African Trypanosomiasis: A Re-emerging Public Health Threat

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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
# African Trypanosomiasis: The Basics

<table>
<thead>
<tr>
<th></th>
<th><strong>West African</strong></th>
<th><strong>East African</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Agent:</strong></td>
<td><em>T. brucei gambiense</em></td>
<td><em>T. brucei rhodesiense</em></td>
</tr>
<tr>
<td><strong>Vector:</strong></td>
<td>riverine tsetse fly</td>
<td>savanna tsetse fly</td>
</tr>
<tr>
<td><strong>Distribution:</strong></td>
<td>west /central Africa</td>
<td>east/south Africa</td>
</tr>
<tr>
<td><strong>Reservoir:</strong></td>
<td>human</td>
<td>antelope, cattle</td>
</tr>
<tr>
<td><strong>Disease:</strong></td>
<td>chronic</td>
<td>rapidly progressive</td>
</tr>
<tr>
<td><strong>Mortality:</strong></td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td><strong>At risk:</strong></td>
<td>rural populations</td>
<td>rural populations</td>
</tr>
<tr>
<td></td>
<td></td>
<td>visitors to game reserves</td>
</tr>
</tbody>
</table>
New Cases of Human African Trypanosomiasis
Data collected by WHO, 1926-2000

* reporting incomplete for 1999 and 2000
New Cases of African Trypanosomiasis Detected in the Democratic Republic of Congo, 1926-2000*

No. of cases

Year

*DRC Ministry of Health statistics
New Cases of African Trypanosomiasis Detected in Angola, 1949-2000*

*Angola Ministry of Health statistics

No. of cases

number of cases number screened

No. screened

0 500 1000 1500 2000 2500 3000 3500

0 5000 10000 15000 20000 25000 30000 35000

Year

1980 1990
Villages in Ezo region, Sudan (n=13)

- Number of villages with sleeping sickness cases: 13 (1988), 7 (1997)
- Prevalence, parasite-confirmed: 9.3% (1988), 0.2% (1997)

(CDC logo)
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
East African Trypanosomiasis in U.S. travelers
1967-2001

No. of cases

- Non-Tanzanian exposure
- Tanzanian exposure
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

<table>
<thead>
<tr>
<th>Disease/Intervention</th>
<th>$ per DALY averted</th>
</tr>
</thead>
<tbody>
<tr>
<td>SS control, southern Sudan 1998 (IMC-CARE-CDC)</td>
<td>28</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Scenario</th>
<th>$ per DALY averted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen at 3 year intervals</td>
<td>10.28 (range 3.84-13.41)</td>
</tr>
<tr>
<td>Delayed intervention at 9 years</td>
<td>17.41 (range 11.97-21.50)</td>
</tr>
</tbody>
</table>

### 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
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
- Problem foci: Angola, Sudan, Uganda
Melarsoprol Treatment Failure Rates, 1997-2001

northern Angola, 25%

southern Sudan, 16-21%

Uganda, 30%
### Melarsoprol Treatment Failure

#### Possible Cause

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

* R. Brun, Swiss Tropical Institute
# Availability of Treatment Drugs for African Trypanosomiasis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Status in summer, 2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>pentamidine</td>
<td>early SS</td>
<td>donation phasing out</td>
</tr>
<tr>
<td>suramin</td>
<td>early SS</td>
<td>halt of production</td>
</tr>
<tr>
<td>melarsoprol</td>
<td>CNS</td>
<td>future production uncertain (environmental concerns)</td>
</tr>
<tr>
<td>eflornithine</td>
<td>CNS, Gambian</td>
<td>not produced</td>
</tr>
<tr>
<td>nifurtimox</td>
<td>CNS, Gambian</td>
<td>halt of production</td>
</tr>
</tbody>
</table>
Finally!
A solution for women who suffer from unwanted facial hair!
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
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
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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