Hurdles Faced in implementing quality clinical research in Human African Trypanosomiasis

Geneva Forum Toward Global Access to Health

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- Introduction to HAT
  - Epidemiology/Clinical picture
- DRC and Africa HAT situation
- Conduct of clinical research experience
  - Partners
  - Preparation/patients inclusion & TTT
  - Difficulties
  - Expectations
  - Win-win situation

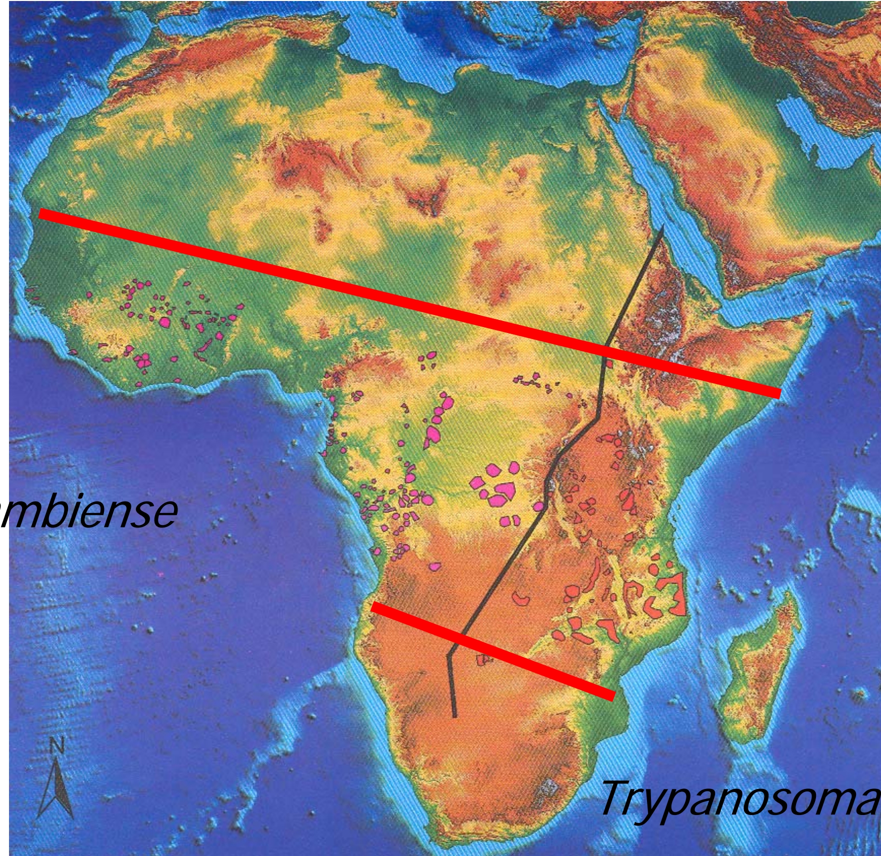
2 SPECIES OF HAT

CHRONIC Form

- West Africa
- Central Africa

Duration: years

Trypanosoma brucei gambiense



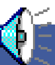
Acute Form

- Est Africa

Duration: max 6 months

Trypanosoma brucei rhodesiense

Geographic distribution: linked to the presence of tse tse fly



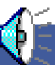
parasite: *Trypanosoma brucei gambiense*

vector: tse-tse fly

patients

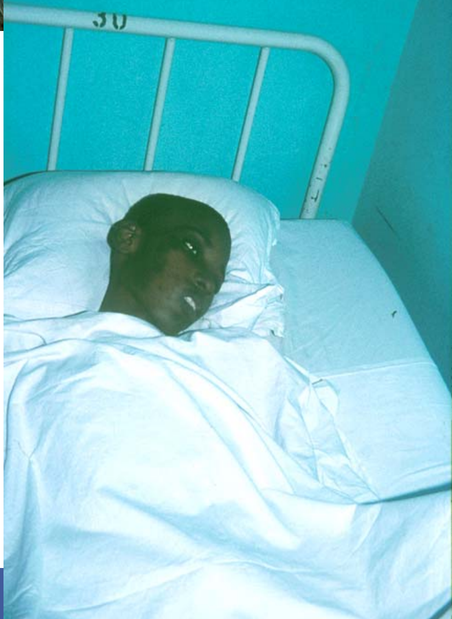
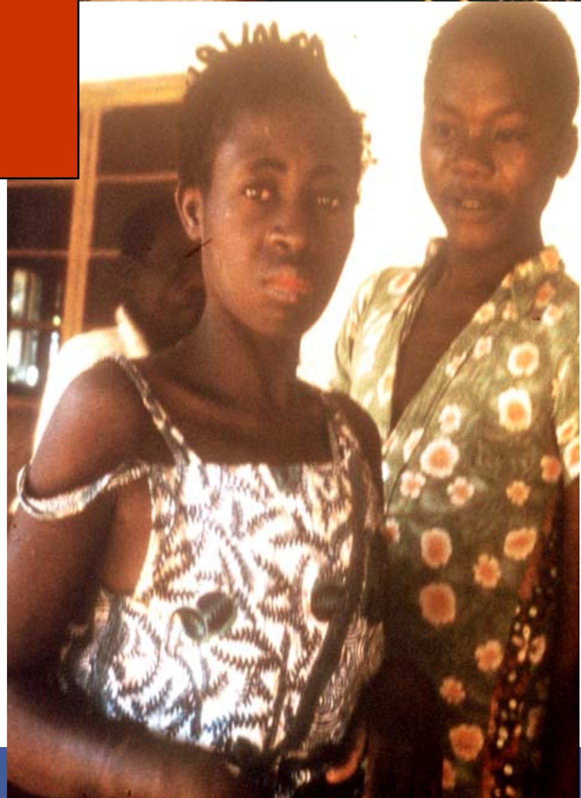
Healthy person

Le contact entre le parasite de l'homme, la mouche tse-tse et l'environnement conditionnent l'évolution épidémiologique

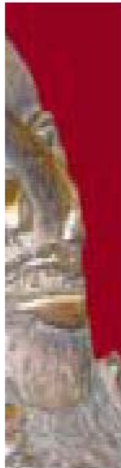


Stage 1 T.brucei gambiense

T.brucei gambiense
stage 2
apathy, unconcerned,
sleepy

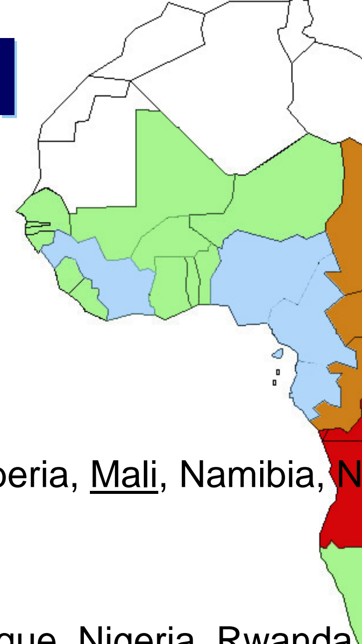
TRYPANOSOMIASE HUMAINE AFRICAINE
HUMAN AFRICAN TRYPANOSOMIASIS



	T.b. gambiense	*T.b. rhodesiense*
PHASE 1	Pentamidine	Suramine
PHASE 2	Melarsoprol	Melarsoprol
	Eflornithine	

WHO surveillance and control

Disease distribution and magnitude



●16 Countries reporting no cases

•Benin, Botswana, Burkina Faso, Burundi, Ethiopia, Gambia, Ghana, Guinea Bissau, Liberia, Mali, Namibia, N
Sierra Leona, Swaziland and Togo.

●12 Countries reporting under 100 cases (2%)

•Cameroon, Côte d'Ivoire, Equatorial Guinea, Gabon, Guinea, Kenya, Malawi, Mozambique, Nigeria, Rwanda,

Zimbabwe.

● 5 Countries reporting between 100 and 1000 cases (14%

•Chad, Central African Republic, Congo Tanzania and Uganda

● 3 Countries reporting more than 1000 cases (84%)

•Angola, Democratic Republic of Congo, Sudan

•In 2006, DRC has reported 8023 HAT cases out of 9223 in Afri

- NGOs
  - Médecins sans Frontières

- Institute of Tropical Medicine, Antwerp (IMTA)
- Swiss Tropical Institute (STI/UNC/LIH)
- Institut de Recherche en Développement (IRD)
- Centers for Disease Control & Prevention (CDC)
- Drugs for Neglected Diseases Initiative (DNDI)
- TDR
  - UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases

Preparation of clinical trials

- Site selection
- Authority approval
  - MoH, Ethics committee
- Information of responsibles & population
- Site improvement
  - Logistics
    - Improvement of laboratories & patient housing
  - Strengthening of local staff
    - Increase staff number
    - Teaching & training
- Case finding
  - Set up of mobile team

Conduct of clinical trials

Logistical improvement

Conduct of clinical trials

Logistical improvement

Conduct of clinical trials

Patient inclusion

- Inclusion of patients
  - Case search and diagnostic:
    - Mobile teams and Treatment centers
  - Clinical and para clinical evaluation:
    - Physician and technical lab assistant
  - Explication and approval of Informed consent:
    - Physician/Responsible person
  - Check of inclusion and exclusion criteria:
    - Physician/Responsible person
  - Completion of CRF:
    - Physician/Responsible person

Treatment of patients

- Application of drugs
- Samples collection
- Follow-up of patients during treatment phase
- Completion of case report form

Difficulties to conduct HAT trials

- Diagnostic
  - Low prevalence disease
    - Examination of many for few enrolled
    - Long-distance trips to find patients
- Informed Consent
  - Unknown before
  - Not or less accepted in our culture
  - Complicated approach

Sleeping sickness – Conduct of trials

Where are the patients ???

Selected teams only	**Viana (Angola)**	**Maluku (DRC)**	**Vanga (DRC)**
Persons screened total	10451	31491	12253
Total new cases	62	298	65
New cases 1st stage	6	115	31
Included	4	28	15
Excluded	5	88	16
Age	3	27	10
Weight	---	14	3
Abnormal ECG	2	11	---
Other reasons	0	36	3

Difficulties to conduct HAT trials

- Biological evaluation
  - Repeated blood sampling is hardly accepted by patients
  - Examinations often upset patient
    - Electrocardiogram
    - Blood analysis
- Need for close supervision
- Post therapeutical follow-up

Difficulties to conduct HAT trials

Summary

- Diagnostic (examination of many for few)
- Patients recruitment (MT, boat/4*4 car)
- Informed consent
- Repeated sample collection
- Close supervision (in country & outside team)
- Post treatment follow up 3,6,12,18 month>80%
- Security? Political stability?

Expectations

- Local capacity building
  - Increased number of adequate treatment centers
  - Strengthening of National programs in research
  - Training of ethical committees
  - Good clinical practice
  - Protocol development
  - Improve fixed laboratories & plan mobile labs for trials
  - Involvement of local medical schools (ARCEAU-RDC)
  - Data analysis

- The hope for better tools in **diagnoses**, **staging**, earlier detection of **treatment failures** and **new treatment …**

Win-win situation

- National expertise in the conduct of research
  - Capacity building
  - Better staff education
  - Support of local diagnostics tools production through study needs (INRB)
- Implementation of a national ethics committee
- Improved patient documentation
- Better understanding of the difficulties of participation in active case search, treatment and follow up
- Improvement of infrastructure:
  Equipment, construction and rehabilitation
- New partnerships
  - Interface between PNLTHA and other agencies to facilitate HAT projects: DNDI, FIND,

Special collaboration

DR Congo – STI Kinshasa Office and DNDI

« HAT Platform Newsletter »

Issue N°1, January 2007

Contents

- A silent anniversary
- Platform activities
- Progress report on clinical trial
- Diary-Events
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Editorial

This new information bulletin is designed to improve communication between HAT platform members. It will provide information relevant to the activities of the platform and the contributions received from each member state.
We wish a long life to this newsletter. We hope that after the inevitable teething problems, and with time and our combined efforts, it will become a reference too for all members of the platform as well as for all researchers working on human African trypanosomiasis.
Each member state will have to contribute to this newsletter with an article on its activities within the platform, or on an interesting subject related to sleeping sickness.
On behalf of the platform's coordination group, and from me, I would like to extend to all of you our best wishes for 2007, which I hope will be seen as a year of genuine achievements for our platform.

Dr. Kadima Ebeja Augustin, platform coordinator

Meeting of HAT platform in Nairobi, September 2006

A silent anniversary

History is being made. The Human African Trypanosomiasis (HAT) platform is not just a passing whim; it is an ambitious project which is now very much alive.
The first strategic meeting on reinforcing the capacities for clinical trials on sleeping sickness was held on August 16-17 2005 in Kinshasa, capital of the Democratic Republic of Congo (DRC). The meeting was organised by DNDi (Drugs for Neglected Diseases initiative), in collaboration with STI (*Institut Tropical Suisse*) and PNLTHA (*Programme National de Lutte contre la Trypanosomiase Humaine Africaine*). The main objectives of this meeting (held as a series of workshops) were to create a network of experts to exchange existing scientific and technical know-how in sub-Saharan Africa on clinical trials on sleeping sickness, and thereby help significantly the clinical trial capacities in the area.

EDITORIAL

In this second newsletter, the HAT Platform renews its communication efforts in order to rally all internal and external actors of the Platform to reinforce clinical trial capacities. Many thanks to those who submitted articles and have helped to publish this second information bulletin on time.

The Platform repeats the wish expressed early in the year, that "2007 be a year of concrete actions".

As always, comments and criticisms to improve the presentation of this bulletin are most welcome.

On behalf of the
HAT Coordination Team,

– Dr. Augustin Kadima Ebeja

1. HIGHLIGHT ON SUDAN

Human African Trypanosomiasis (HAT) appeared for the first time in South Sudan in 1906. The country has since experienced several epidemics, largely limited to the southern district of the Equatorial region. Recent HAT epidemics have been caused in part by the collapse of health services due to the civil war, which has raged in the region for the past fifty years. Continued insecurity hampers the efforts of the NGOs working to improve disease control. These difficult conditions, which have also prompted massive population movements, are responsible for the recent resurgence of several historical foci (Yei, Kajo keji, Nimule, Yambio) of human African trypanosomiasis.

Active and passive surveillance systems were used to monitor HAT in the country, but certain areas were not covered. Between 2002 and 2006, 8,568 people were diagnosed with and treated for sleeping sickness. A high number of relapses were recorded, particularly in cases treated with melarsoprol.

In the current post-war environment, there is an urgent need for essential measures, such as implementing active and passive screening, mapping the incidence of human African trypanosomiasis, as well as developing new treatment pro-

HAT Platform team in Kampala, Uganda

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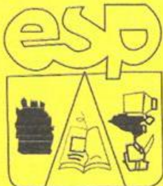
ARCEAU RDC

HBMM



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- All partenairs in the field (MSF/S,B

Thank you for your attention

MERCI
AKSANTI
SHUKRANI
OBRIGADO