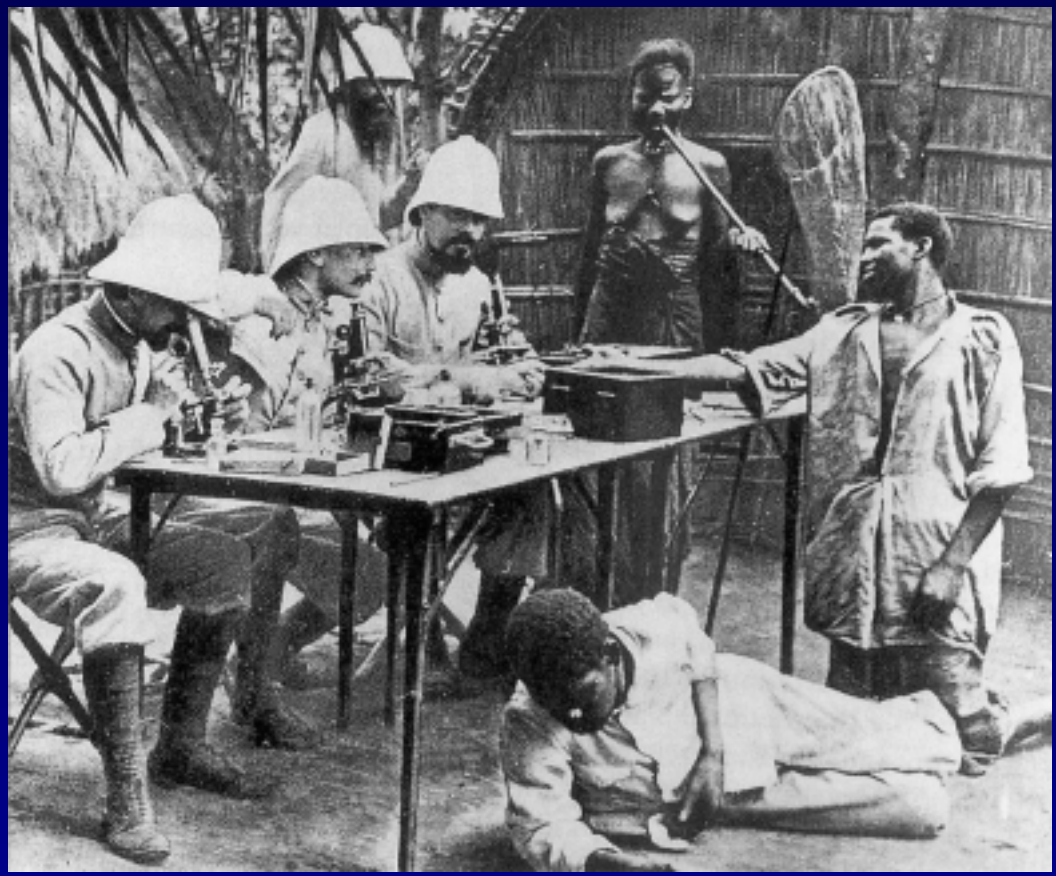
African Trypanosomiasis: A Re-emerging Public Health Threat



Anne C. Moore
Division of Parasitic Diseases
Centers for Disease Control and Prevention

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African Trypanosomiasis: Background

- a classic example of an emerging infection, 1890-1930
- the leading public health problem in Africa in the first half of the 20th century
- nearly eliminated by 1960 using population screening, case treatment, chemoprophylaxis
- currently a re-emerging infection in central Africa

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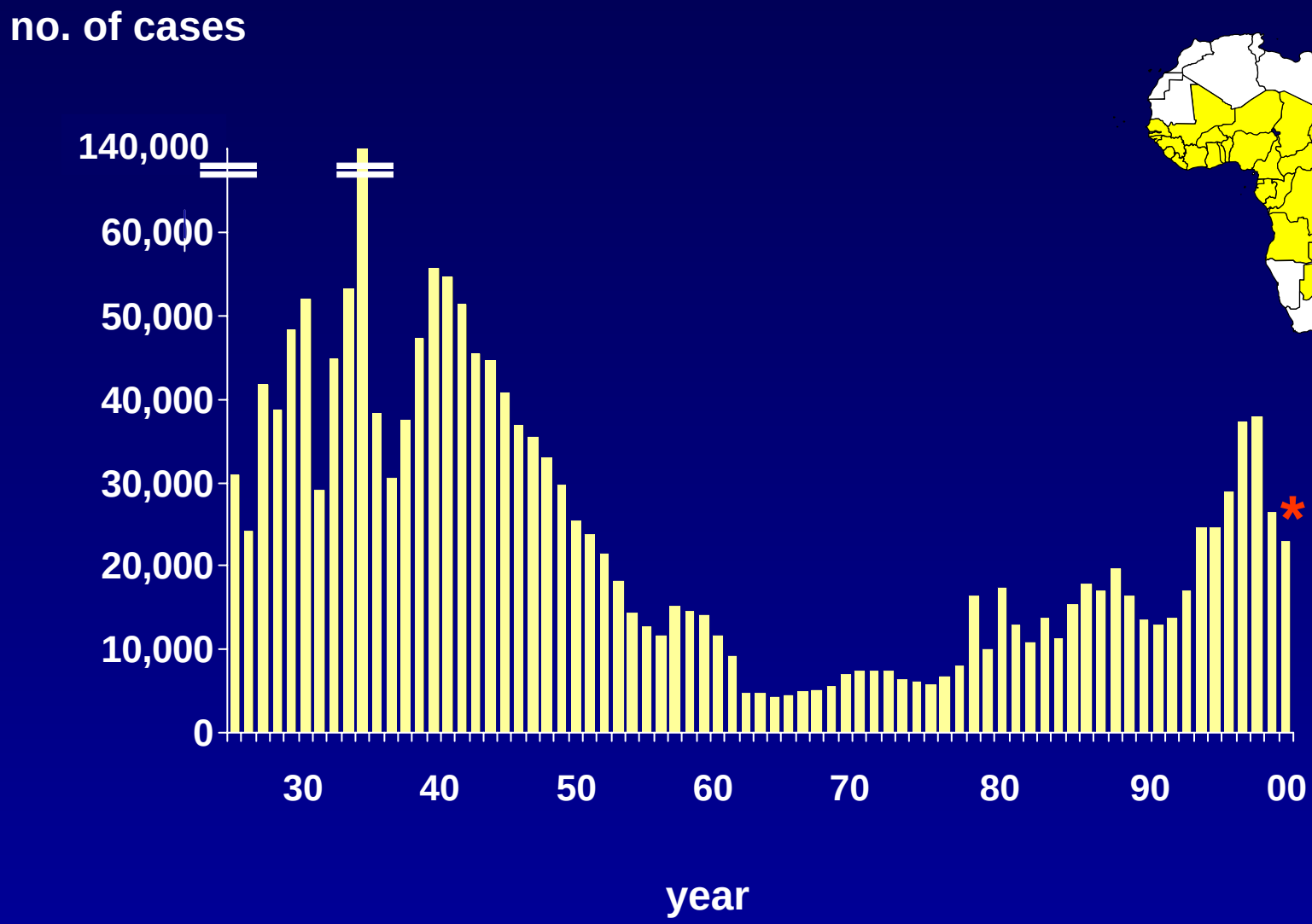
African Trypanosomiasis: The Basics

	West African	East African
Agent:	*T. brucei gambiense*	*T. brucei rhodesiense*
Vector:	riverine tsetse fly	savanna tsetse fly
Distribution:	west /central Africa	east/south Africa
Reservoir:	human	antelope, cattle
Disease:	chronic	rapidly progressive
Mortality:	100%	100%
At risk:	rural populations	rural populations visitors to game reserves

New Cases of Human African Trypanosomiasis
Data collected by WHO, 1926-2000



* reporting incomplete for 1999 and 2000

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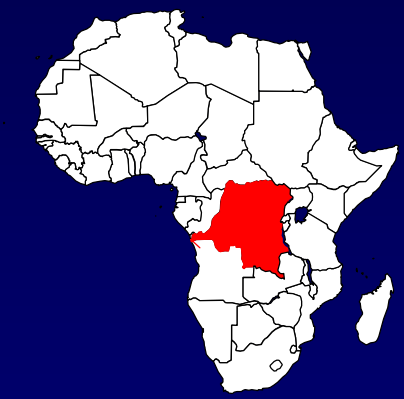
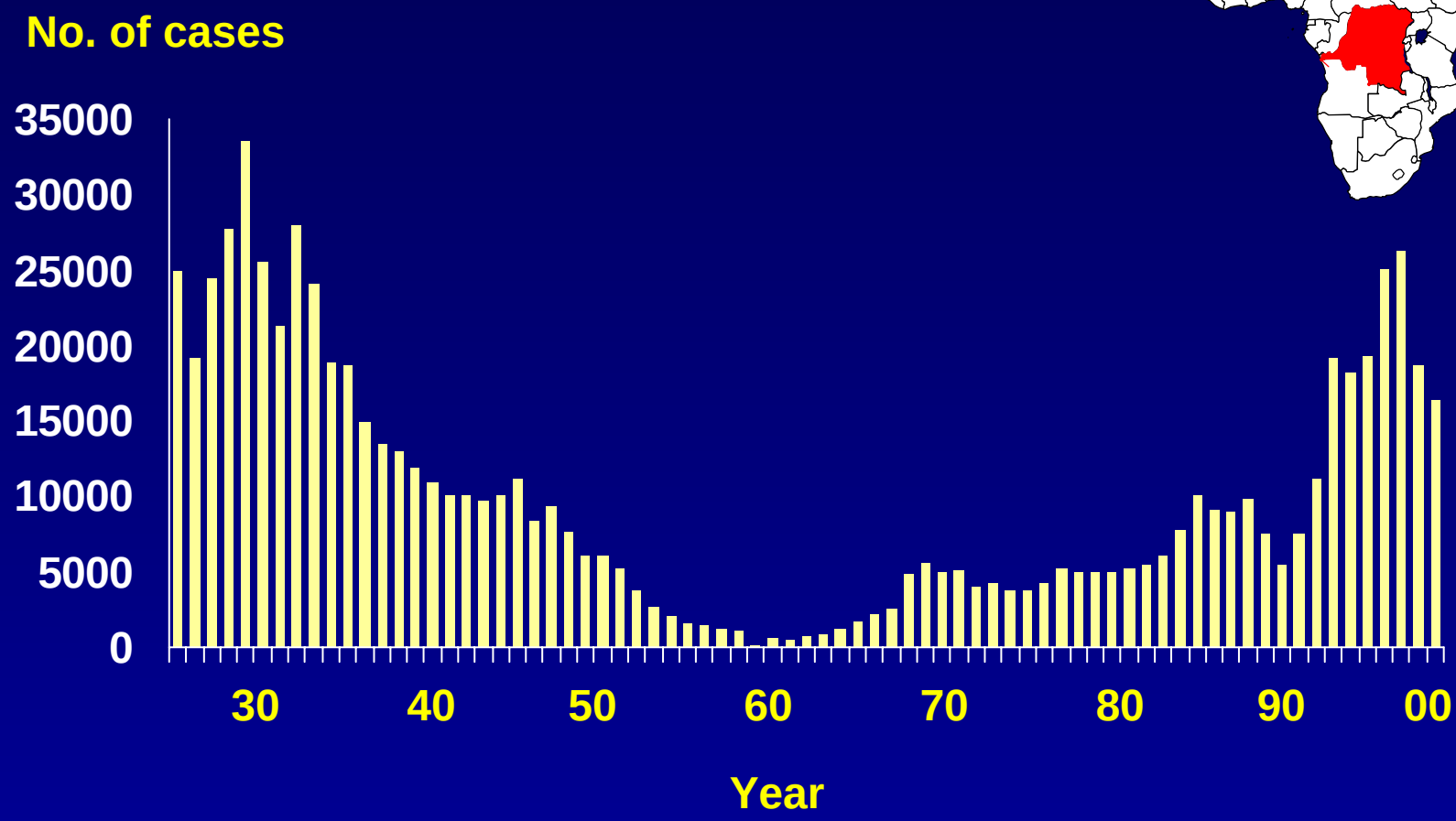
New Cases of African Trypanosomiasis Detected in the Democratic Republic of Congo, 1926-2000*





*DRC Ministry of Health statistics

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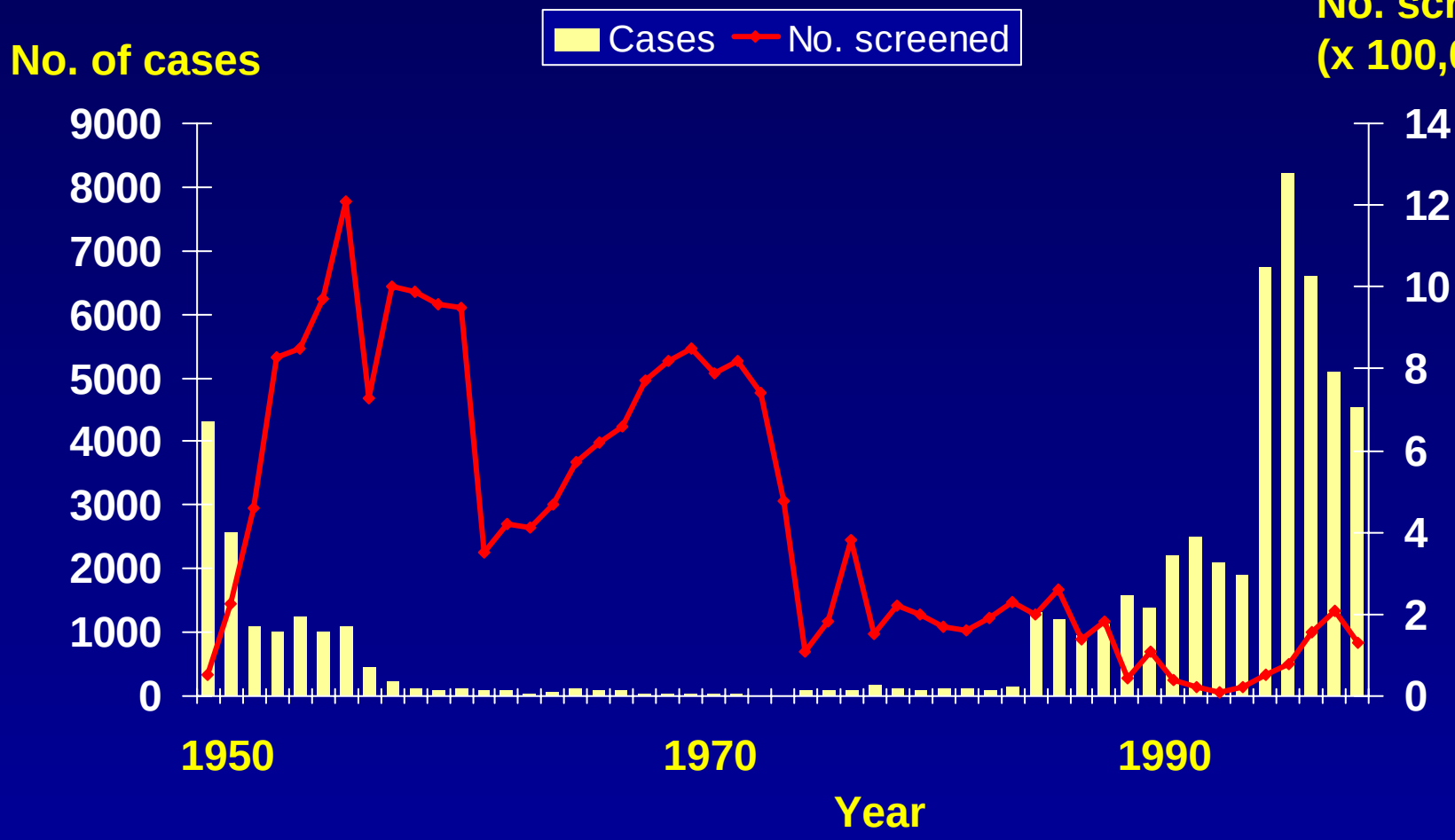
New Cases of African Trypanosomiasis Detected in Angola, 1949-2000*



*Angola Ministry of Health statistics

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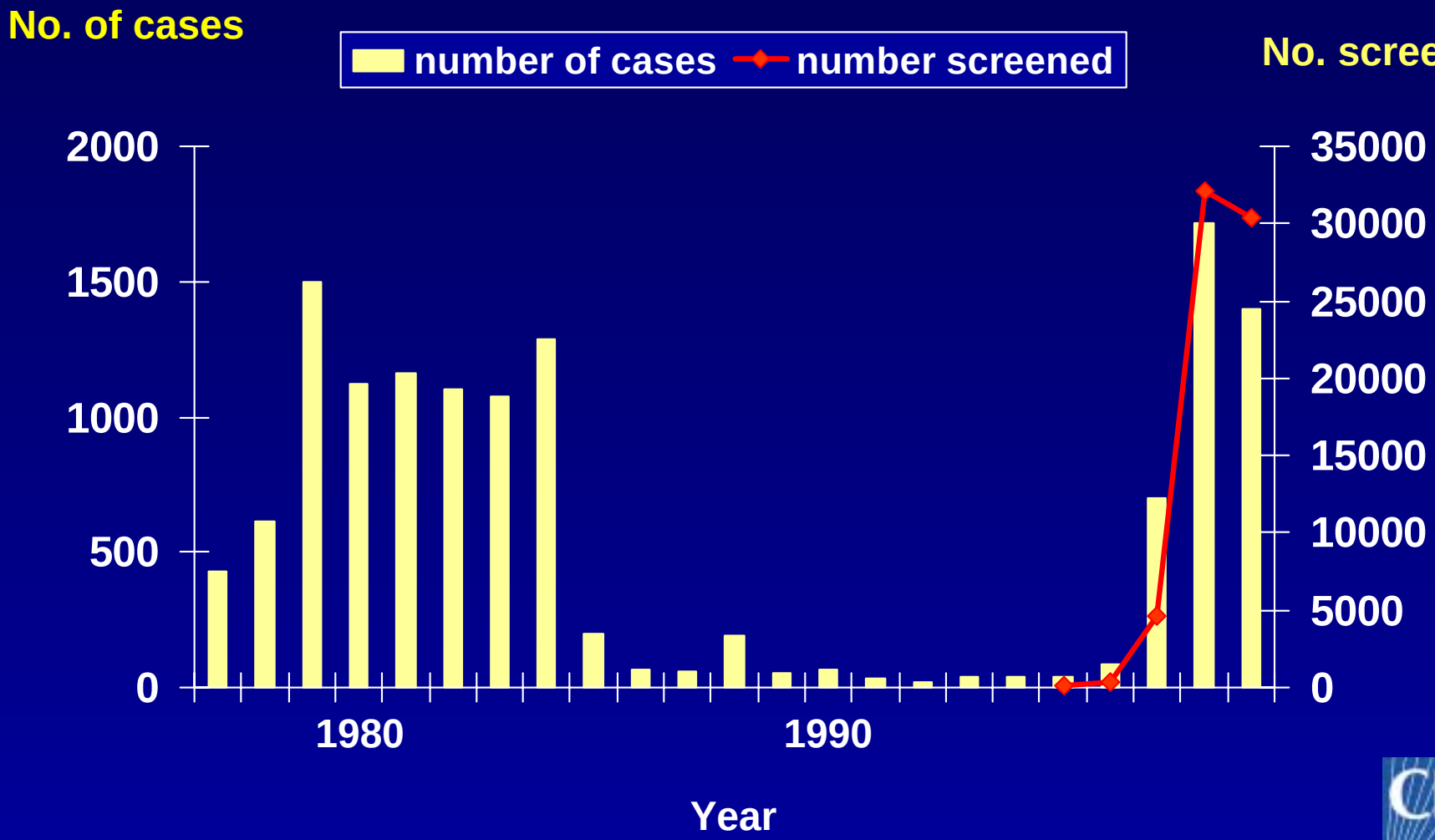
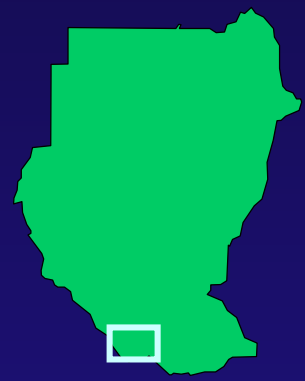
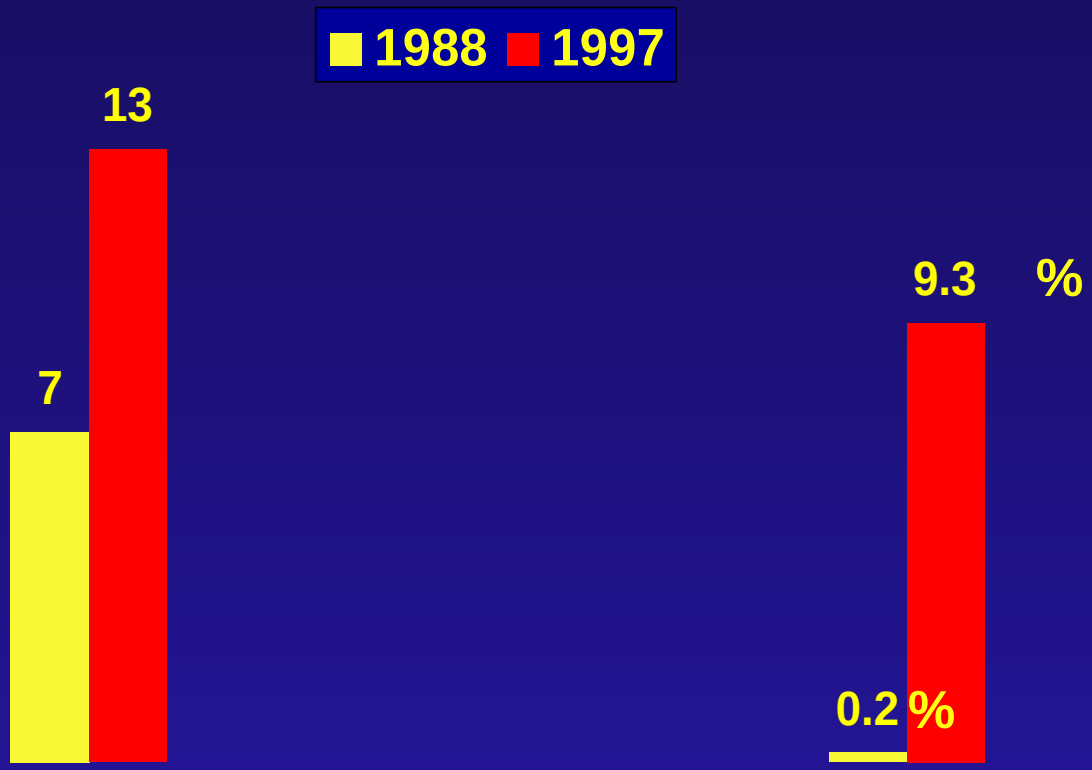
New Cases of African Trypanosomiasis Detected in Sudan, 1977-1999



Population Screening for Trypanosomiasis, 1988-1997
Villages in Ezo region, Sudan (n=13)





number of villages with sleeping sickness cases

prevalence, parasite-confirmed

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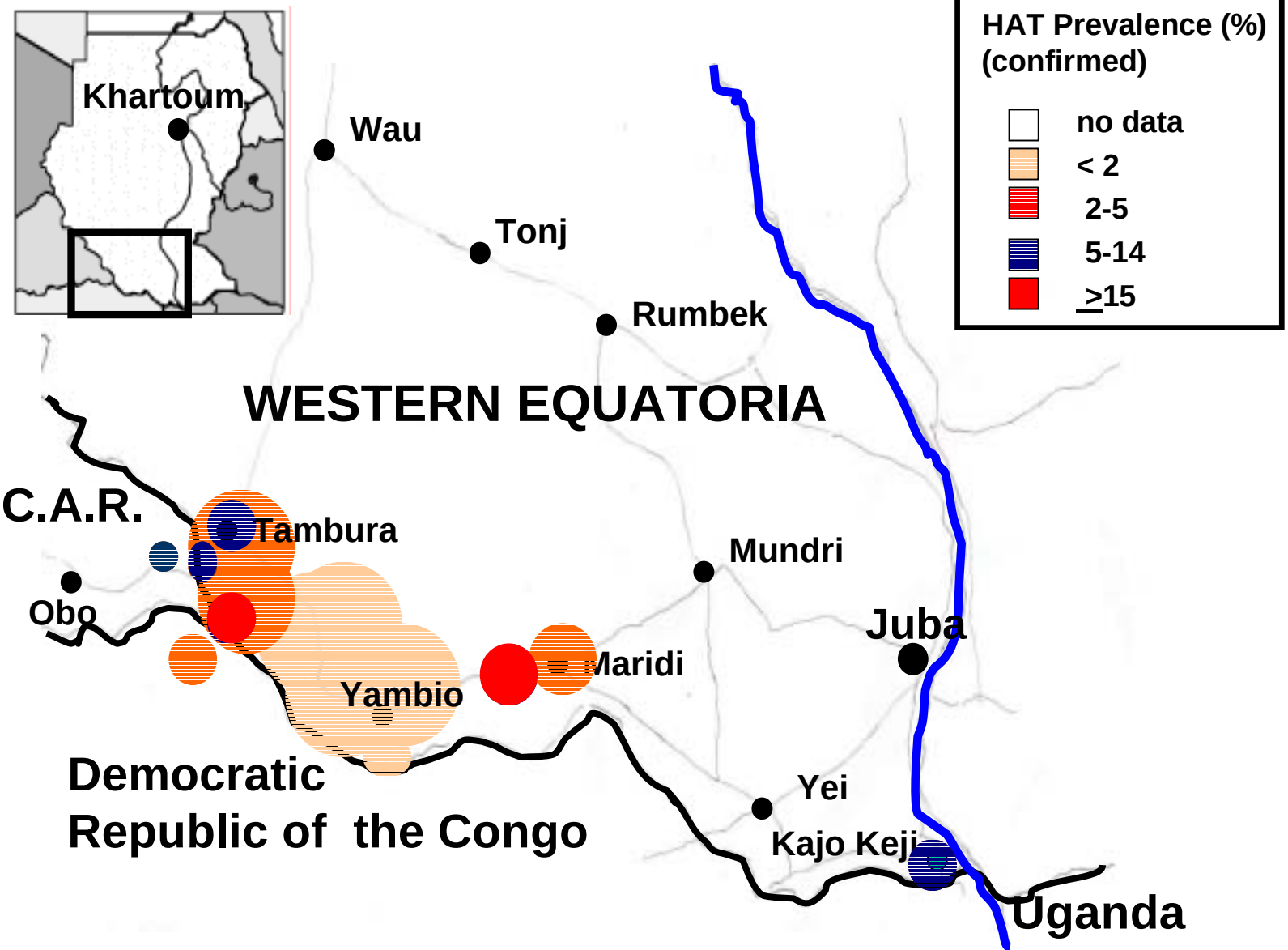
Prevalence of Sleeping Sickness
Southern Sudan, 1998



West African Trypanosomiasis: Problems in Accurately Estimating the Burden

- Inadequate levels of active case detection
  - At risk: 60 million
  - Screened for infection: < 2 million
- Disease distribution is uneven
- Passive case detection only minimally helpful
  - No health facilities in many areas at risk
  - Conflict or insecurity in epidemic foci
  - Clinical diagnosis is difficult until late in disease
  - Low sensitivity of parasitological diagnosis

→ Epidemic disease often remains unrecognized, even where there are functioning health facilities

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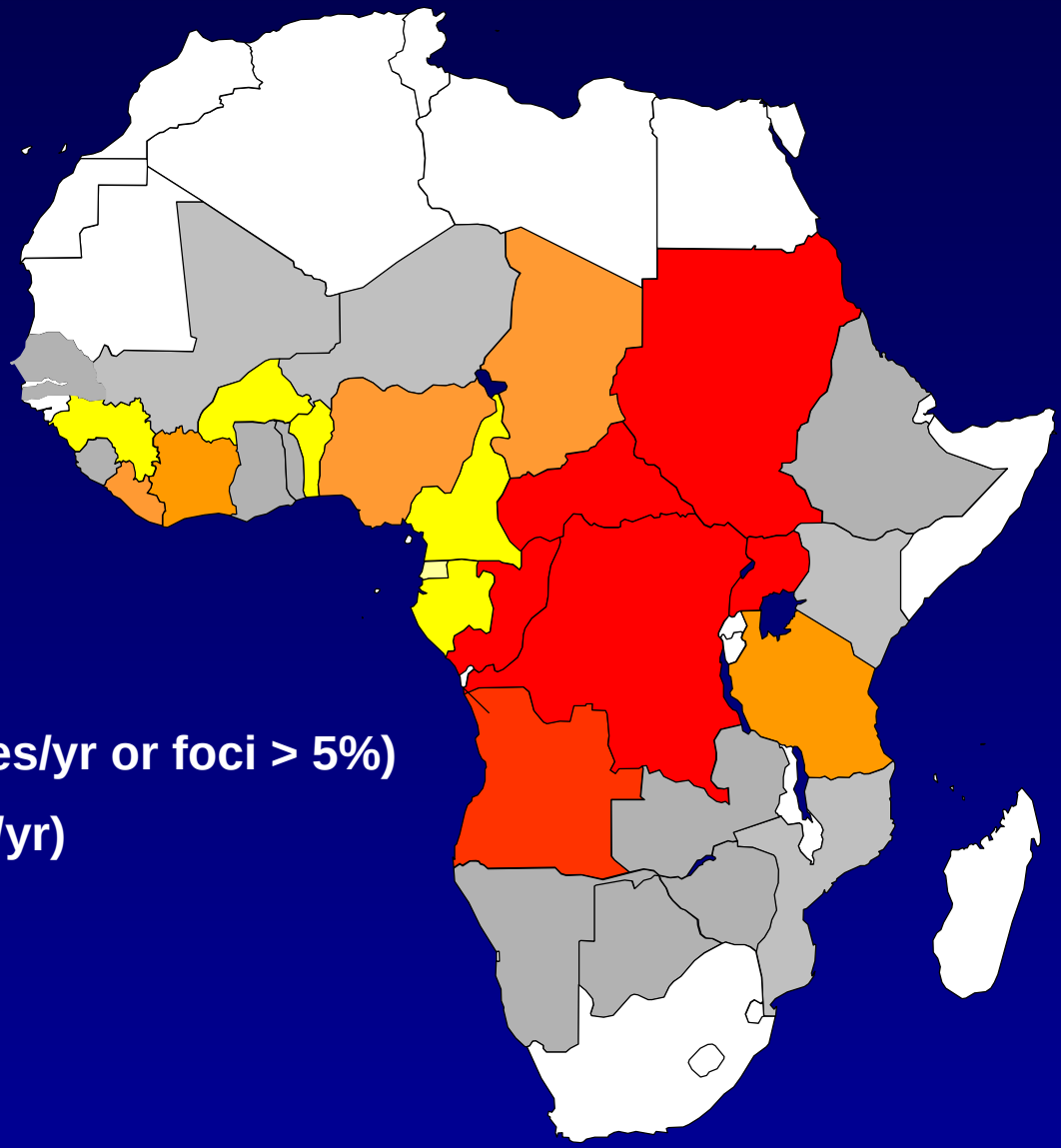
New Cases of African Trypanosomiasis, 1995-2000



- High/epidemic (>1000 cases/yr or foci > 5%)
- Moderate (100-1000 cases/yr)
- Low (25-100 cases/yr)
- Very low or unknown

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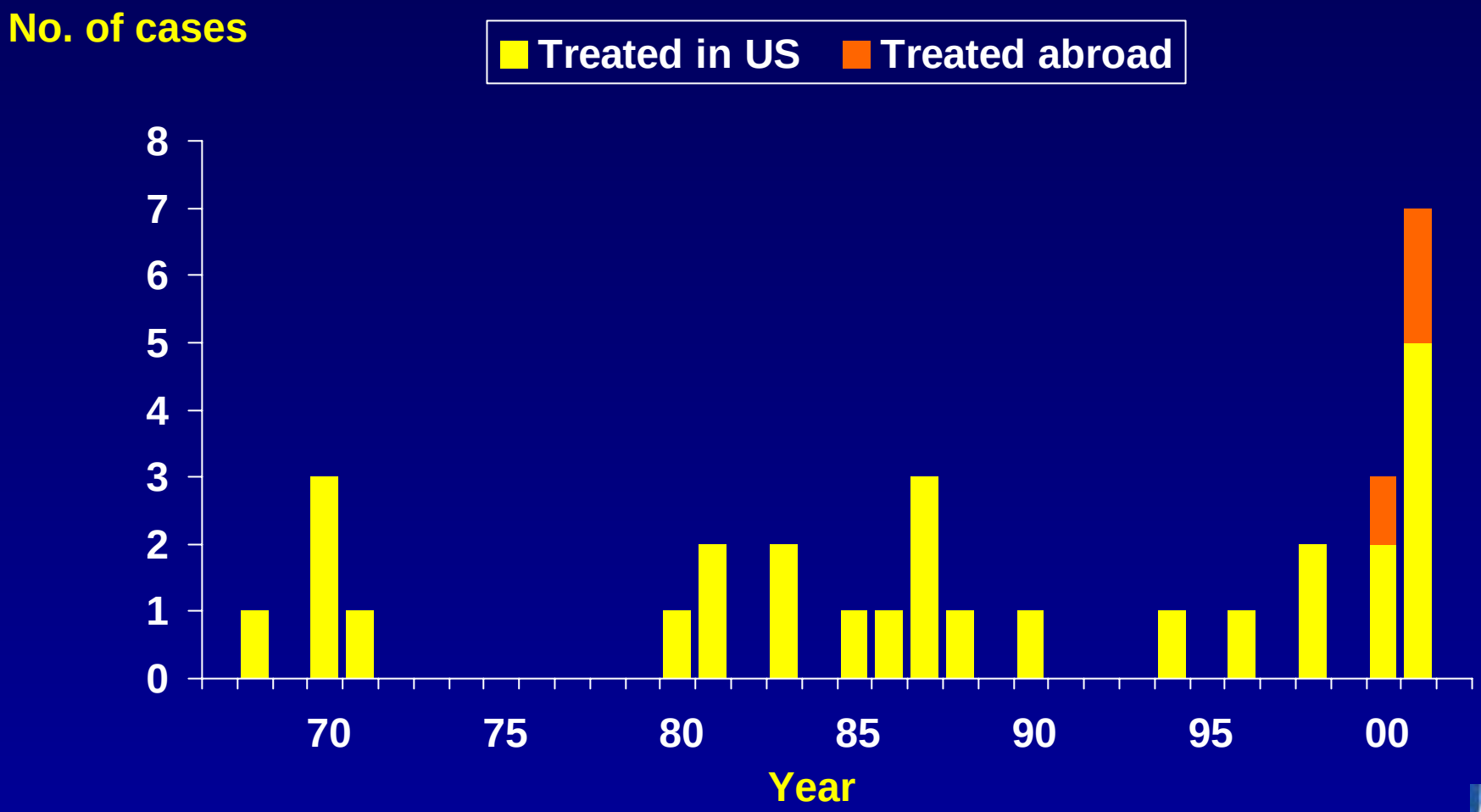
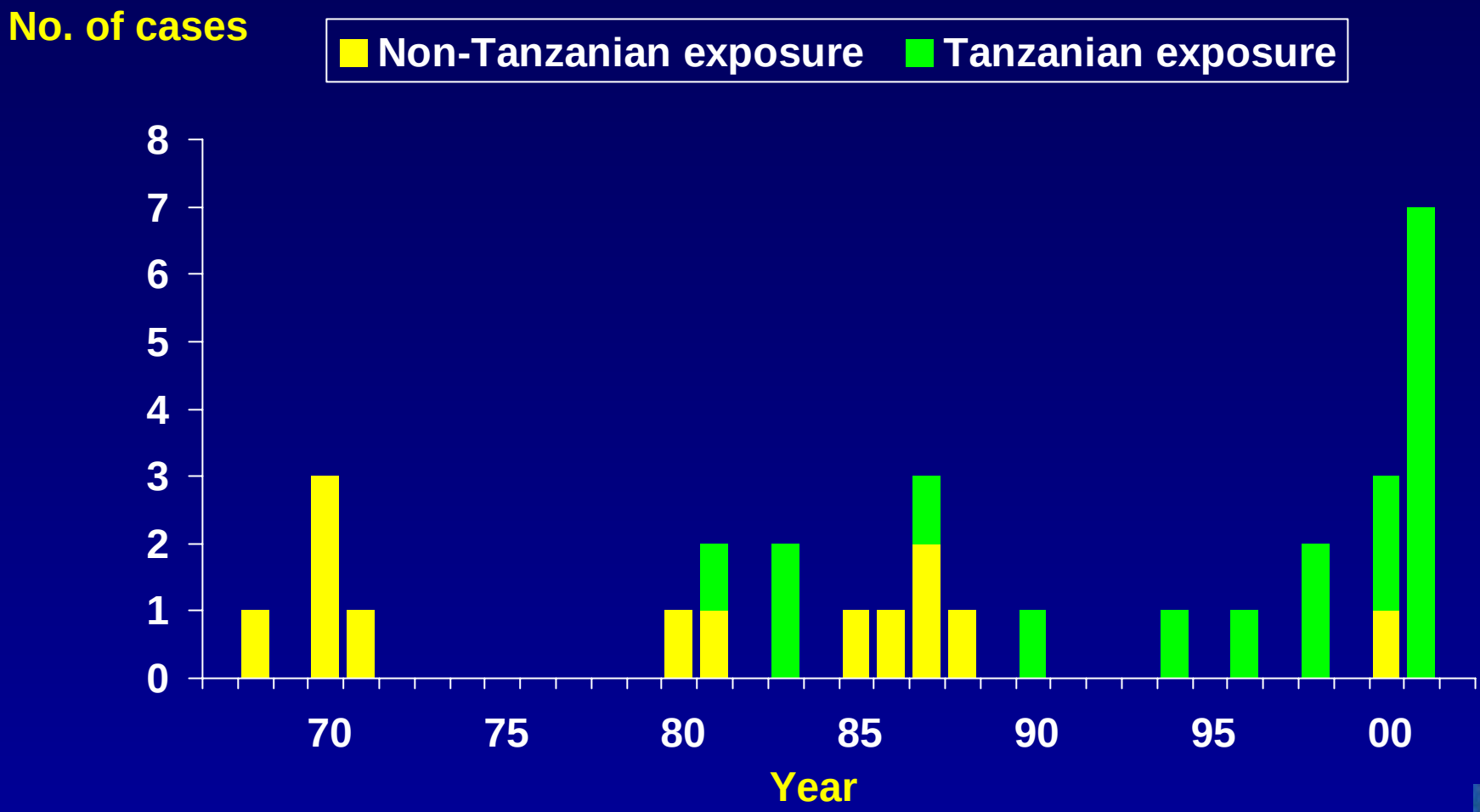
East African Trypanosomiasis in U.S. travelers 1967-2001



East African Trypanosomiasis in U.S. travelers 1967-2001



African Trypanosomiasis: Public Health Burden

Estimated prevalence: 350,000-500,000 cases
>95% *T. b. gambiense*

Health Burden: 2.05 million DALYS
(WHO, 2000)

For Africa, compare with:

malaria	**36.8 DALYS**
tuberculosis	**8.7**
meningitis	**3.6**
schistosomiasis	**1.6**
polio	**0.8**

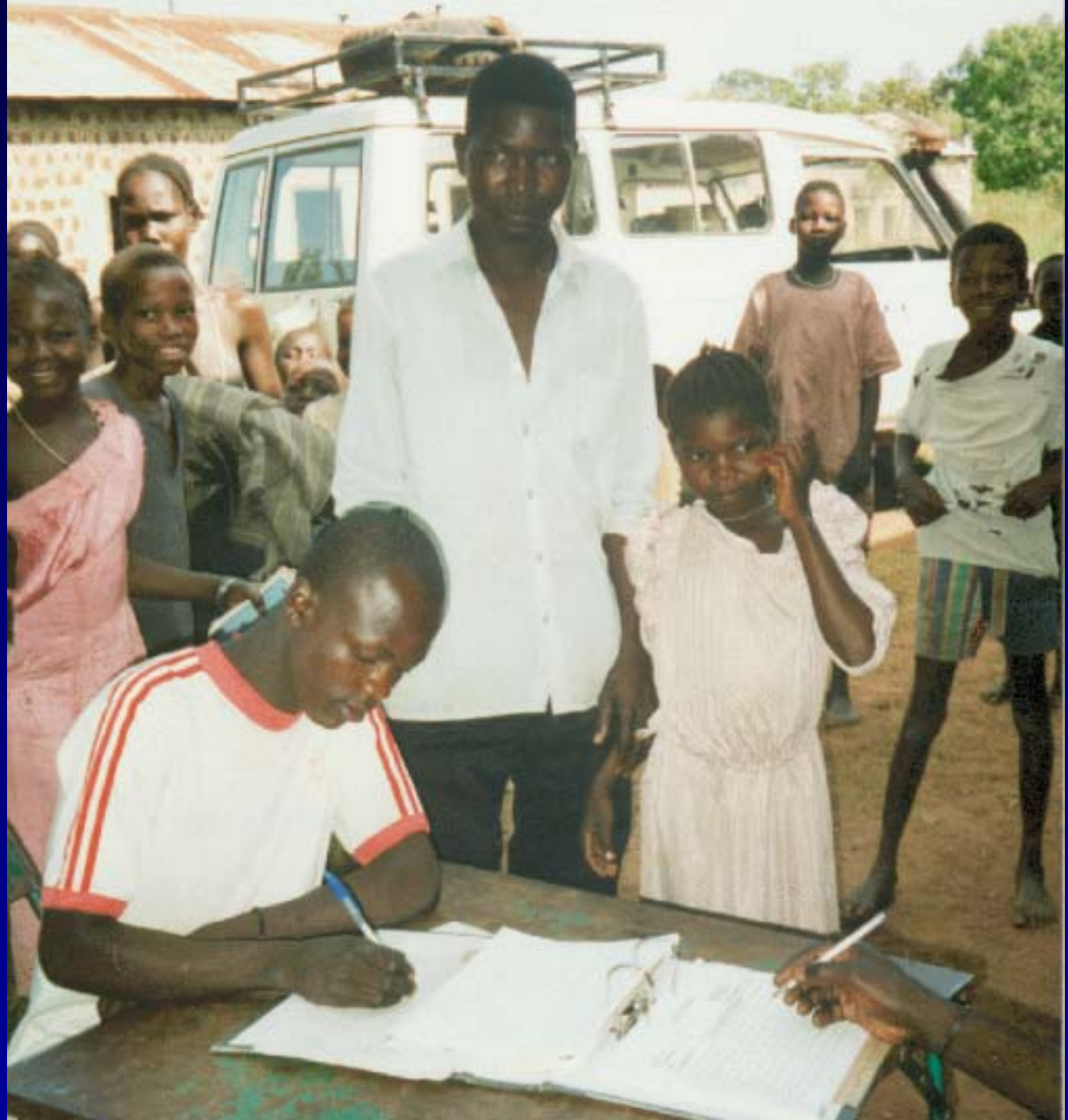
Control of West African Trypanosomiasis

Primary strategy:

- **Active case detection/population screening**
- **Case treatment**
  - **reduce mortality**
  - **reduce disease reservoir**

Adjunct strategy:

- **Vector control (traps)**
  - **Reduce man-tsetse contact**



Cost-effectiveness of African Trypanosomiasis Control

Disease/Intervention	$ per DALY averted
SS control, southern Sudan 1998 (IMC-CARE-CDC)	28
Compare with:	
“good value” for $	25
TB treatment (not DOT)	3
visceral leishmaniasis, Sudan epidemic	18
immunization DPT, polio, measles	25
acute respiratory infection	20--50
Malaria (bed nets + insecticide)	19--85

Cost-effectiveness of African Trypanosomiasis Control Periodic Screening vs. Delayed Intervention

Scenario	$ per DALY averted
Screen at 3 year intervals	10.28 (range 3.84-13.41)
Delayed intervention at 9 years	17.41 (range 11.97-21.50)

Assumptions:

- basic health infrastructure exists
- analytic horizon is fixed at 9 years
- SS duration untreated is 3 years
- population screening decreases prevalence by 2/3
- population is 50,000 and is static except for SS deaths
- Initial SS prevalence 0.5%
- SS prevalence doubling time 1.75 years

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Barriers to Control of African Trypanosomiasis

- Insufficient resources
- War and civil disturbance
- Crisis in African trypanosomiasis chemotherapy
  - Rising rates of melarsoprol treatment failure
  - Disappearing arsenal of therapeutic drugs

Melarsoprol Therapy for African Trypanosomiasis

- **Introduced:** 1949
- **Indication:** CNS African trypanosomiasis
- **Use:** 60-90% of patients
- **Efficacy:** 92-95% for almost 5 decades
- **New Trend:** *T. b. gambiense* treatment failure, 1997-2001
- **Problem foci:** Angola, Sudan, Uganda

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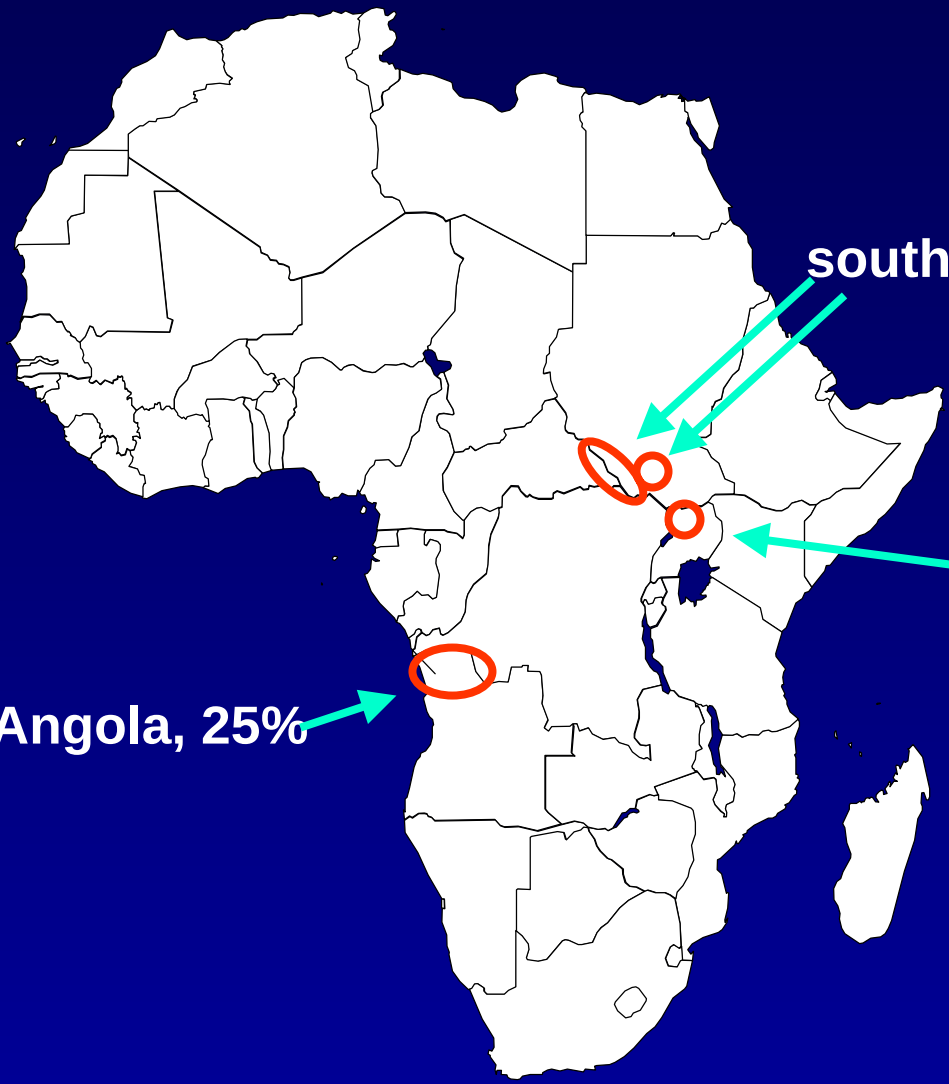
Melarsoprol Treatment Failure Rates, 1997-2001



Melarsoprol Treatment Failure

Possible Cause	Available Data
▪ pharmacokinetic differences	identical drug levels in responders and relapse patients
▪ HIV co-infection	more data needed
▪ drug resistance	very few isolates tested for susceptibility IC_{50} 9-36 ng/ml Uganda relapses (n=3)* IC_{50} 9-72 ng/ml Uganda responders (n=8)* IC_{50} 1-14 ng/ml banked Ivory Coast relapses (n=10)*
▪ altered affinity for protected sites	no data

* R. Brun, Swiss Tropical Institute

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Availability of Treatment Drugs for African Trypanosomiasis

Drug	Indication	Status in summer, 2000
pentamidine	early SS	donation phasing out
suramin	early SS	halt of production
melarsoprol	CNS	future production uncertain (environmental concerns)
eflornithine	CNS, Gambian	not produced
nifurtimox	CNS, Gambian	halt of production

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VANIQA™
(eflornithine HCl) Cream, 13.9%

Finally!
A solution for women
who suffer from unwanted facial hair!

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African Trypanosomiasis: Recent developments

- All 5 drugs are being produced
- All 5 drugs are donated to WHO for sleeping sickness treatment for 5 years
- New drug research and development
  - Consortium for sleeping sickness drug discovery and development ((U of North Carolina, Gates Foundation)
  - MSF Drugs for Neglected Diseases initiative

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African Trypanosomiasis: Additional Recent Developments

- WHO-coordinated activities to strengthen surveillance, control, research (support from Aventis)
  - GIS-based global disease surveillance
  - Sentinel surveillance for treatment failure and drug resistance
  - Financial and technical support for training, population screening, treatment center rehabilitation
  - Formation of a clinical trials group
  - Creation of a specimen bank

- PATTEC (Pan African Tsetse and Trypanosomiasis Eradication Campaign), October 2001

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Summary: African Trypanosomiasis

- A re-emerging infection of serious dimensions in central Africa
- Resurgence has not led to expanded control measures
- Effective treatment and disease control are threatened by
  - increasing treatment failure rates
  - lack of secure, long-term availability of therapeutic drugs

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