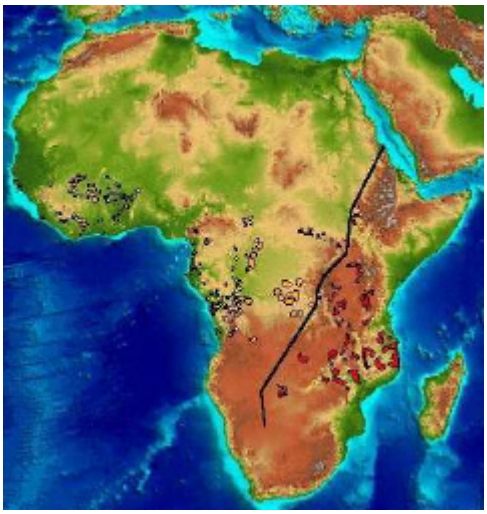
Sleeping sickness

Gambiense chronic disease recently resurged in the Democratic Republic of **Congo** (DRC), **Angola**, **southern Sudan** and **northwest Uganda**

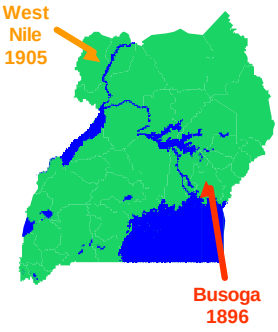


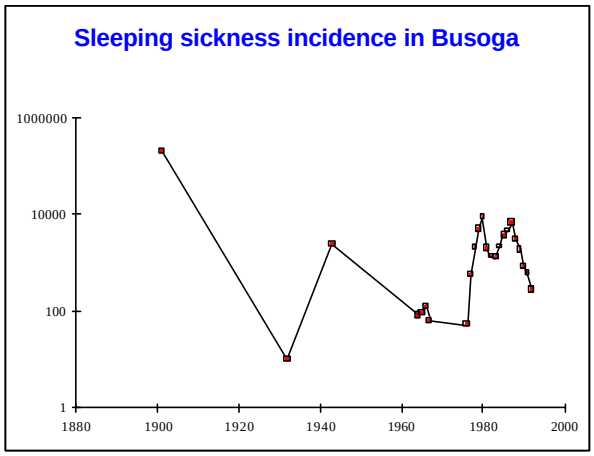
Rhodesiense acute disease serious epidemics in **southeast Uganda** from 1940s onwards

Uganda remains the only country with foci of both **Gambiense** and **Rhodesiense** sleeping sickness

Three major epidemics in SE Uganda last century

1900, 1940, 1980





1900s *G. palpalis*
1908 1/3 population dead (c. 300,000)
1909 survivors evacuated
From Congo ?

1940s *G. pallidipes*
1942 2,432 cases
274 deaths
From Zambia via Tz?

1980s *G. f. fuscipes*
Epidemic peaks:
1980 9,000 cases
1987 7,000 cases

Evidence for the zoonotic reservoir of *T. b. rhodesiense*

Wild animal reservoir

Bushbuck

1950's (Heisch, McMahon and Manson-Barr)
Shores of Lake Victoria
Used human 'volunteers' to differentiate parasite

Domestic livestock reservoir

Cattle

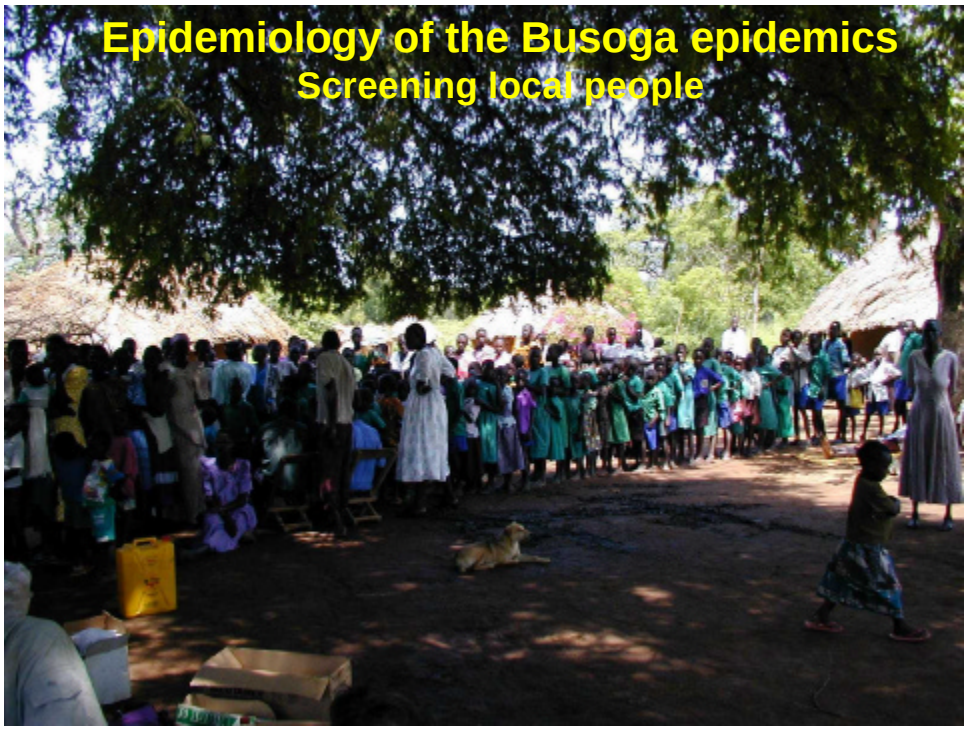
1960's (Onyango and de Raadt)

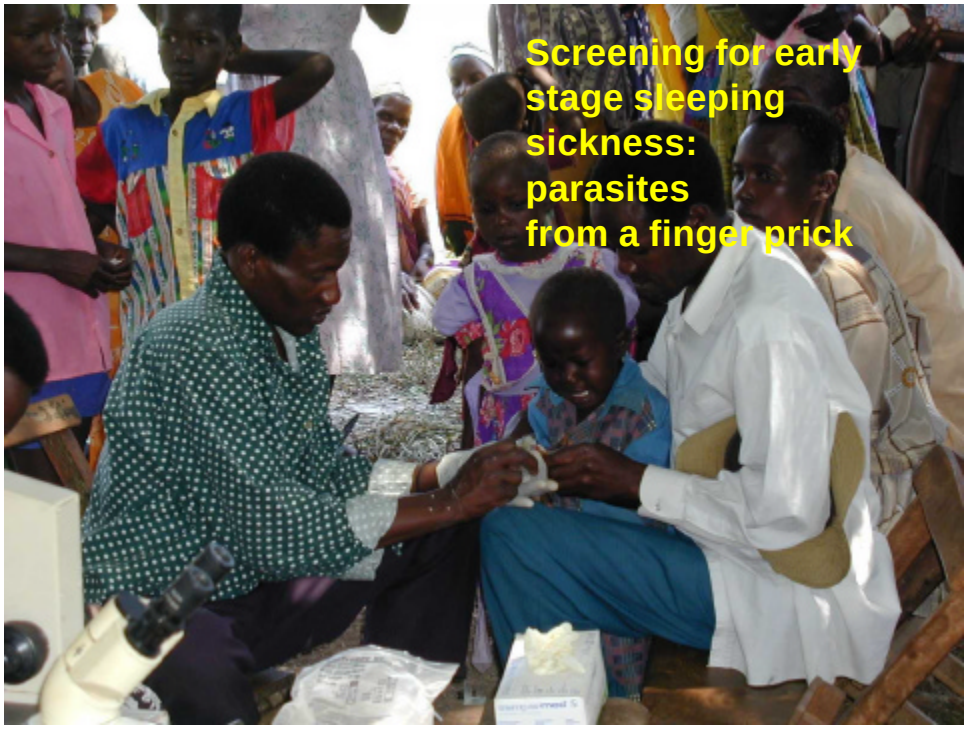
Alego outbreak – shores of Lake Victoria
Differentiation by human 'volunteers'

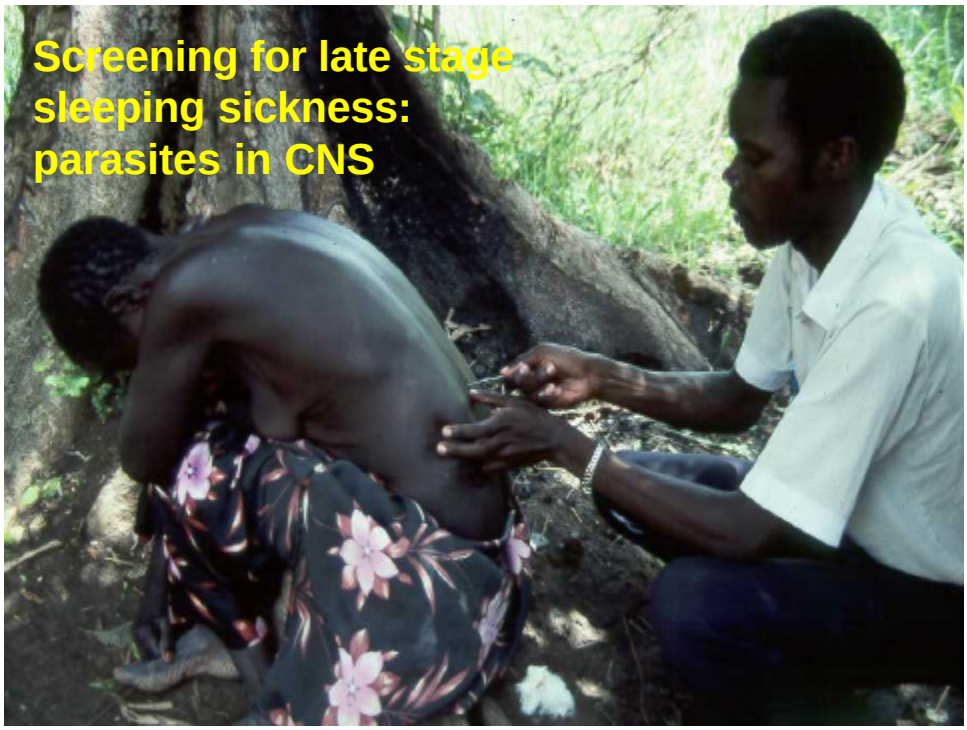
Vector

G. pallidipes **moved into SE Uganda 1940s carrying zoonotic infection from game (MacKitchan, 1944)**


How important is the animal reservoir?

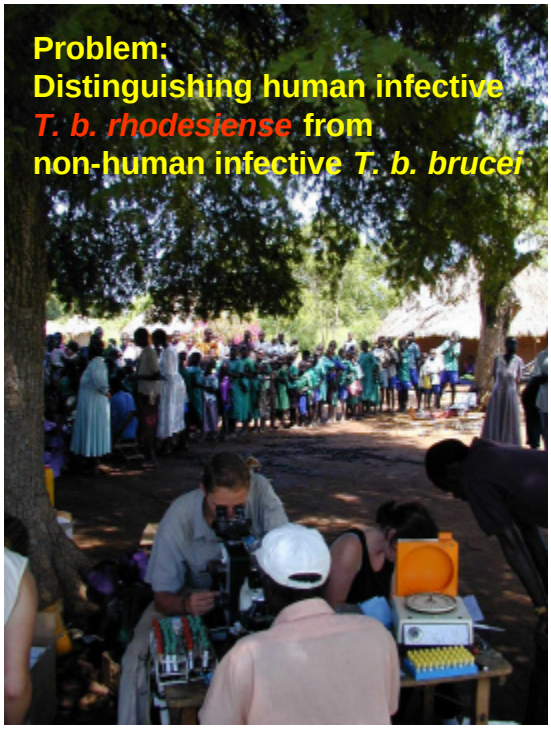

Epidemiology of the Busoga epidemics
Screening local people


Screening for early
stage sleeping
sickness:
parasites
from a finger prick


Screening for late stage
sleeping sickness:
parasites in CNS

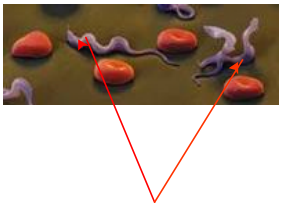

Trapping tsetse for infection rates
and bloodmeal analysis


Sampling cattle



T.b.rhodesiense sleeping sickness parasites are simple to identify in patients from a wet blood film.

Animals can harbour both ***T.b.rhodesiense*** and ***T.b.brucei*** - technical problem: how to distinguish morphologically identical parasites in animal blood



T.b.rhodesiense or ***T.b.brucei****?*

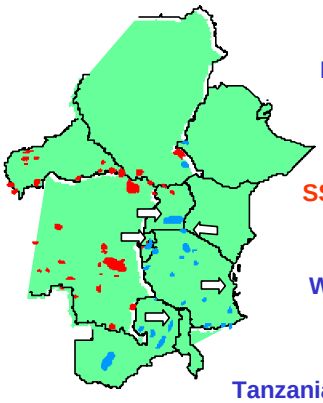
Origins of sleeping sickness epidemics in Busoga
Insights through technology

- **Improvements in sample collection methods and geo-positioning**
  - **Increased sensitivity of analysis**
- **DNA technology**

•Strain genotyping – species-specific PCR, RFLP, AFLP, minisatellites, MGE-PCR to
•determine geographical range of specific genotypes
•derive insights into origins of disease
•distinguish human infective *T. b. rhodesiense* from morphologically identical non-human infective *T. b. brucei* in animals *SRA single gene PCR*

Suggested 'spread' of *T.b.rhodesiense* 1910 – 1950 from Zambia by human carriers

'New' vector
G. pallidipes
moved into SE Uganda carrying **zoonotic** infection from **game animals**
(MacKitchan, 1944)



Ruanda/Burundi
1954

SS reaches SE Uganda
1940's

W Tanzania
1920's

Kenya
1942

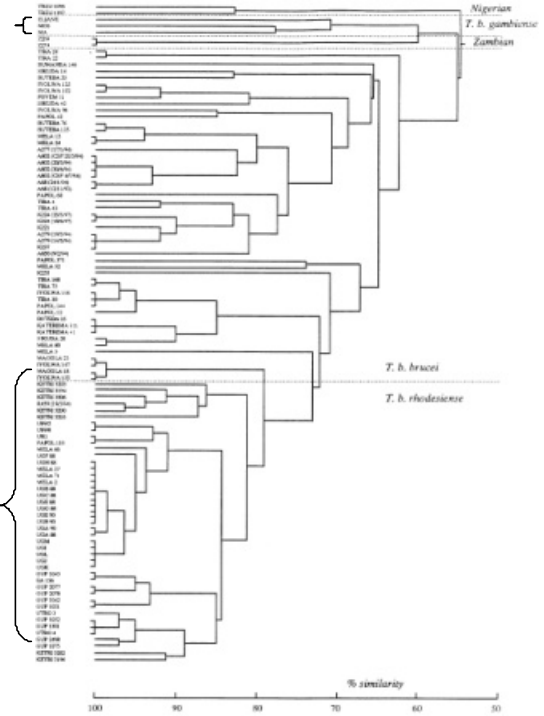
Tanzania/Mozambique
1911

Busoga 1942
2,432 cases
274 deaths

'Discovery' in Zambia 1910
Stephens & Fantham

Cluster analysis of RFLP shows that *T. b. rhodesiense* from Zambian and Ugandan/ Kenyan sleeping sickness foci are not related

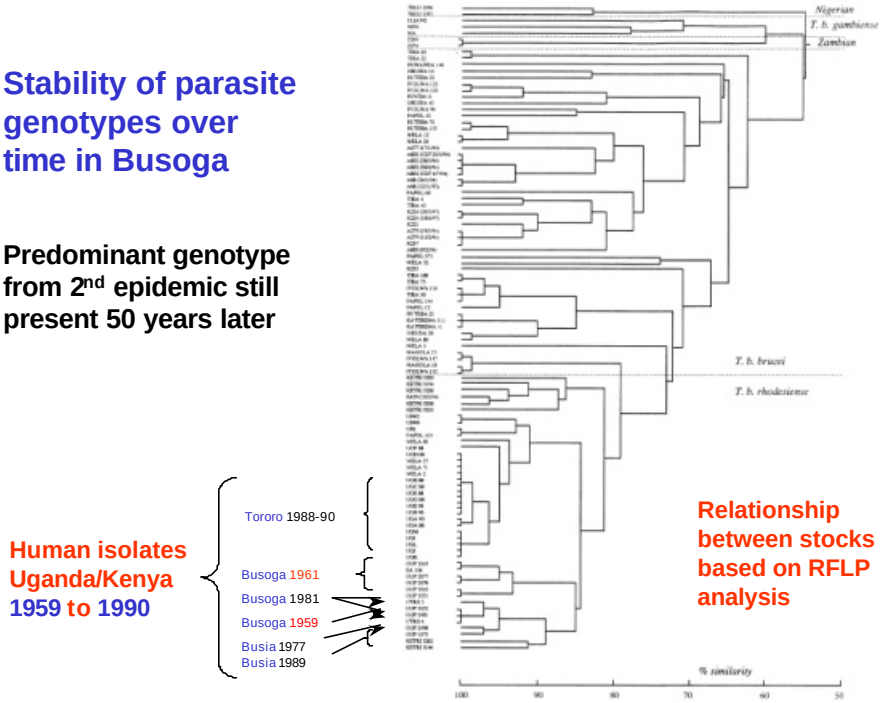
T.b. rhodesiense
Zambia 1983



T.b. rhodesiense
Uganda/Kenya
1959 to 1990

Stability of parasite genotypes over time in Busoga

Predominant genotype from 2nd epidemic still present 50 years later



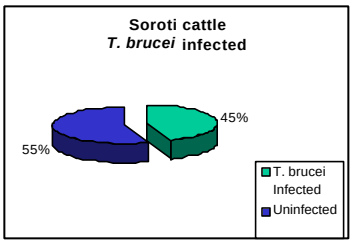
Human isolates Uganda/Kenya 1959 to 1990

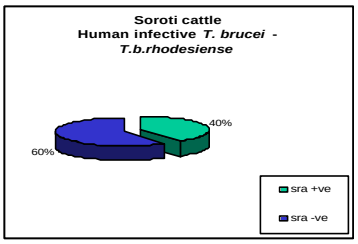
Relationship between stocks based on RFLP analysis

T.b. rhodesiense in the cattle reservoir

SRA **(serum resistance associated gene)**

PCR analysis of cattle - Soroti district (Lancet 2001)



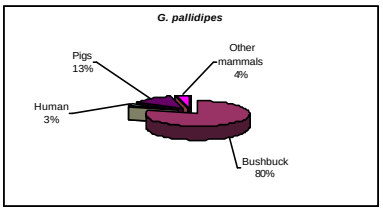


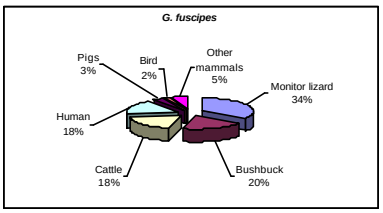
Point prevalence of *T. brucei* in cattle in Soroti 45% of which 40% have *SRA* gene.
18% of cattle in Soroti carrying human infective *T. b. rhodesiense*.

Previous best estimate human infective cattle:
c. 1% prevalence (23% of the 5% *T. brucei* infections)

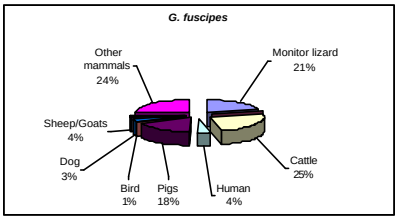
Tsetse hosts SE Uganda

1950's **2000**





Loss of *G. pallidipes* as main vector
Loss of bushbuck as reservoir host
Cattle now main reservoir host



Measuring the risk of cattle as reservoir of sleeping sickness in SE Uganda – *SRA* analysis

Human Sleeping sickness rate: 0.6 % (6 people/1000)

$p2_M$ 0.006

$p1_M$ 0.035

$p3_M$ 0.0002

Fly biting rate human 9% cattle 23% (from bloodmeal analysis)

$p1_C$ 0.26

$p3_C$ 0.04

Cattle 234 X more likely to be source of infection than another human

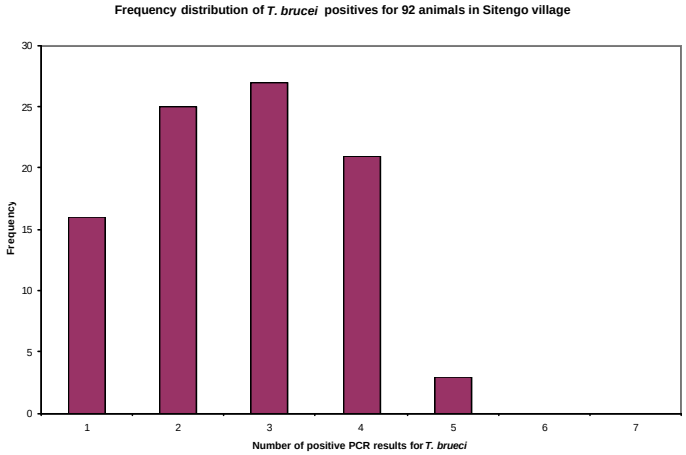
Cattle
***T.b. brucei* prevalence 45%**
***T.b. rhodesiense* 40% of *T.b. brucei* (18%)**

$p2_C$ 0.18

Six month longitudinal survey of *T. brucei* s.l. in cattle in SE Uganda

82.6 % cattle positive for *T. brucei* s.l

17.4 % of cattle were never positive during this period



92 cattle in total, 7 sampling dates (644 observation in total)

Measuring the risk of warthog as reservoir of sleeping sickness in Serengeti – *SRA* analysis

Human Sleeping sickness rate: 0.0028 %

$p2_M$ 0.000028

$p1_M$ 0.001

$p3_M$ 2.8 x 10^8

Fly
biting rates:
human 0.1%
warthog 32%

$p1_C$ 0.32

$p3_C$ 0.03

Warthog
>1 million X more likely to be source of infection than another **human**

Warthog
9.5% SRA +ve

$p2_C$ 0.095

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