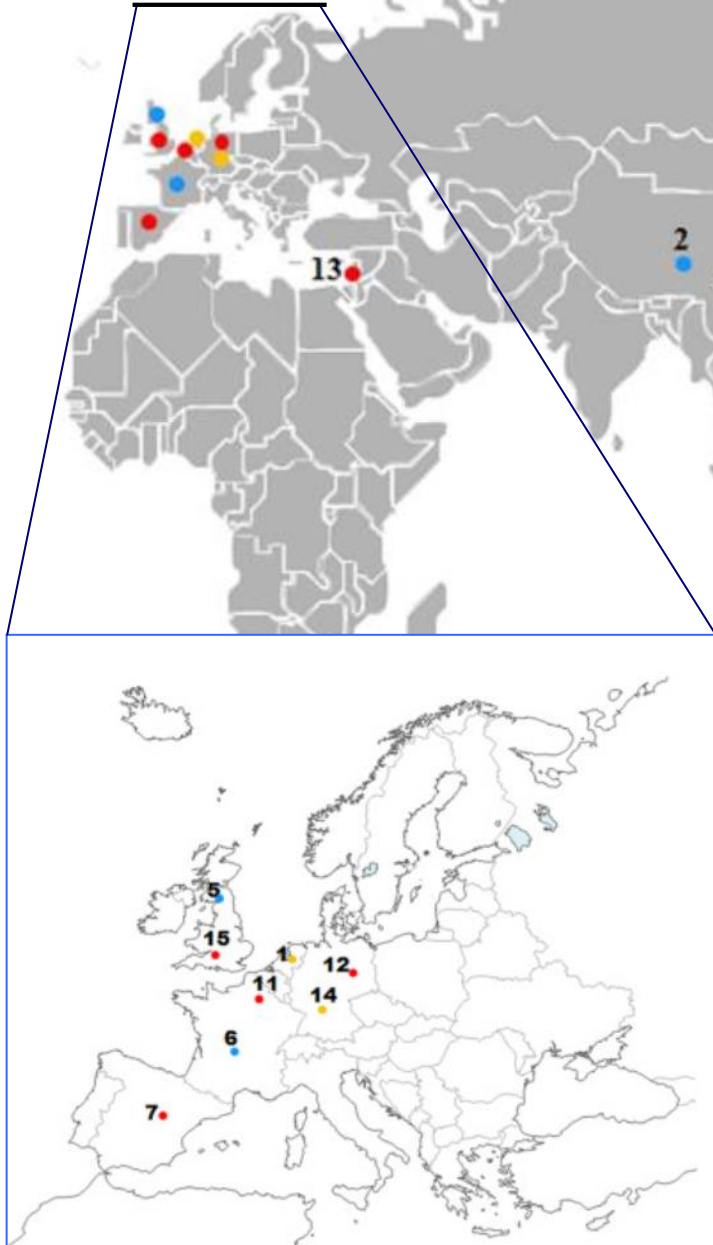
© 2018 The Authors. Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Fig. 1. Biopsia de linfonodo mostrando *T. brucei gambiense*



A

EUROPA



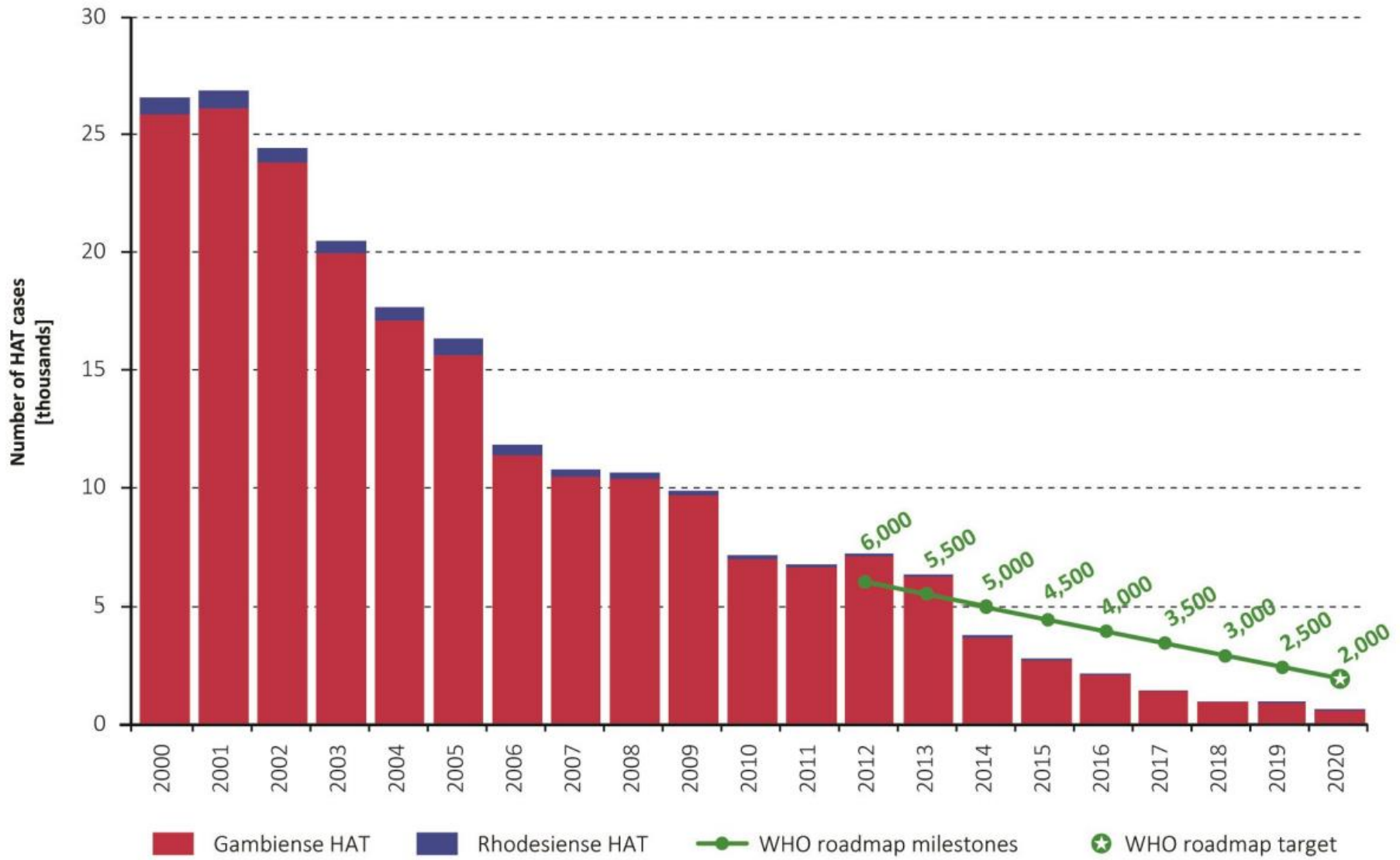


Fig 1. Total number of reported cases of HAT (gambiense and rhodesiense) per year (2000–2020). The green line and the green circles show the milestones and target set in the WHO road map for HAT elimination [14].

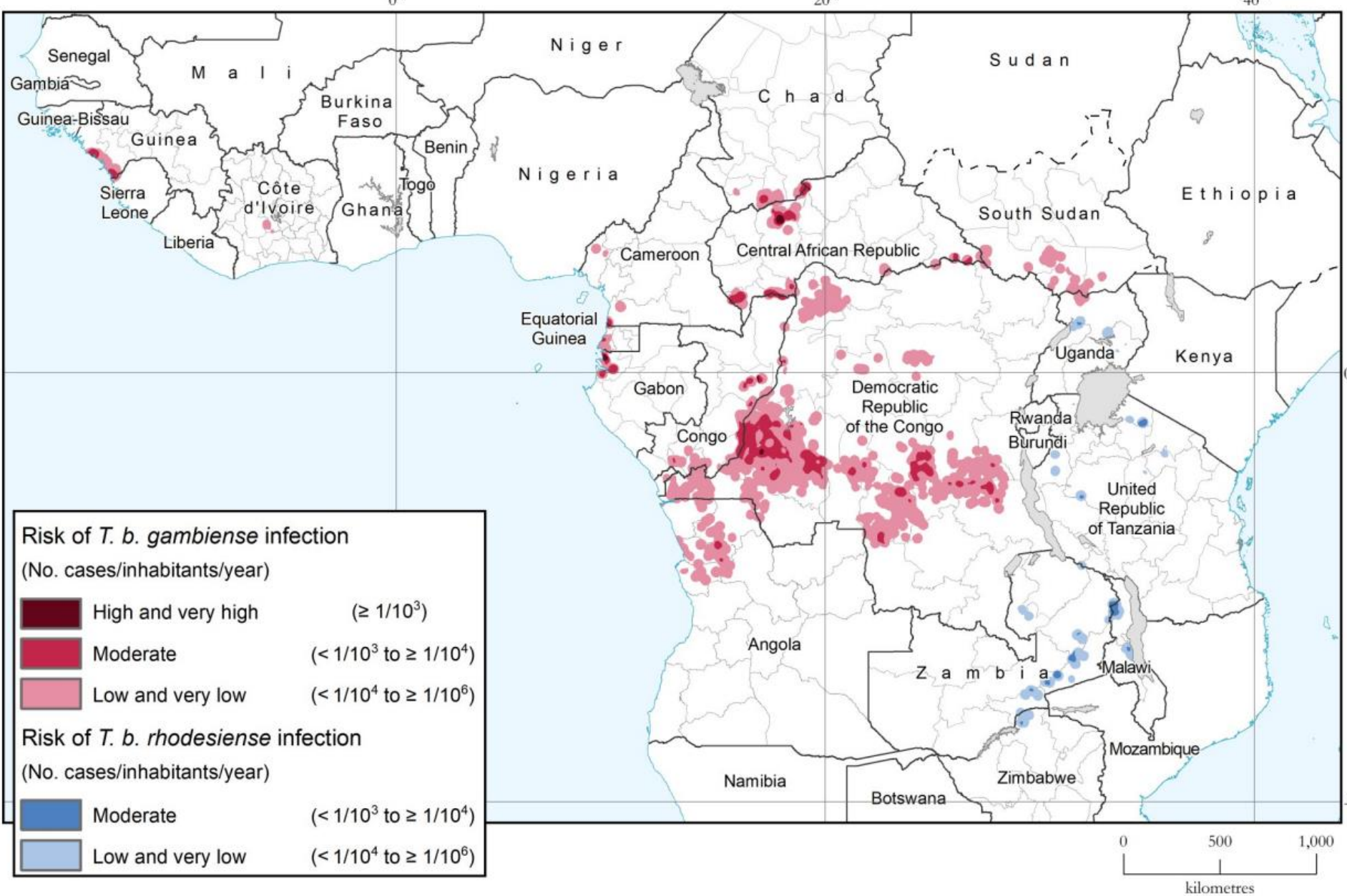


Fig 4. Areas at risk of HAT infection. Period 2016-2020 (Franco et al., 2022)

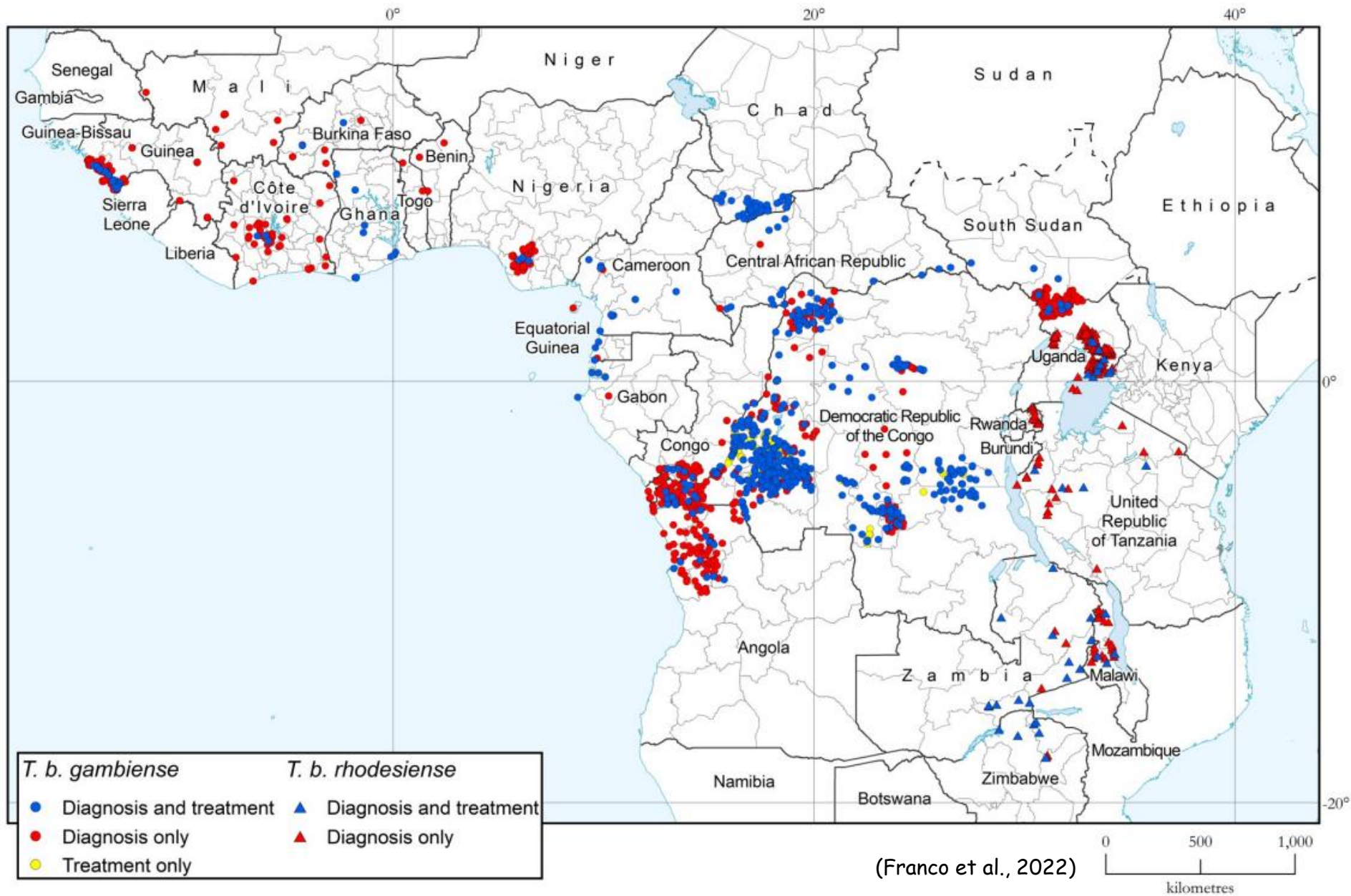


Fig 5. Geographical distribution of fixed health facilities offering diagnosis and treatment of gambiense and rhodesiense HAT. Data were collected by WHO from National Sleeping Sickness Control Programmes in June 2021. The base layers used in this map are the FAO Global Administrative Unit Layers (GAUL), Global Administrative Areas and FAO Inland water bodies in Africa.

T. congolense (genótipos), *T. vivax* e *T. b. brucei*



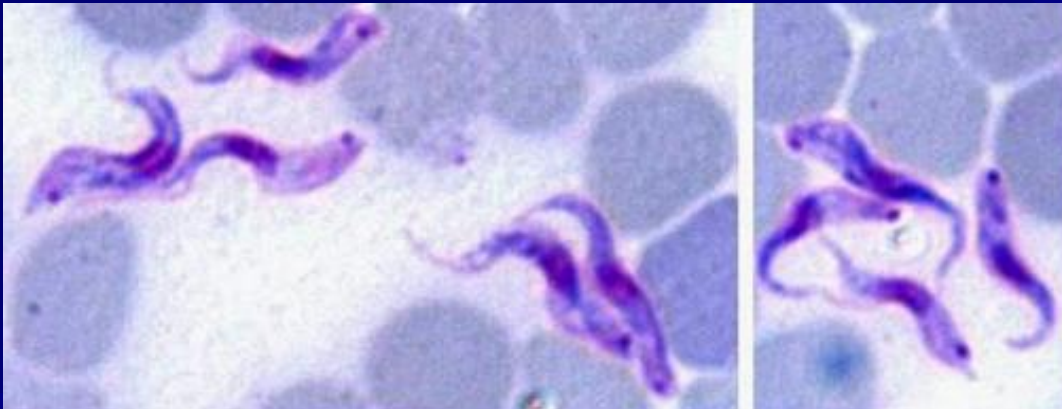
Nagana – tragédia na África



Trypanosoma congolense (genótipos)

Hospedeiros:

animais domésticos (boi, cabra, ovelha, porco, equinos)
ruminantes silvestres – assintomáticos
outros animais silvestres – leões



Mais
patogênico

Exclusivo
sangue

Anemia

Restrito África

Nagana

T. congolense

T. vivax

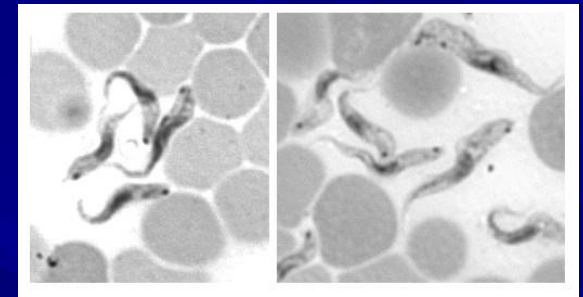
T. b. brucei

Patogênico

Prevalente

Amplamente distribuído

T. congolense



Savannah

Vários ungulados
Carnívoros

Muito patogênico

Forest

Porcos, Cabras
Bois, Cachorros

Pouco patogênico

Kilifi

Bois, Ovelhas
Cabras

Não patogênico

Mammal

Tsetse

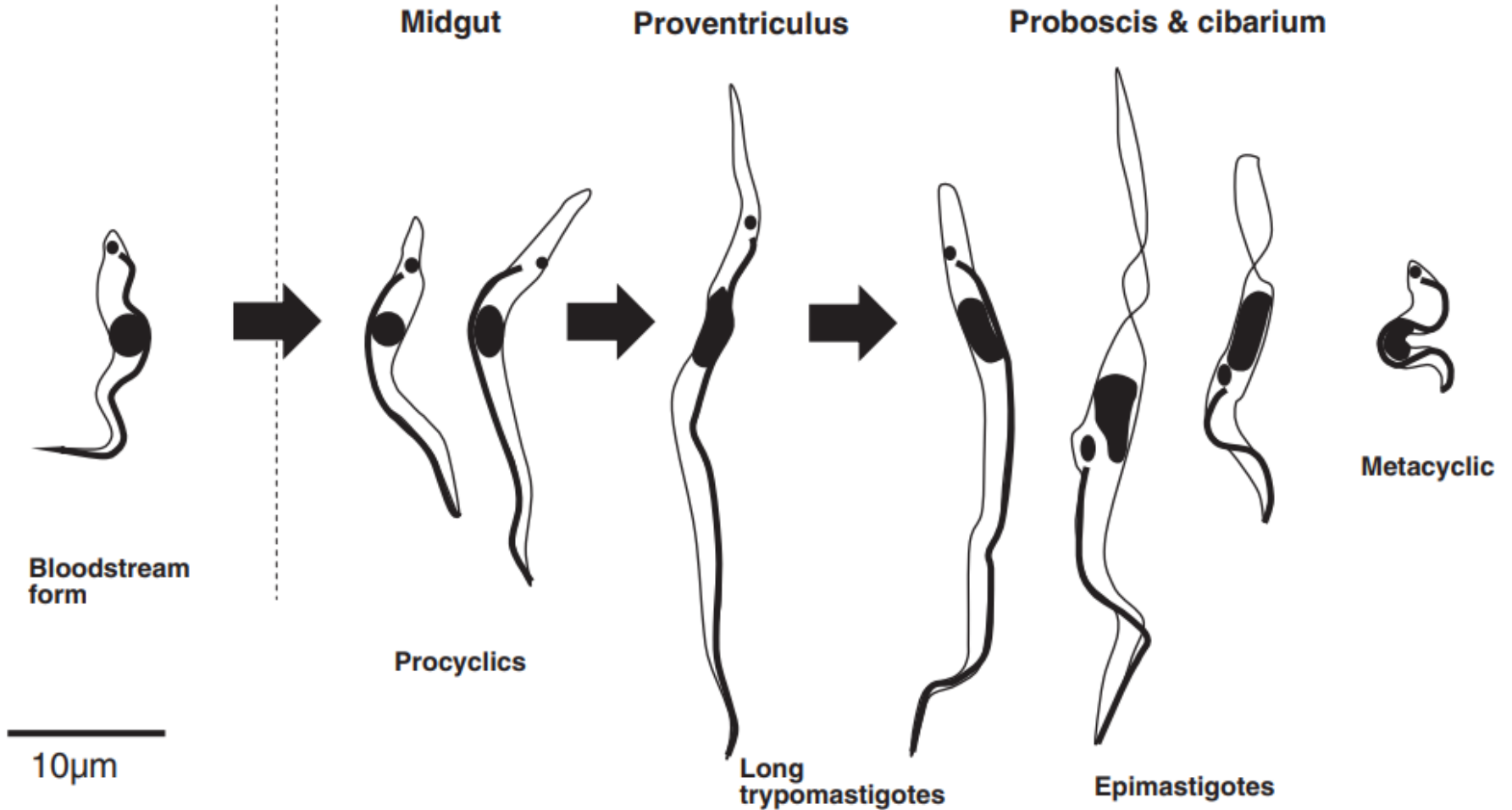
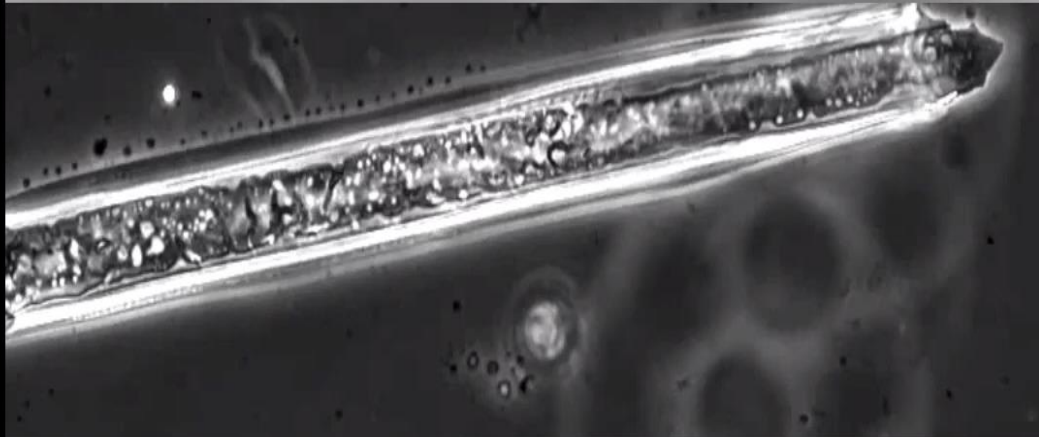


Figure 9 *T. congolense* life cycle stages.

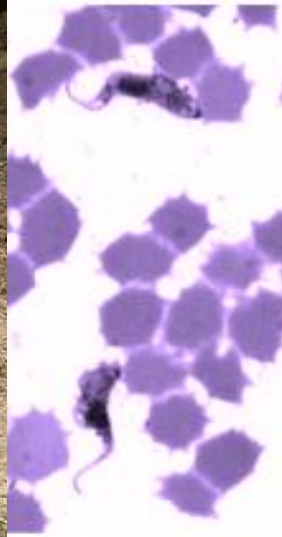
Representative life cycle stages are shown in their respective locations in the mammalian or tsetse hosts. Bloodstream forms taken up by the fly (arrow) differentiate to procyclics in the fly midgut and grow in length. In the proventriculus the procyclics cease division and become uniform in size and shape. These trypomastigotes migrate to the cibarium and proboscis, where they differentiate to epimastigotes; some of these forms have extremely long or truncated posterior ends as shown in these examples. The infective metacyclics are very small and do not divide. The exact sequence of events between proventricular trypomastigotes arriving in the proboscis/cibarium and production of metacyclics is uncertain, and whether there are gradual or abrupt transitions between stages remains to be elucidated.

**Hypopharynx infected with
*Trypanosoma congolense***

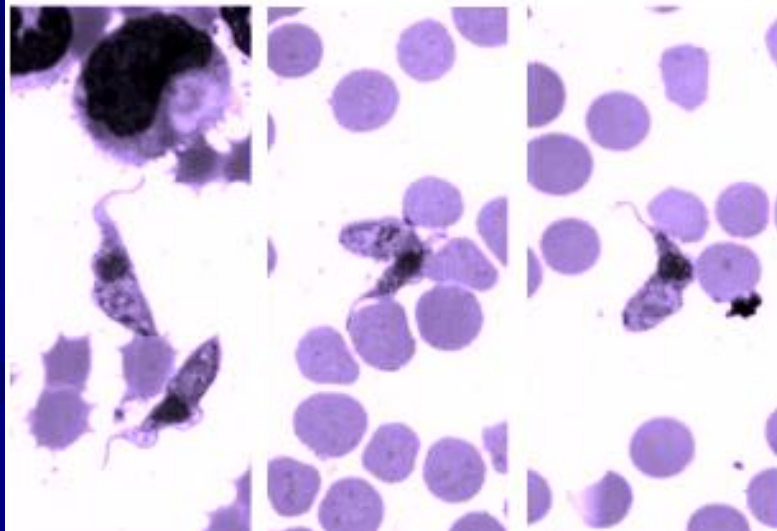


**Microarchitecture of the tsetse fly
proboscis. Wendy Gibson, Lori Peacock,
and Rachel Hutchinson**

Trypanosoma simiae, *T. simiae* Tsavo,
T. godfreyi



Restrito África



reservatório

Diferenças biológicas de tripanossomas que infectam porcos

T. (N.) simiae

T. (N.) godfreyi

T. (N.) congolense

produz doença **aguda e fatal**;

produz infecção **subaguda**;

produz doença **crônica**.

(Janssen & Wijers, 1974; McNamara et al., 1994).

Morfologia indistinguível

T. simiae

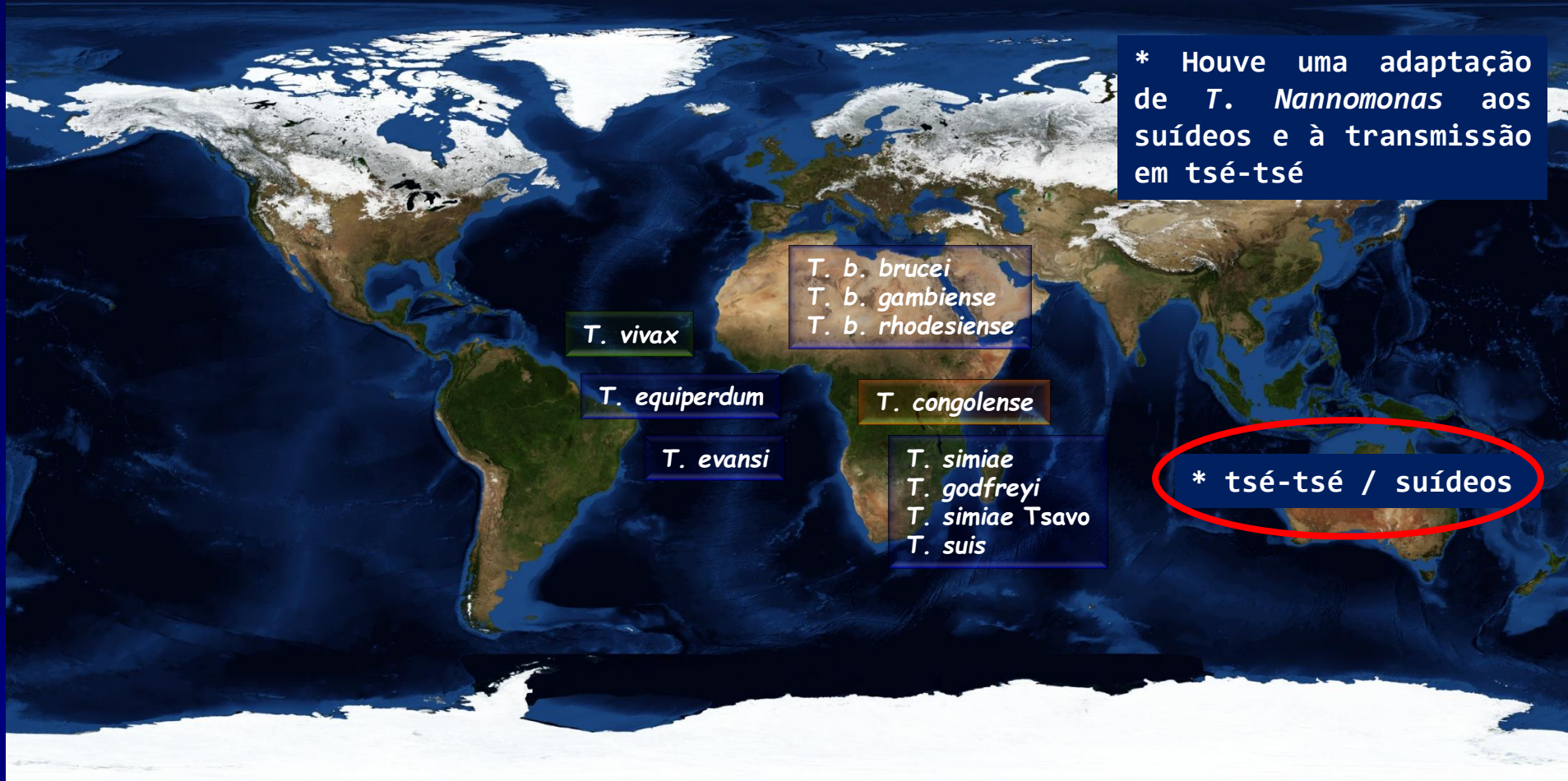


Todos se desenvolvem sequencialmente no intestino médio e probóscide das glossinas

Tripanossomas africanos de suídeos



Facóquero (Warthog)
Moscas tsé-tsé
África



* Houve uma adaptação de *T. Nannomonas* aos suídeos e à transmissão em tsé-tsé

T. vivax

T. equiperdum

T. evansi

T. b. brucei
T. b. gambiense
T. b. rhodesiense

T. congolense

T. simiae
T. godfreyi
T. simiae Tsavo
T. suis

* tsé-tsé / suídeos

Tripanossomas de suídeos



Phacochoerus africanus
Moscas tsé-tsé
África

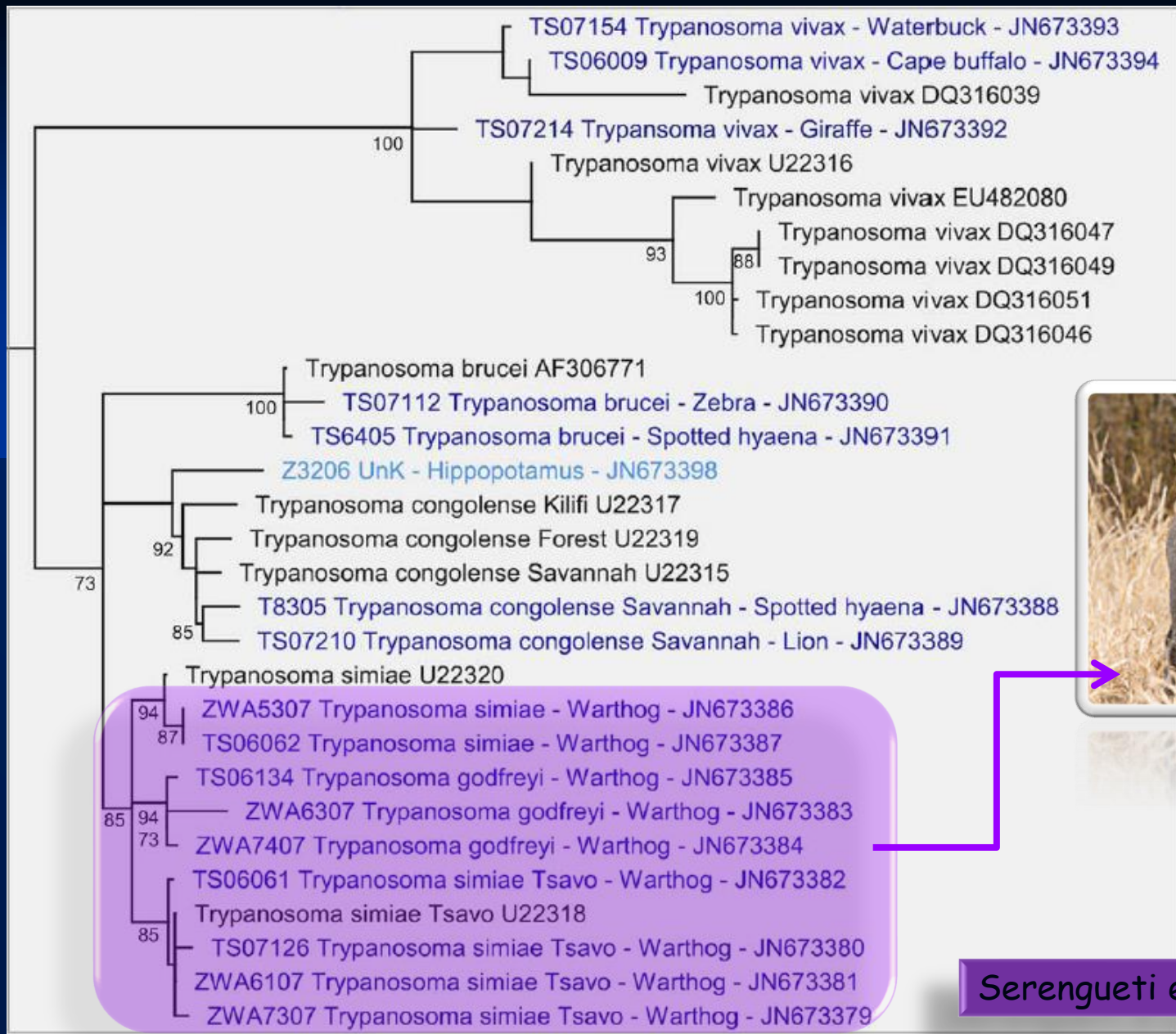
- Muito da história evolutiva dos tripanossomas africanos foi compartilhada com suídeos.
- A fonte alimentar preferencial de glossinas são suídeos. Muitas espécies atuais são específicas de porcos.



Phacochoerus africanus



Ancestrais de suídeos e hipopótamos
(Anthracotheriidae)



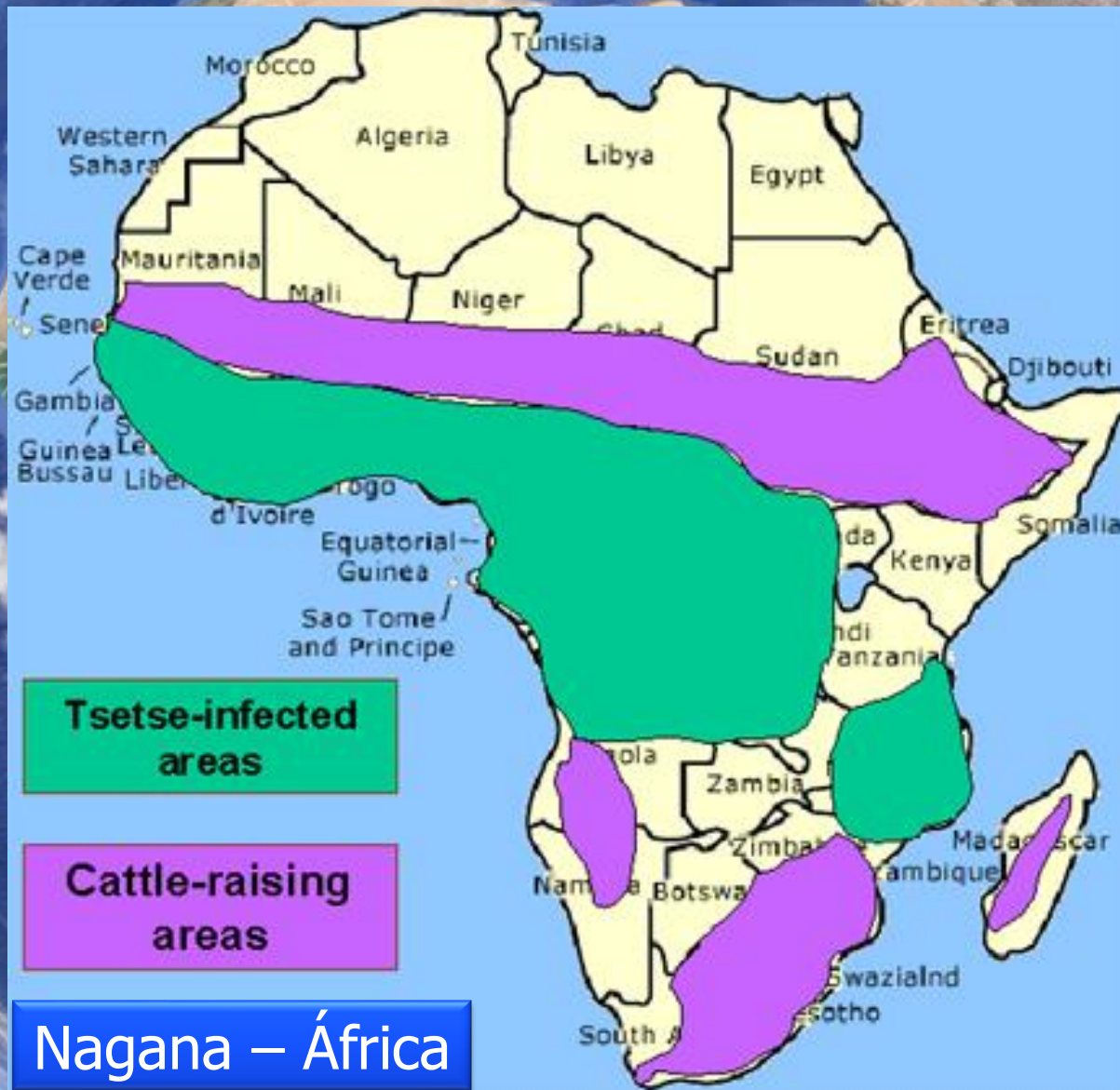
Phacochoerus africanus



Serengueti e Luangwa Valley

0.03

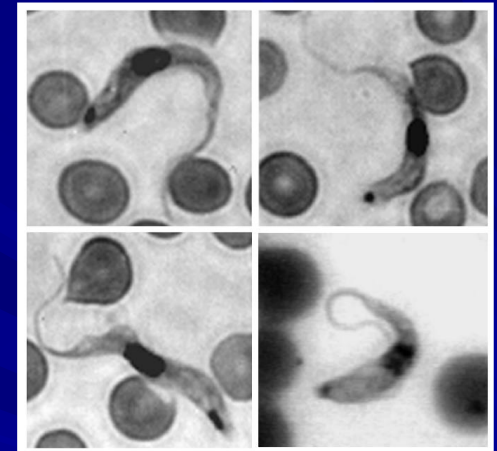
(ITSrDNA - Auty et al., 2012)



Trypanosoma vivax

- **Na África** – bovídeos infectados totalmente assintomáticos - infecções com severa anemia, emagrecimento e morte
- Doença crônica
- Raças tripanotolerantes
- Equinos – mais resistentes
- Reservatórios – ruminantes (búfalos e antílopes)

T. vivax



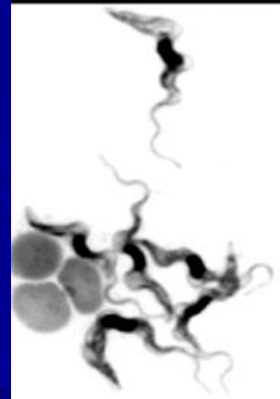
Trypanosoma (Trypanozoon) evansi

(Evans Griffiths 1880)

Maior distribuição geográfica entre os tripanossomas africanos patogênicos: África, Ásia, Oceania, Américas do Sul e Central

- Maior número de hospedeiros

T. evansi



Brasil

- capivaras, quatis, porcos selvagens, morcegos etc.
- bovinos, búfalos - infecções assintomáticas
- doença grave em equinos e cães **X**

Hospedeiros

Enzootia



cotia

A GRANDE FUGA...

TRENDS in Parasitology Vol.17 No.2 February 2001

Trypanosoma vivax – out of Africa

Tudor W. Jones and Alberto M.R. Dávila

Mutation Research, 2015

Kinetoplast adaptations in American strains from *Trypanosoma vivax*

Gonzalo Greif^{a,1}, Matías Rodríguez^{b,1}, Armando Reyna-Bello^{c,d}, Carlos Robello^{a,e},
Fernando Alvarez-Valin^{b,*}



Adaptations of *Trypanosoma brucei* to gradual loss of kinetoplast DNA: *Trypanosoma equiperdum* and *Trypanosoma evansi* are petite mutants of *T. brucei*

De-Hua Lai^{*†}, Hassan Hashimi^{*†}, Zhao-Rong Lun[†], Francisco J. Ayala^{§¶}, and Julius Lukeš^{**†¶}

PNAS, 2008

Opinion Trends in Parasitology, 2010

Trypanosoma brucei: two steps to spread out from Africa

Zhao-Rong Lun^{1,5}, De-Hua Lai^{1,2,5}, Feng-Jun Li³, Julius Lukeš² and Francisco J. Ayala^{1,4}

Cell
PRESS

Research Focus

What happens when *Trypanosoma brucei* leaves Africa


Robert E. Jensen¹, Larry Simpson² and Paul T. Englund³

¹ Department of Cell Biology, Johns Hopkins Medical School, Baltimore, MD 21205, USA

² Department of Microbiology, Immunology and Molecular Genetics, UCLA, Los Angeles, CA 90095, USA

³ Department of Biological Chemistry, Johns Hopkins Medical School, Baltimore, MD 21205, USA

Trends in Parasitology, 2008



Se adaptaram a
transmissão mecânica
fora da África

T. evansi
T. vivax

T. congolense
T. simiae
T. godfreyi
T. brucei



Brasil (endêmica) -
Pantanal

Tripanossomas Africanos nas Américas:

T. vivax e T. evansi

Introduzidos pelos colonizadores

Animais trazidos das colônias africanas

Adaptação à transmissão mecânica



Moscas dos estábulos
Stomoxys sp.



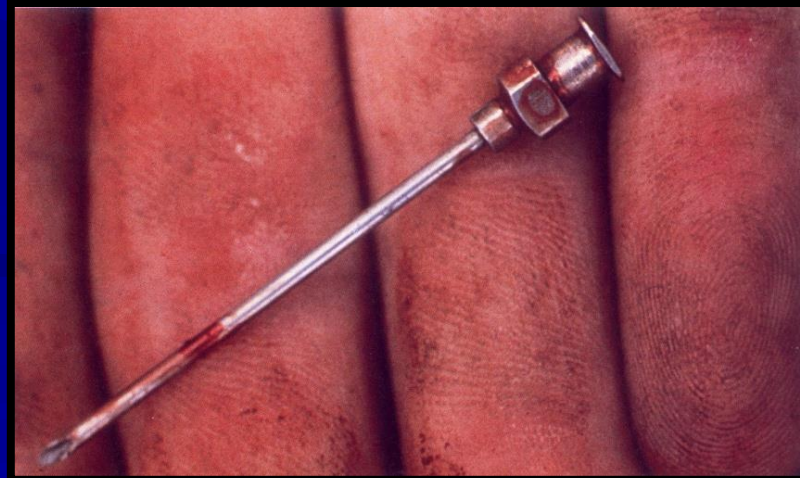
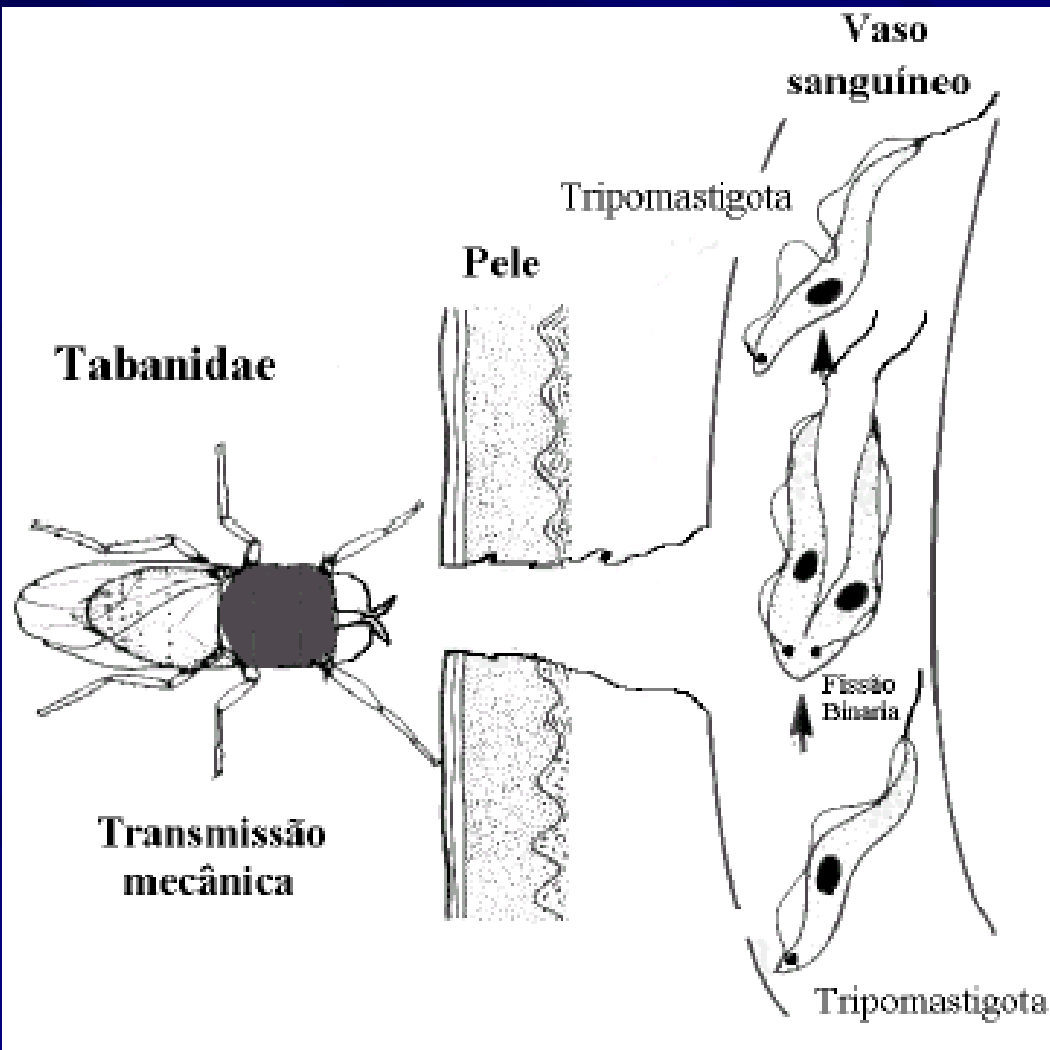
Tabanídeos



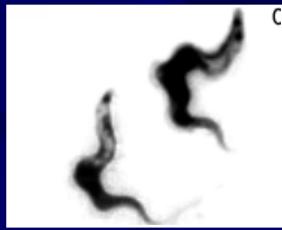
Stomoxys sp. & *Haematobia* sp.
(5–9 & 2.5–4 mm)

T. vivax e *T. evansi*
transmissão mecânica

Só transporta os tripomastigotas sanguícolas na proboscide

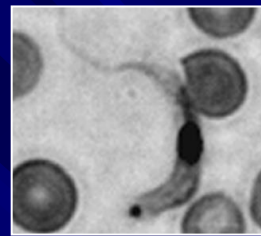


T. evansi



Perdeu capacidade de desenvolver ciclo em mosca tsetse

T. vivax



Se adaptou a transmissão mecânica fora da África

Oeste e Sul da Ásia
Sudeste da Ásia e Oceania
América Central
América do Sul
Iran/Iraque*



Epidemiologia

Trypanosoma vivax

Ziemann 1905
(Camarões)

Tejera, 1920
Shaw e Lainson, 1972

Na América do Sul

- bois e búfalos assintomáticos nas áreas endêmicas
 - equilíbrio enzoótico
 - surtos doença grave – áreas não endêmicas
- reservatórios silvestres ?

Trypanosoma vivax Área endêmica



PANTANAL

(Paiva et al., 2000; Madruga et al., 2006;
Osório et al., 2008; de Mello et al., 2019).

Trypanosoma vivax
Área endêmica



AMAZÔNIA

(Shaw e Lainson, 1972; Lanham et al., 1981;
Madruga et al., 2006; Guedes et al., 2008;
Garcia et al., 2020).

Trypanosoma vivax

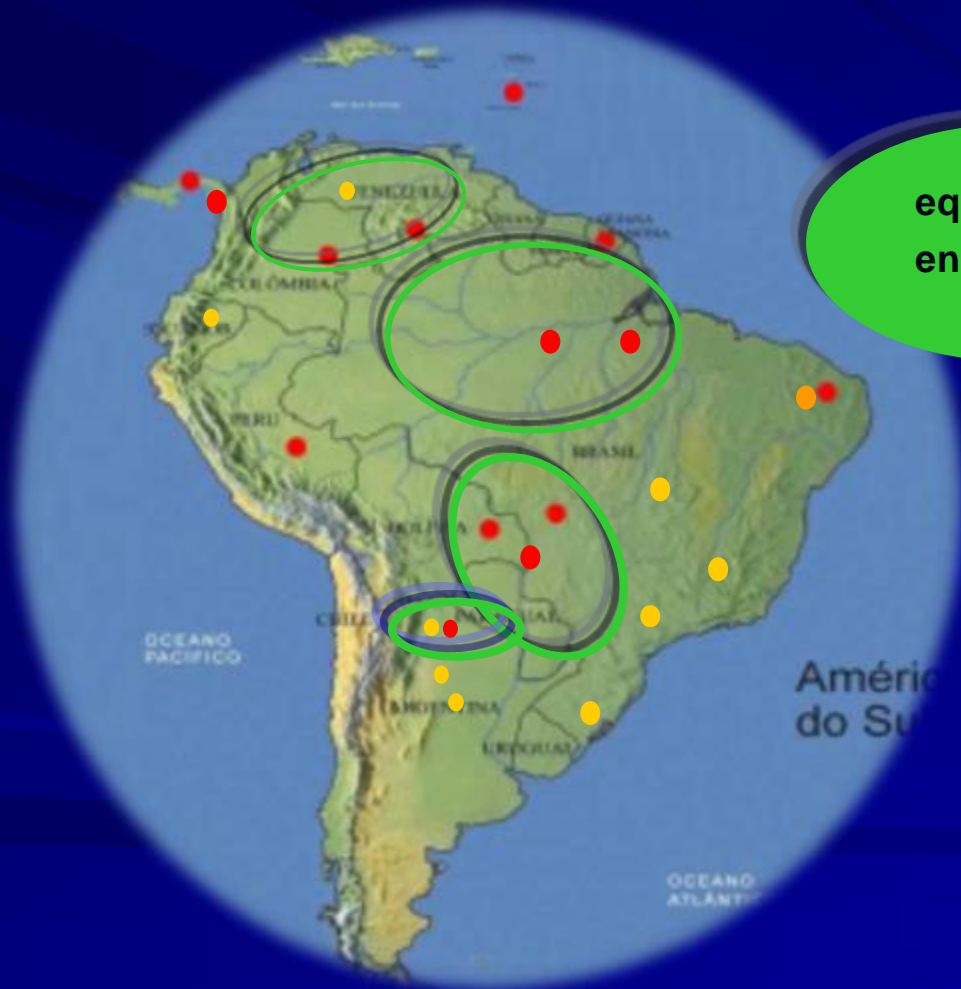
SURTOS

*Animais infectados de
Áreas endêmicas*



Trypanosoma vivax

Área endêmica - área não endêmica



equilíbrio
enzoótico

● SURTOS

- Infecção aguda
- Alta letalidade
- Vacas leiteiras
- Ovelhas
- Cavalos

Trypanosoma vivax surtos - semiárido



Figura 1 - Localização da zona do Semiárido brasileiro.

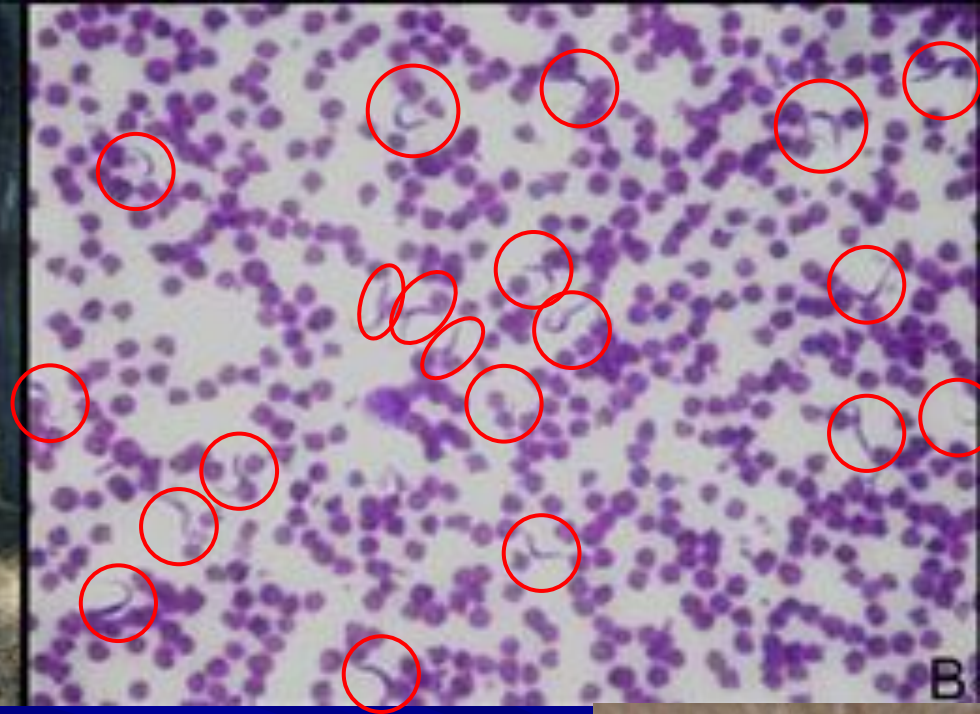


Reservatórios?

África -assintomáticos

Trypanosoma vivax

Sangue – tecidos
SNC



Doença aguda

Anemia
Alterações cardíacas
incoordenação
Meningite e meningoencefalite –
morte
abortos

Doença crônica

Menor produtividade
• Distúrbios reprodutivos
machos e fêmeas
• Abortos
• Redução produção leite

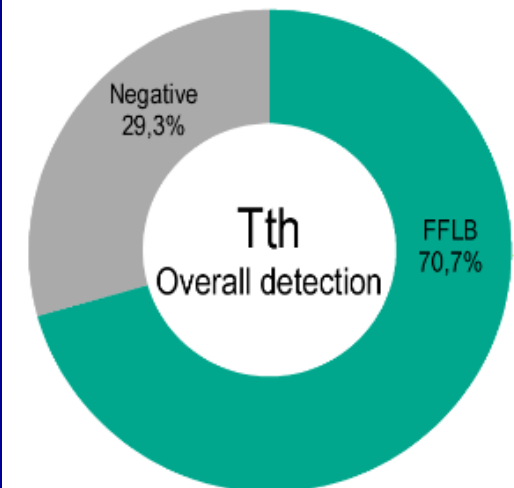
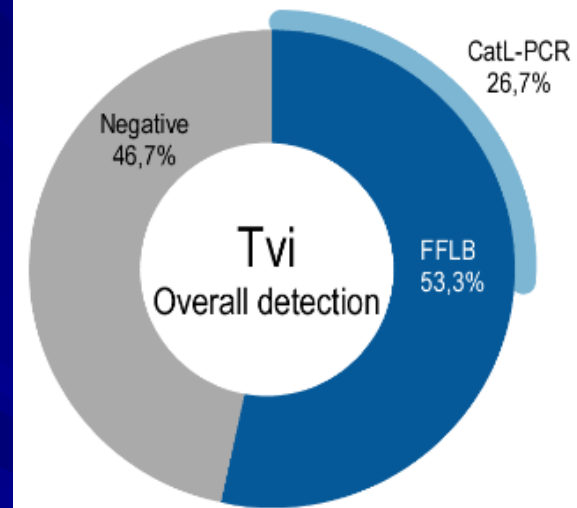


High *Trypanosoma vivax* infection rates in water buffalo and cattle in the Brazilian Lower Amazon



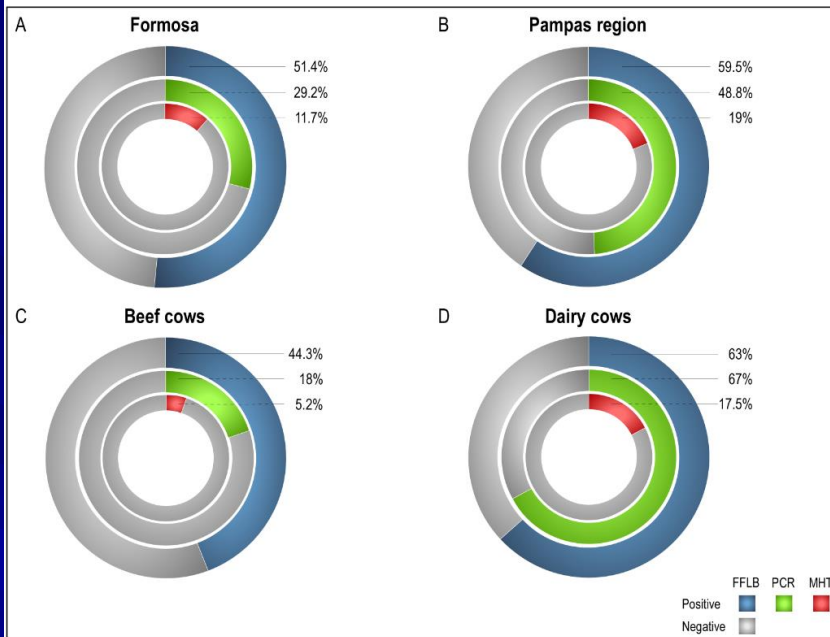
Herakles Antonio Garcia Pérez^{a,*}, Carla Monadeli Filgueira Rodrigues^{a,b,1}, Isis Helga Vivas Pivat^c, Adriana Carlos Rodrigues Fuzato^a, Erney P. Camargo^{a,b}, Antonio Humberto Hamad Minervino^d, Marta Maria Gerales Teixeira^{a,b}

Parasitology International 79 (2020) 102162



Molecular epidemiological insights into *Trypanosoma vivax* in Argentina: From the endemic Gran Chaco to outbreaks in the Pampas

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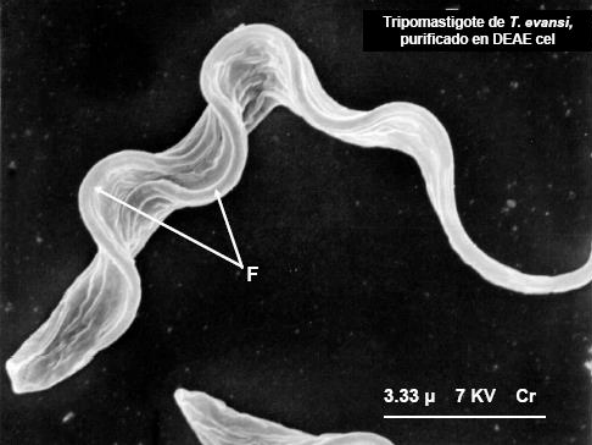
Trypanosoma evansi - área endêmica



PANTANAL

(Nunes e Oshiro 1990; Franke et al. 1994; Silva et al. 1995; Dávila et al., 2003; Herrera et al., 2004)





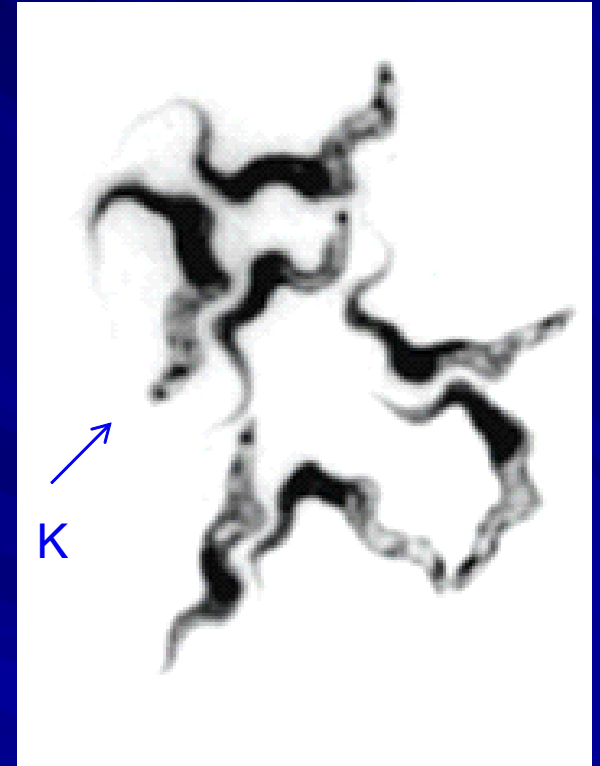
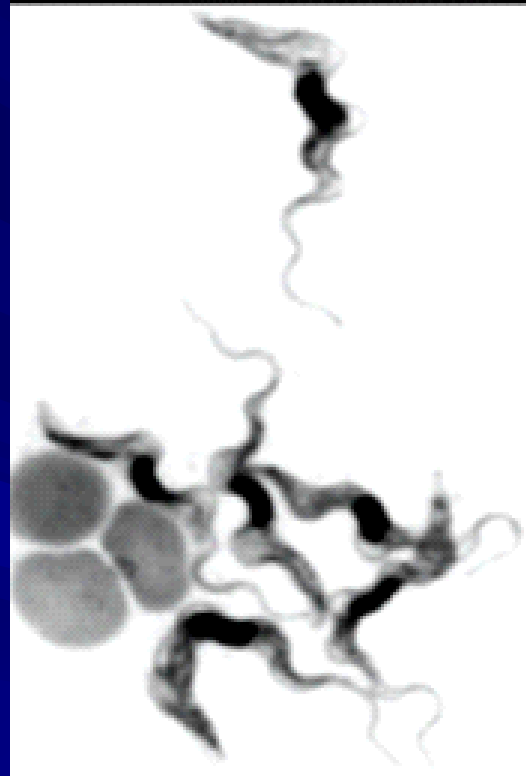
T. evansi

T. brucei

**Ausência
DNA
Mitocondrial**



**Impede
Desenvolvimento
Insetos**



Sangue - LCR - cérebro

Infecção *T. evansi*- Sinais clínicos

- anemia;
- emagrecimento progressivo;
- incoordenação e atrofia dos membros pélvicos;
- dificuldade para levantar, fraqueza muscular;



Infecção *T. evansi*

Sinais clínicos



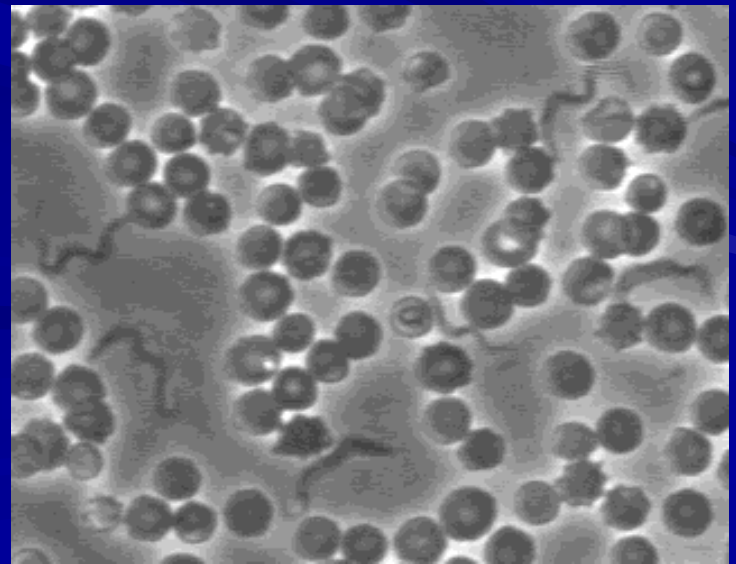
- edema subcutâneo da região posterior e das patas;
 - rebaixamento da região traseira (mal de cadeiras);
 - manifestações no sistema nervoso central
- doença SNC - sem recuperação**



Mal de cadeiras



Síndrome Neuromotor



“Mal de Cadeiras”



Fatal para cães se não tratada rapidamente

T. evansi: zoonose emergente? = aHT

2004 - Índia (Maharashtra)*

(Joshi et al., 2005; Powar et al., 2006; Joshi et al., 2006)

N. ENGL J MED - Demonstrou mutação no gene APOL1
(Vanhollebeke et al., 2006)

2006 - Índia (divisa com Bangladesh) Óbito do paciente

(Touratier and Das, 2006)

2006 - Índia (Maharashtra). Screening serológico ~2000
(CATT / *T. evansi*) = 4.5% prevalência. Não parasitemia
por microscopia. Exposição frequente aos parasitas

(Shegokar et al., 2006)

- 2010 - Egito - Fazendeiro positivo por microscopia. Não houve pesquisa clínica nem diagnóstico adequado

(Haridy et al., 2011)

- 2016 - Vietnam. Infecção de paciente sem mutações nos genes da APOL1. Pós-parto inicial - Altíssima parasitemia.

(Van Vinh Chau et al., 2016)

- 2022 - Índia (divisa com Bangladesh). Screening CATT / *T. evansi* (5%) - Microscopia (-) e PCR (VSG-gene) (3%). Exposição frequente aos parasitas e risco de infecção.

(Sengupta et al. 2022)

Diagnóstico da tripanossomíase

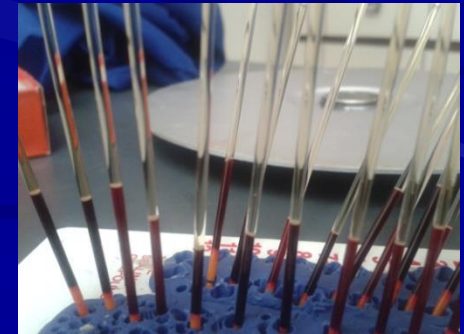
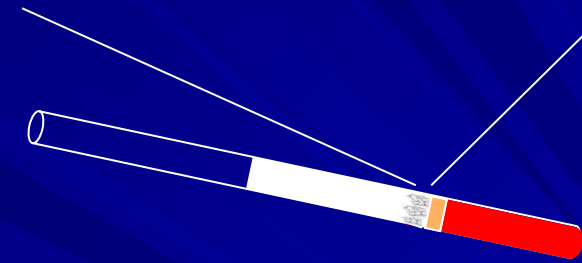
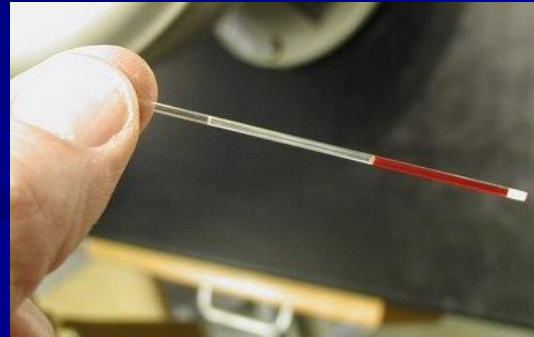
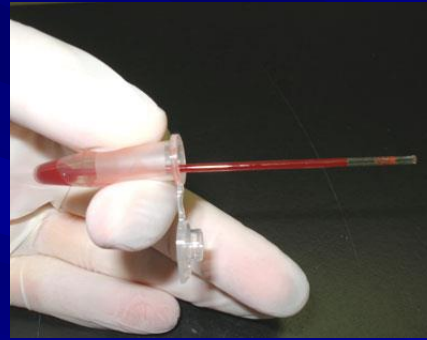


Tripanossomas africanos

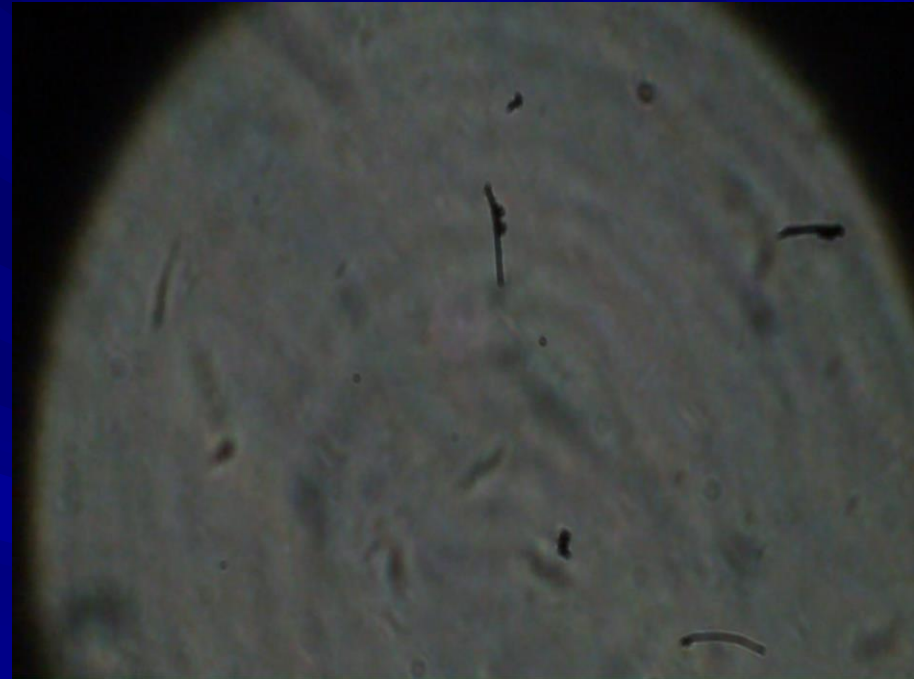
Diagnóstico

- **Microhematócrito**
- **Esfregaço sanguíneo: morfologia**
 - **Sorologia: inespecificidade**
 - **PCR: sensível e específico**

Microhematócrito



Diagnóstico da tripanossomíase



- Avaliação do Microhematócrito

Tratamento da tripanossomíase

Bovinos, pequenos ruminantes, equídeos, cães

Tratamento pode ser curativo ou preventivo

Aceturato de Dimenazene - cura
Beronal, Veribem, Ganaseg, Ganatet

Cloreto de Isometamidium- prevenção
Samorim, Trypamidium, Vivedium

*SNC - Não são eficientes
recidivas (parasitas SNC e olhos)*

Resistência a drogas - África



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Obrigado

