Leiden University
Medical Center

Werkgroep klinische parasitologie
"Malaria - Why would you still do microscopy?"

Based on a previously presented case

Lisette van Lieshout

Parasitology

LEIDEN UNIVERSITY MEDICAL CENTER

Met dank aan Carolien Wijsman, Jaap Hanssen,
Henk Scheper en Leo Visser (INZI LUMC/Alrijne)
ITM - Antwerp
en alle laboratoriumedewerkers van het KML

Case – October 2016

Alrijne ZKH:

- Pt vd S, 54 years (F)
- Visit: (Sunday Oct 2nd) fever, headache since 5 days; following a holiday visit to the tropics
- Clinical history: migraine, spinal disk herniation, microscopic haematuria eci

- Amnestic:
  - 7-16 Sept. Masai Mara (Kenia), safari
  - 16-21 Sept Serengeti en Ngorongoro (Tanzania), safari
  - 21 -24 Sept Kenia & return to NL
  - During travel: mild diarrhoea. No reported insect bites.
  - Used malaria prophylaxis.

Case – October 2016

- First symptoms: started Sept 29th , 5-6 days after return: nausea, vomiting, diarrhoea, headache and a fever.
- Monday October 3rd *(Leids ontzet)*: visit ED because of headache & fever.

- Physical examination: moderately ill - without fever.
- Malaria RDT: negative.
- Send home: gastroenteritis.

- Microscopy slides & EDTA arrived late afternoon October 4th at LUMC, only for confirmation (Q: malaria? no patient info)

- October 5th at 14:00 the LUMC reported: microscopy slides & ICT& QBC negative (PCR not included)

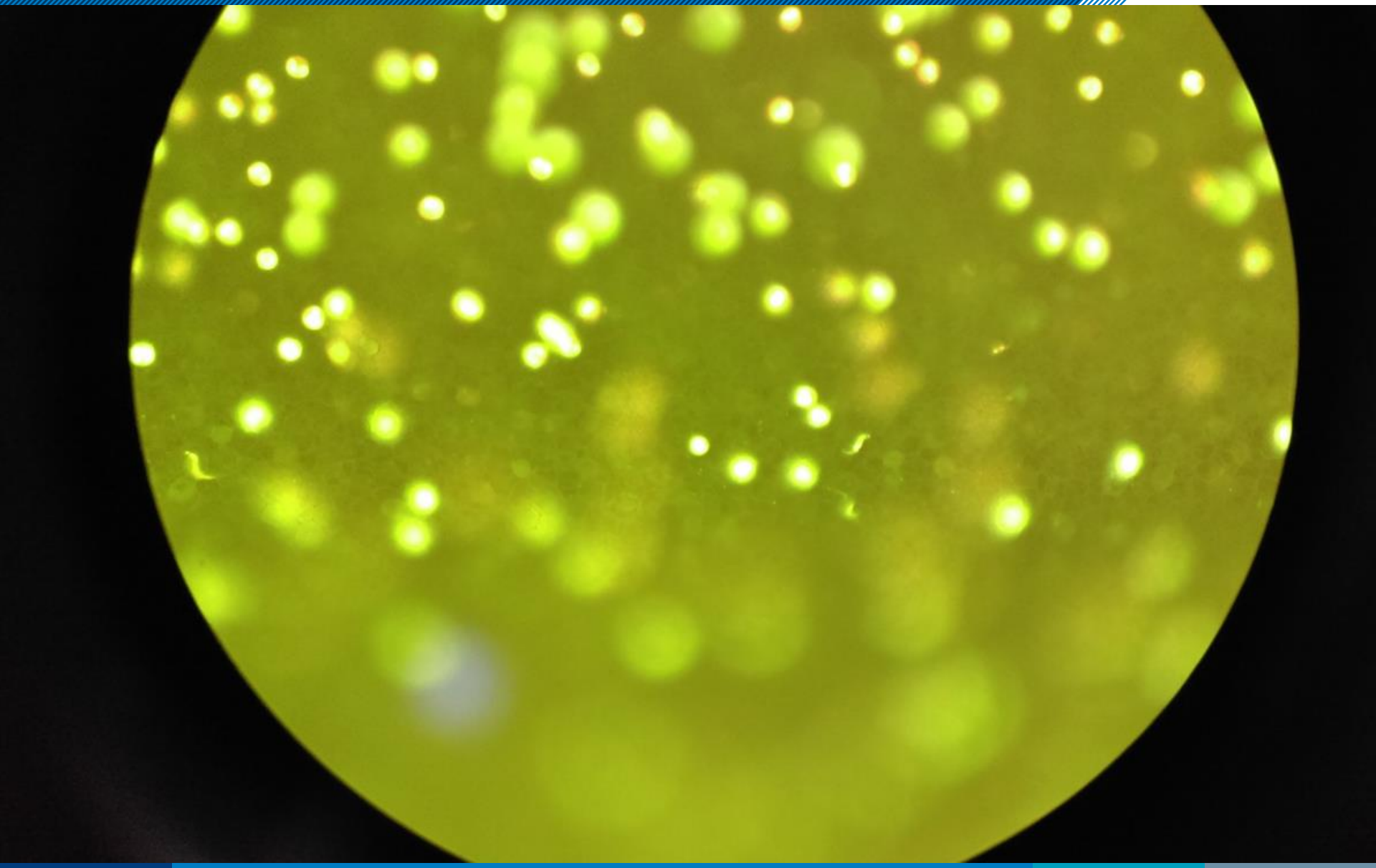
Case – October 2016

- Second visit October 5th: admission because of fever, persistent nausea, headache and malaise.

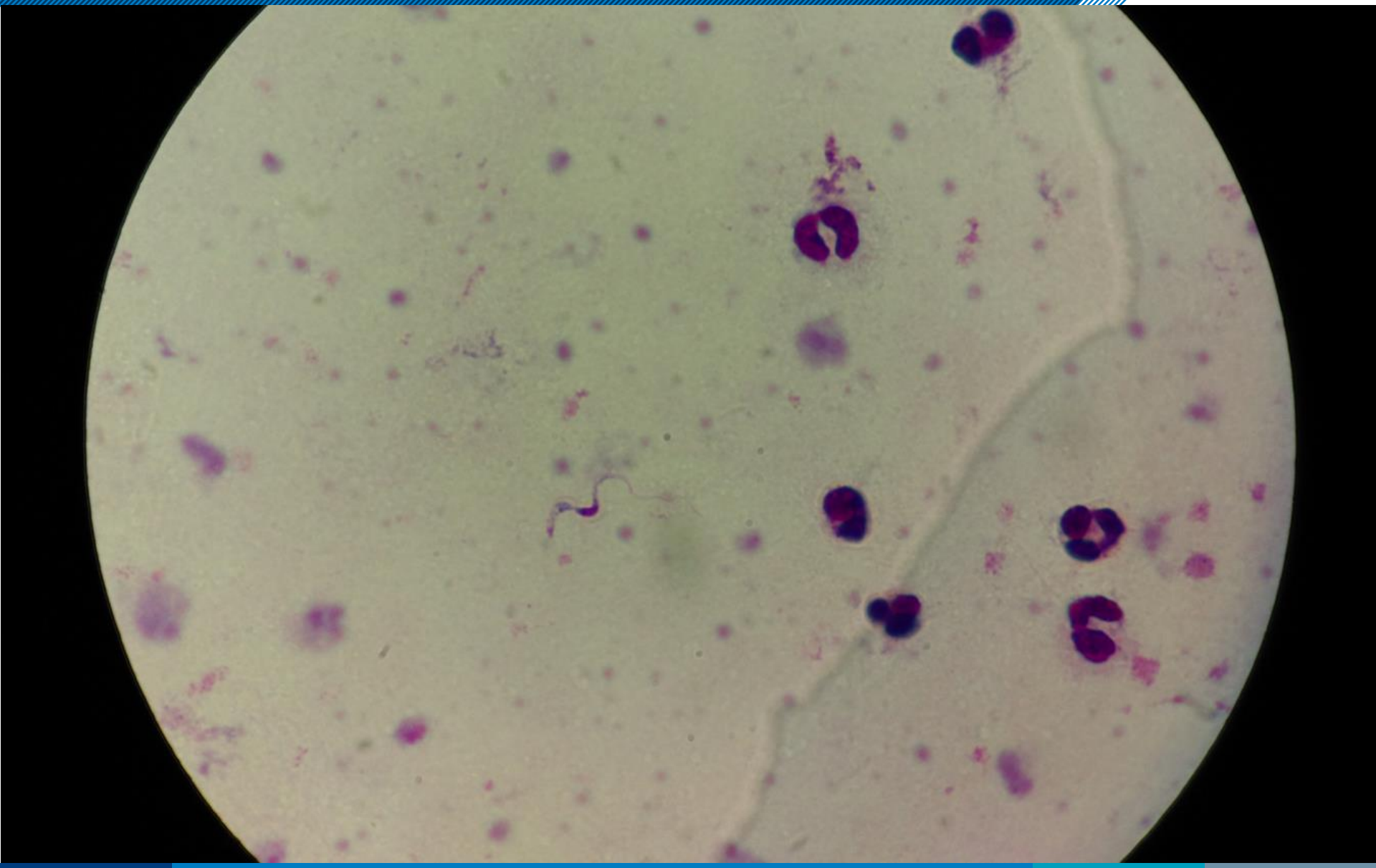
- No lymphadenopathy.
- Low Hb (5.7) and haematocryte (0.270)
- Low leukocytes count (1.46 x 10^9/L), low thrombocyte count (48 x 10^9/L)
- Mild hepatitis: ↑liver enzymes, high bilirubin (51 µmol/L) of which 33 µmol/L conjugated
- Mild haematuria
- Ultrasound abdomen: normal
- Malaria RDT: negative

- Microscopy slides +EDTA (taken at 16:40) arrived at October 6th at LUMC (10:20) only for confirmation (Q: malaria? no patient info)

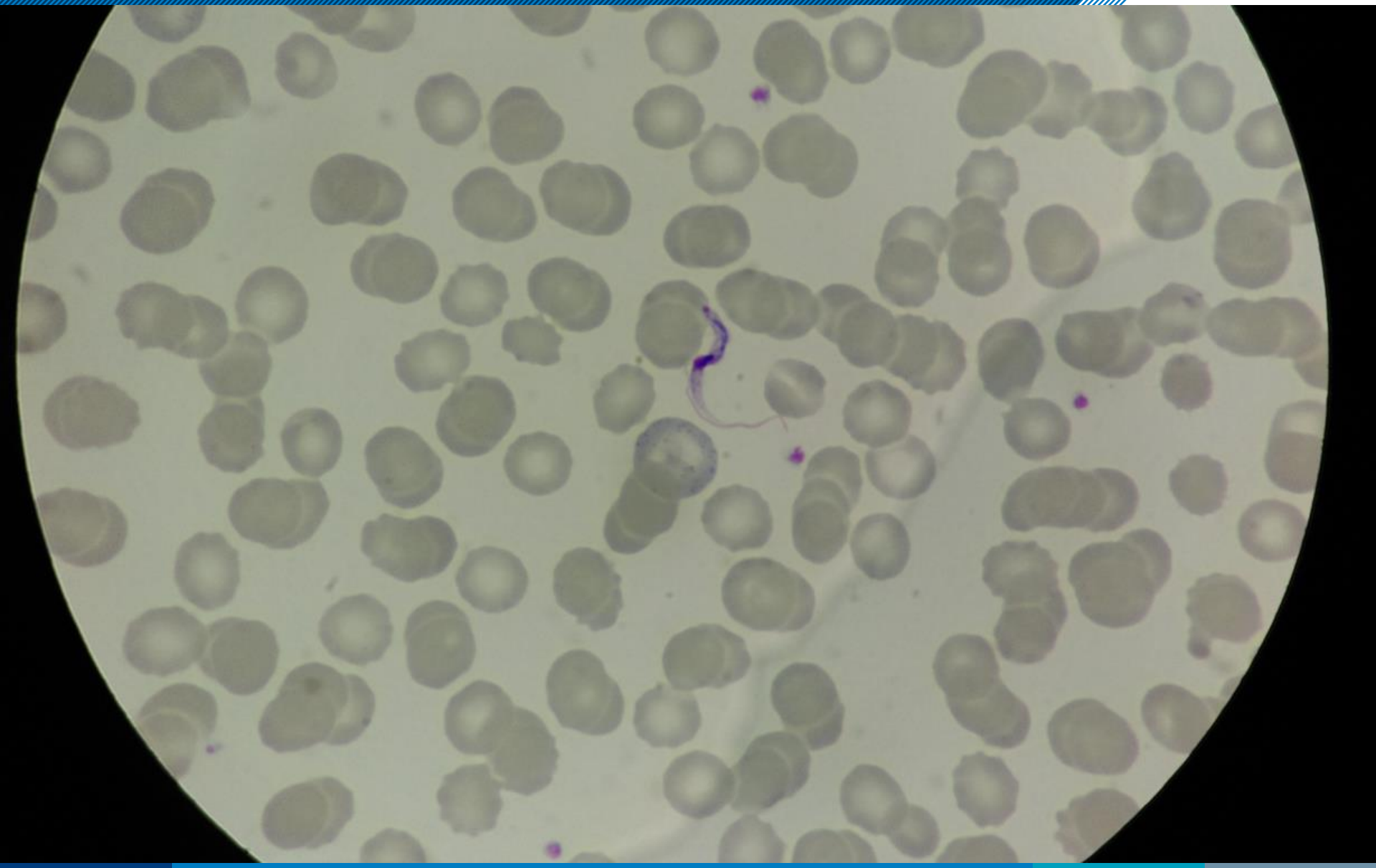
Microscopy LUMC - QBC



Microscopy LUMC – Thick smear

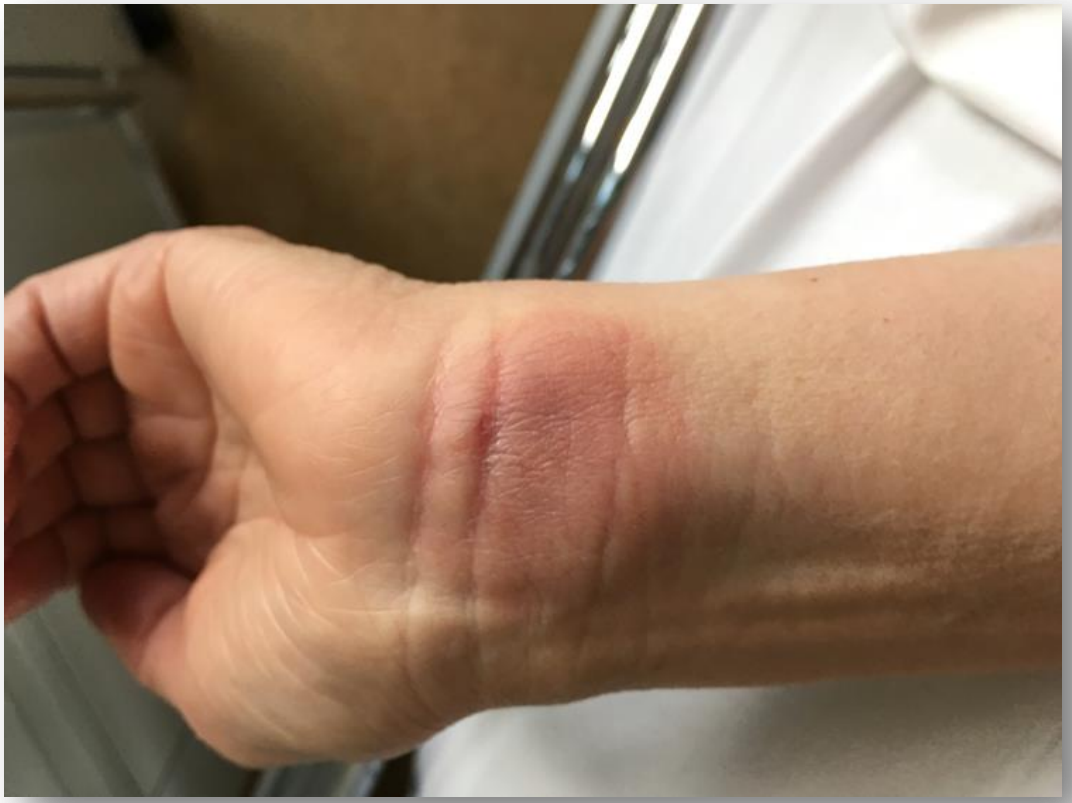


Microscopy LUMC – Thin smear



Transfer to LUMC – October 6th

- Lab: 1-10 trypomastigotes per field in thin smear
- At LUMC: left wrist: painless erythematous plaque, softened centre without central necrosis and a diameter of approximately four cm.
- Lumbar puncture:
  - one leukocyte
  - normal protein
  - absence trypanosomes



First stage East-African trypanosomiasis

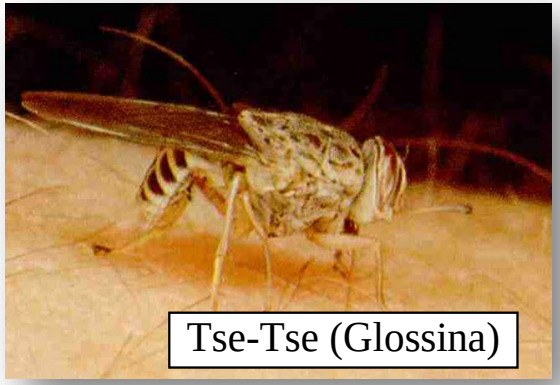
Human African Trypanosomiasis (HAT) Protozoa

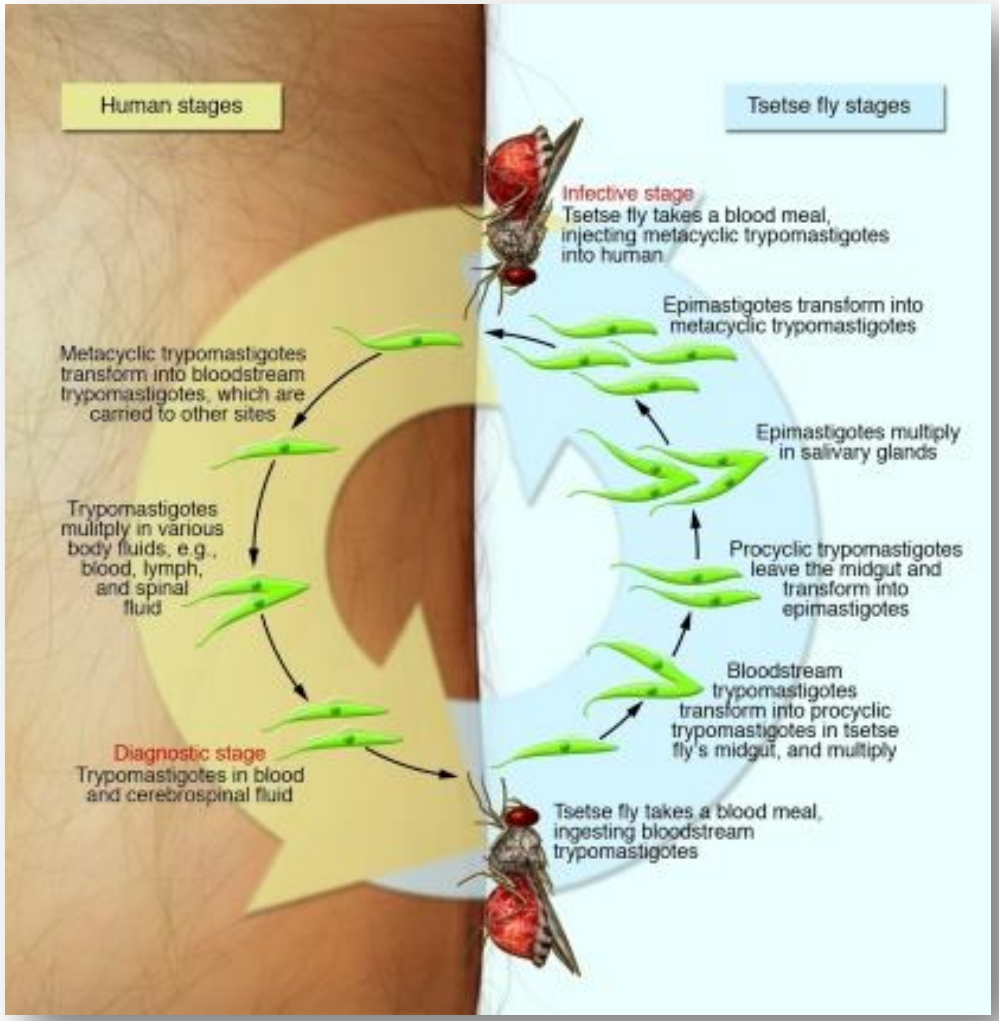
Trypanosoma brucei rhodiense

- East Africa (zoonotic)
- Acute presentation
- Fatal <6 months

Trypanosoma brucei gambiense

- West and Central Africa (98%)
- Chronic presentation


Tse-Tse (Glossina)



Kennedy *et al.,* (2013) Lancet Neurol 12: 186-94

Geographical distribution HAT
Human African Trypanosomiasis

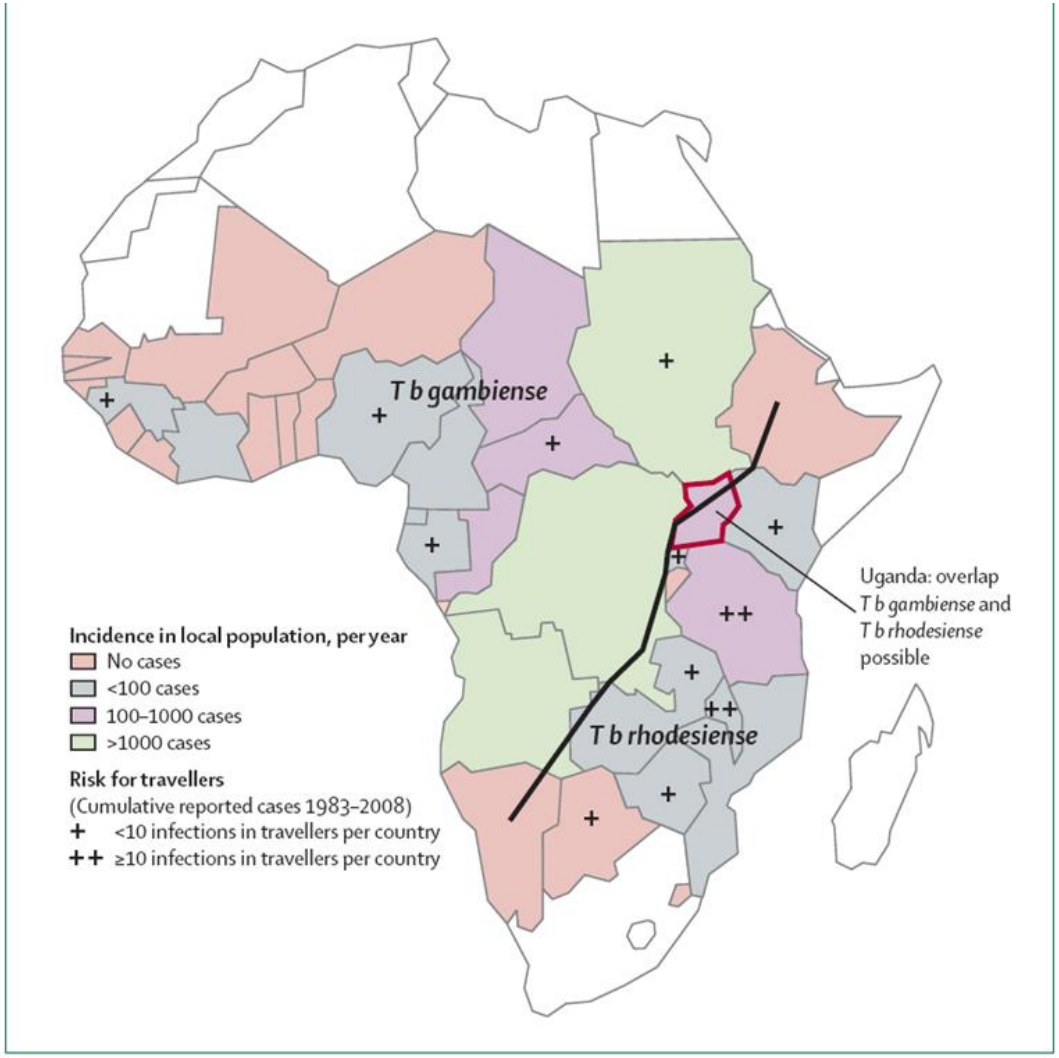


Figure 1: **Distribution of human African trypanosomiasis with incidences and risk for travellers**
The black line divides the areas in which *Trypanosoma brucei gambiense* prevails and those in which *Trypanosoma brucei rhodesiense* predominates (J Blum, Swiss Tropical Institute).

Brun *et al.,* (2010) Lancet 375: 148-59

History of WHO reported cases
Human African Trypanosomiasis

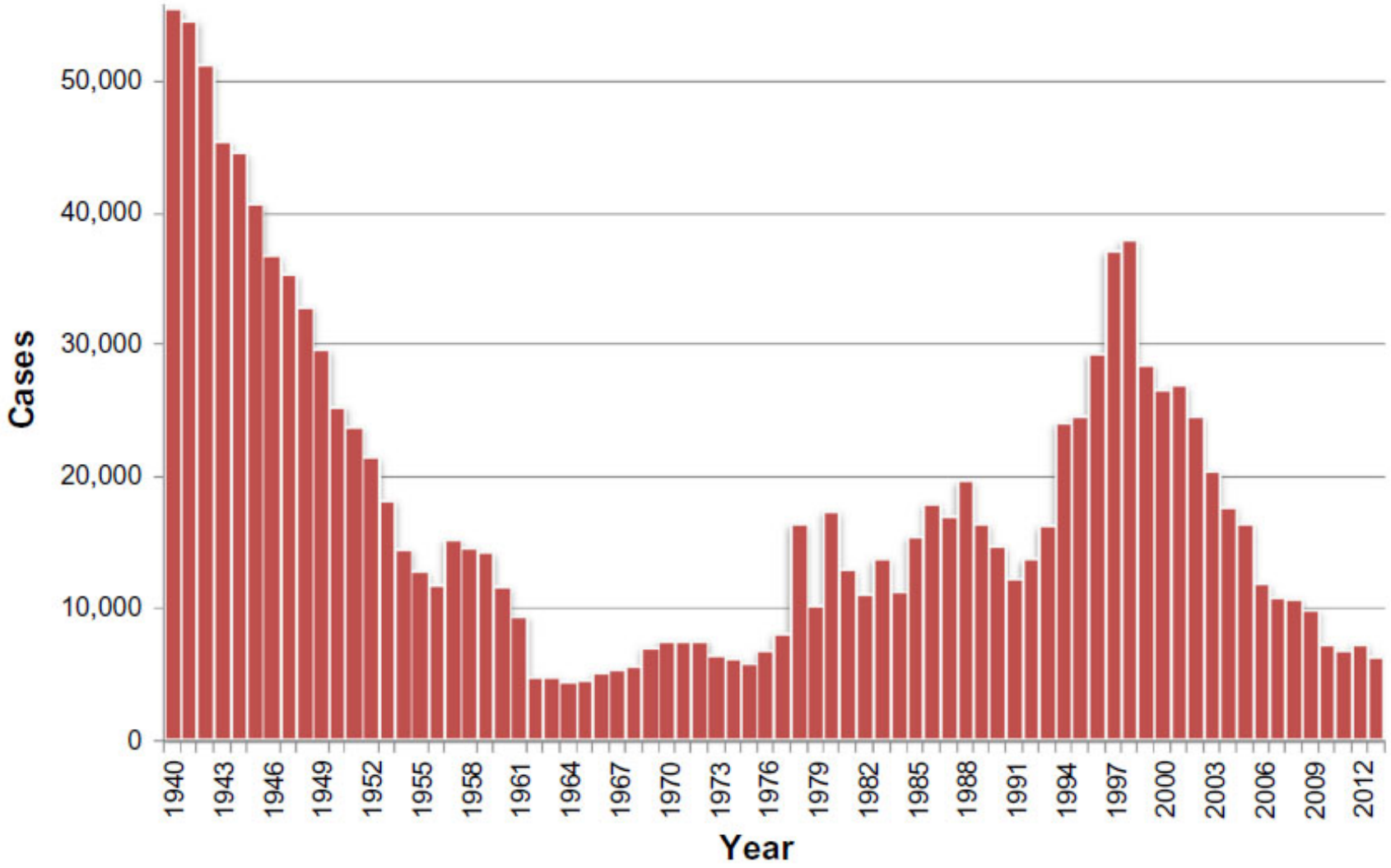


Figure 1 Total number of new cases of human African trypanosomiasis reported to the World Health Organization, 1940–2013.

Franco *et al.,* (2014) Clinical Epidemiology 6:257-75

Imported cases – in non-endemic regions
Human African Trypanosomiasis

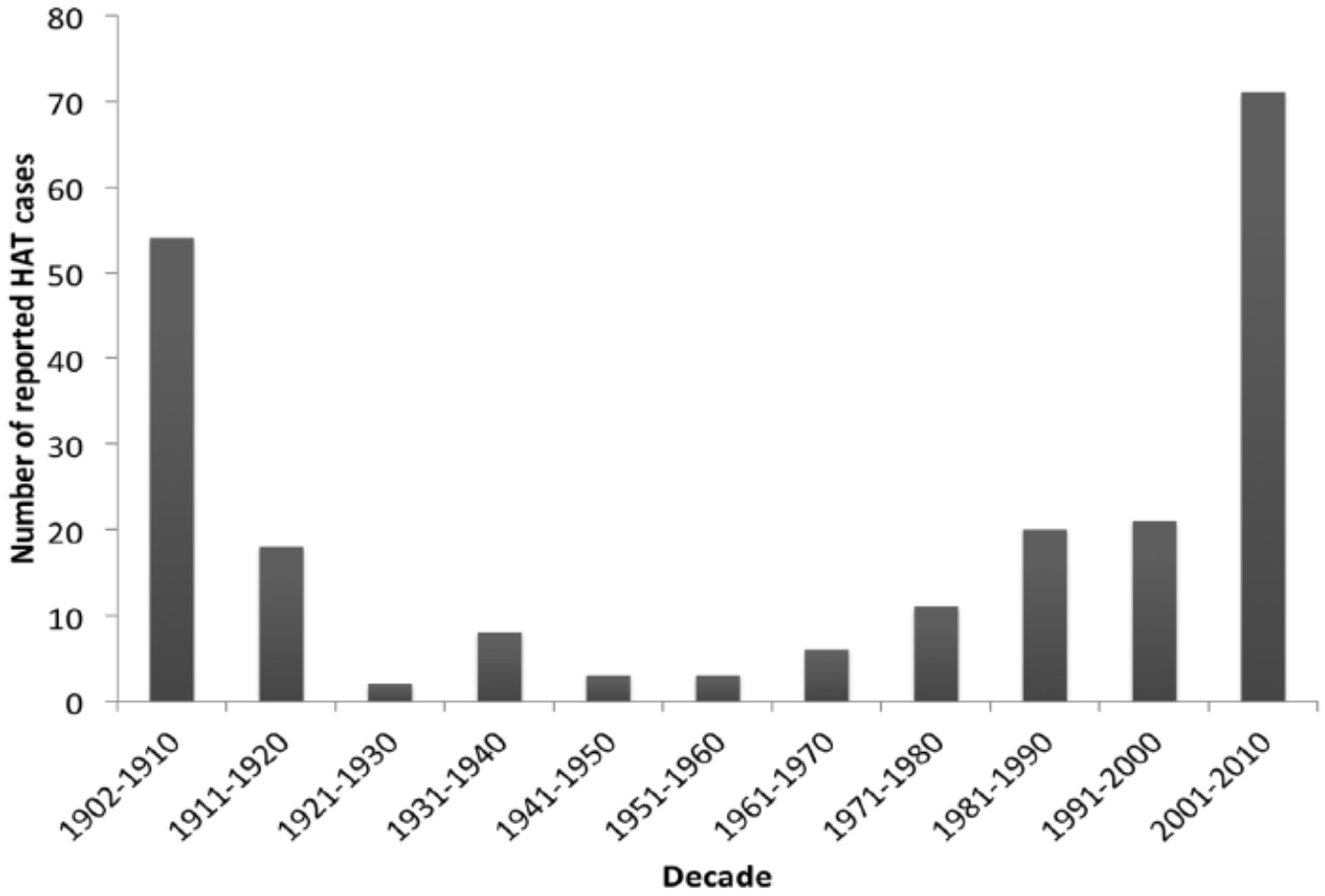


Figure 1. Number of reported HAT cases among patients from non-endemic countries per decade.

Neuberger *et al.*, (2014) PLosOne e88647

Imported cases – in non-endemic regions
Human African Trypanosomiasis

Table 1. Epidemiologic data and mortality rates of patients from non-endemic countries who acquired Human African Trypanosomiasis during the colonial period (1902–1966) and during the post-colonial period (1967–2012).

	Colonial period	Post-colonial period	P-value
Age, years (average±SD)	32.5±7.8	43.0±16.1	p<0.001
Gender, females/all patients (% female)	11/110 (10%)	32/134 (23.9%)	p<0.001
Occupation/purpose of visit:			p<0.001
• Tourist	0/86 (0%)	91/125(72.8%)	
• Expatriate	34/86 (39.5)%	14/125 (11.2%)	
• Missionary	15/86 (17.4%)	3/125 (2.4%)	
• Military	15/86 (17.4%)	4/125 (3.2%)	
• Others*	22/86 (25.6%)	13/125 (10.4%)	
T. brucei subspecies**:			p<0.001
• T. b. rhodesiense (%)	24/110 (21.8%)	98/128 (76.6%)	
• T.b. gambiense (%)	86/110 (76.2%)	30/128 (23.6%)	
Mortality (%)	6/43(14%)[Ŧ]	4/98(4.1%) E HAT 1/30 (3.3%) W HAT	N/A

SD, standard deviation; E HAT, East African Trypanosomiasis; W HAT, Western African Trypanosomiasis;
*Others : Medical personnel, teachers, sailors, scientists;
**Subspecies according to microbiologic diagnosis or likely place of infection;
Ŧmostly West African Trypanosomiasis.

Neuberger *et al.*, (2014) PLosOne e88647

Reporting period 2010 - 2014 HAT
Historically low numbers

89-90% reduction since 1999

2015 WHO:

2733 *T.b. gambiense*

71 *T.b. rhodesiense*

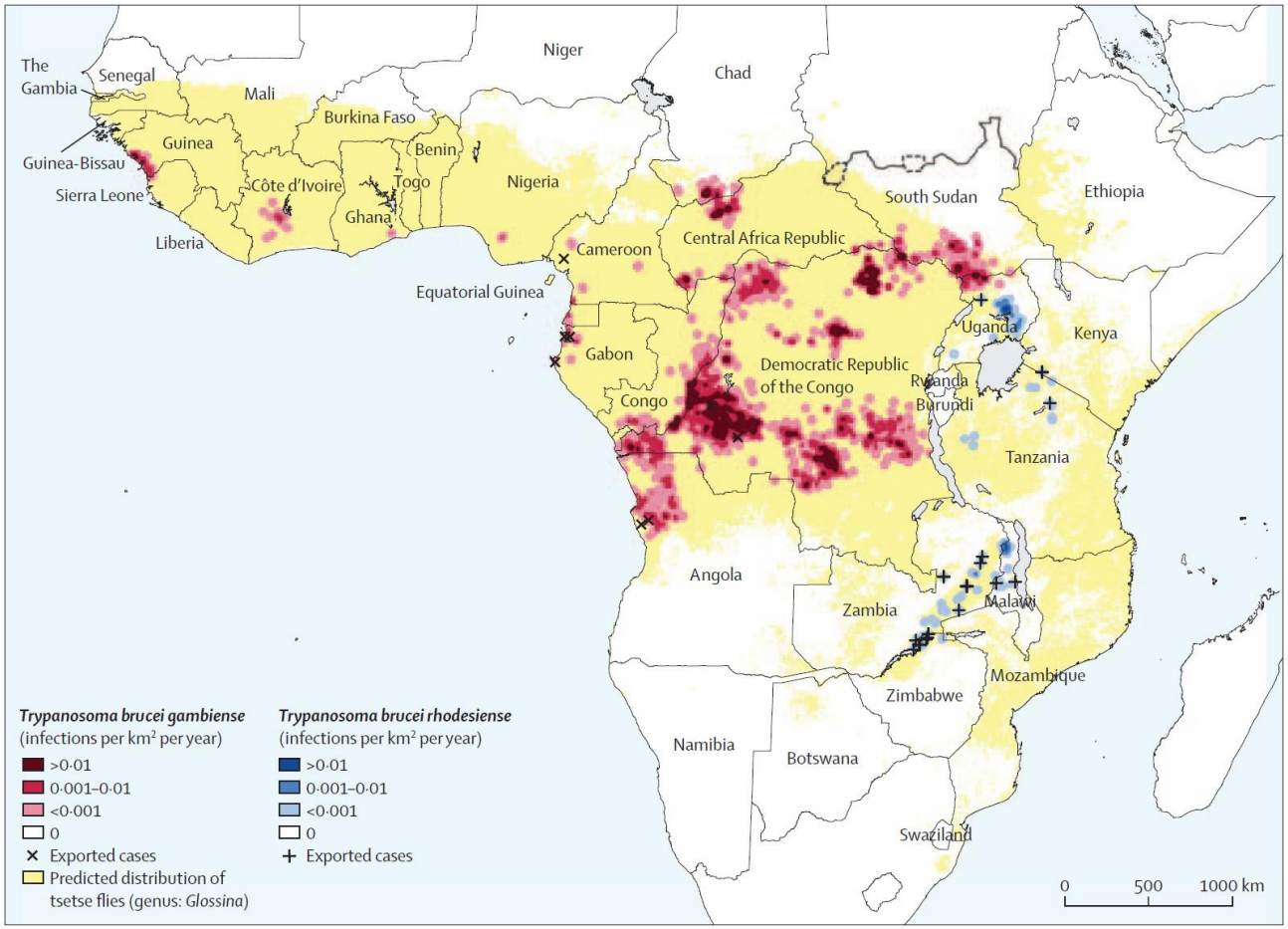


Figure 1: **Geographical distribution of reported infections of human African trypanosomiasis (reporting period 2010–14)**
Trypanosoma brucei gambiense disease is found in western and central Africa, whereas *Trypanosoma brucei rhodesiense* disease is found in eastern and southern Africa. The source of reported infections is the WHO Atlas of human African trypanosomiasis.[1,13] The density of reported infections (ie, the number of reported infections per km² per year) was obtained from village-level data by kernel smoothing,[14] with a search radius of 30 km.[15] Exported cases (ie, those diagnosed in non-endemic countries) are mapped in the probable place of infection.[3] The predicted distribution of tsetse flies was provided by the Programme against African Trypanosomosis.[16]

Büscher et al., (2017) Lancet 390: 2397-409

Our Case – follow-up

Suramin treatment – non-availability issues

Another 14 hours after LUMC admission (from Basel)

Treatment started with pentamidin 300 mg iv.

Suramin challenge dose of 100 mg

- followed by another 400 mg the same day
- 500 mg on day two
- 1000 mg on day 8, 15 and 22

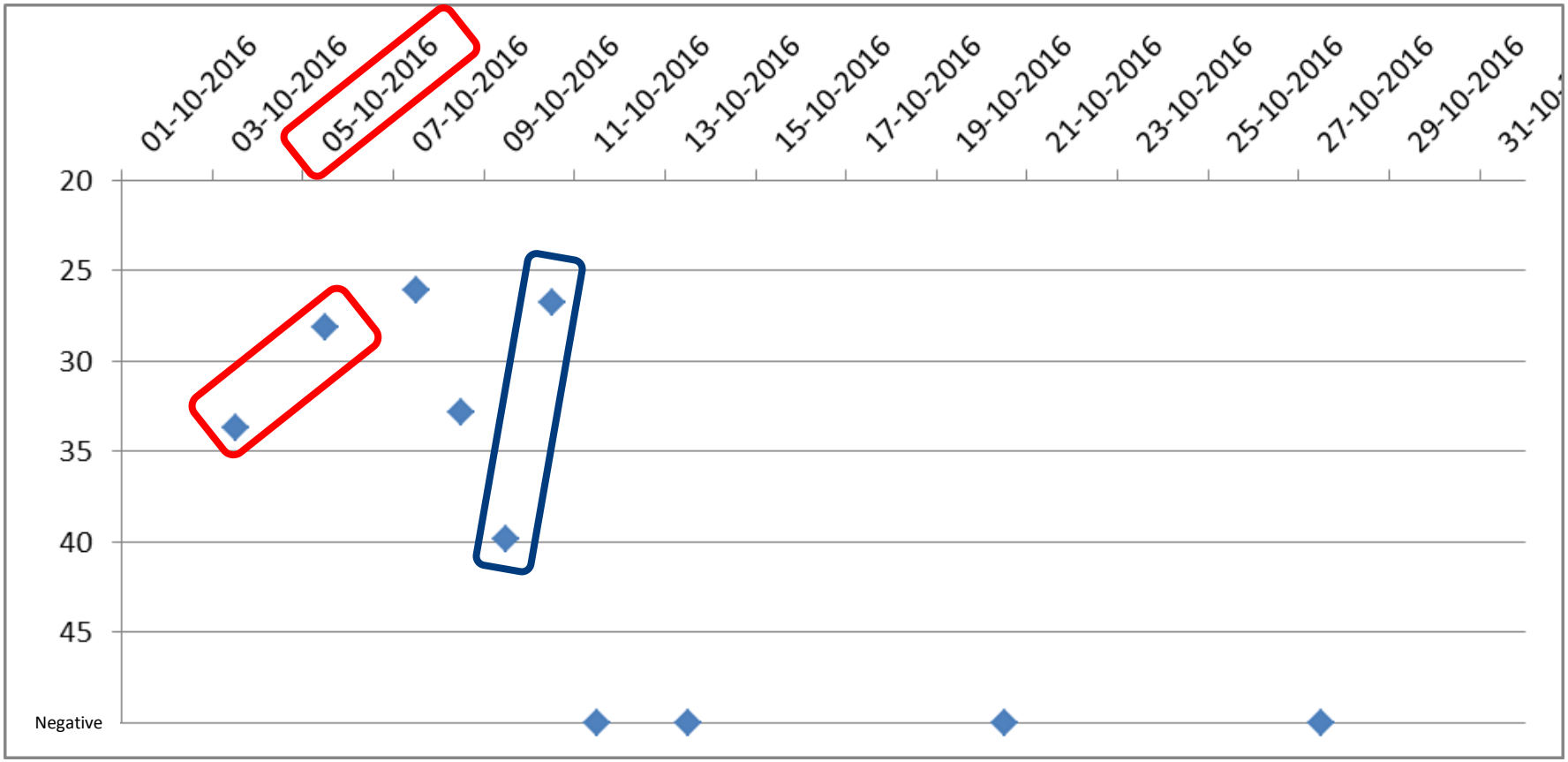
Microscopy:

Decline starting day 2 of treatment

Negative day 4 (October 9th)

Retrospective PCR analysis of blood samples

ITM – Antwerp (T.b. rhodesiense)



- PCR positive before microscopy
- CSF negative
- PCR negative 2 days later than microscopy

Diagnostic delay…… if focus is on malaria RDT

Or in case RDT in combination with malaria PCR would have been performed

- Clinical information and travel details to the laboratory!!!
- Even when HAT-PCR would replace microscopy
- More delay in the diagnosis if HAT not considered