

State of the art on Diagnosis and

Treatment of HAT



Pretoria - October 2nd, 2003

The way from empiricism to rationality and from
dogma to curiosity

Ibn Khaldun'

1406

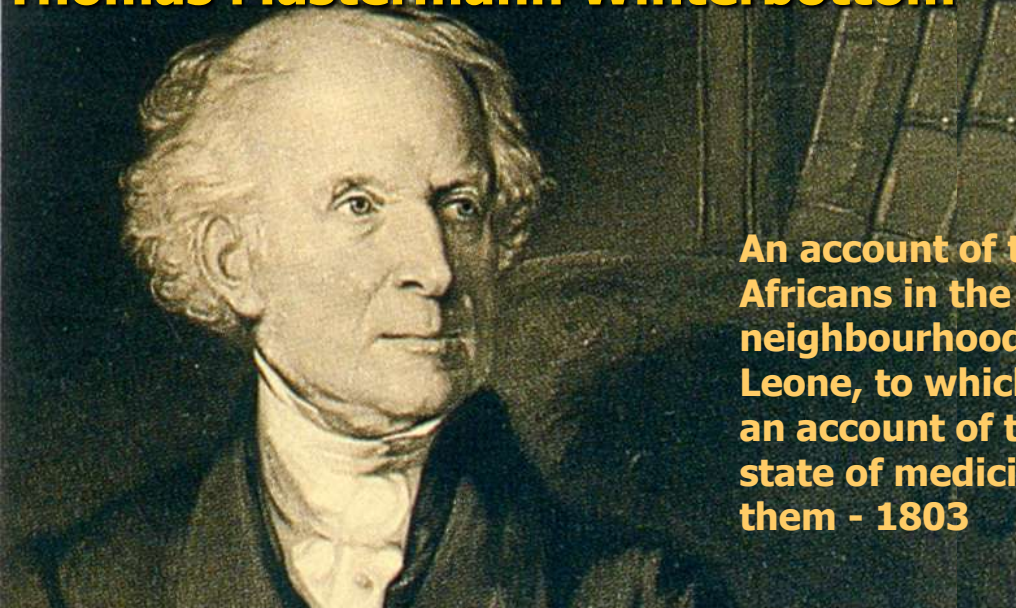
Kitab al-Ibar wa-Diwan al-mubtada wa'l-khabar

Mort du Sultan Mari Djata II (Soudan)

Edition Bulaq (Cairo), AH
1284/AD 1867, 7 vols;

ملكه ما بقصر الموالنة بلدي داركلا وقوة سلطانه فلقى منه منزه و ترجيا و وعدة
بالمظاهرة والقيام بخاره واصحبه الي بلده اخبرني وهو اللغة قال حكنا
بواكبة انا و ابو اسحاق الطويحي دون وزيرانه ووجه قومه فناخذ باطراف
الاخاديت فمستغ وكان يخفنا في كل منزل بطرف الماكل والحلاوات قال والذي
يجل علمه الله وجزئته من الوصايف خاصة التي عشر افا لاسية اقبية الريح
والحرير البياقي قال الحاج بوسن ترجمان هذه الامة بمصر هذا الملك منسبا
موسى من بلده ثمانين حملا من الثبر في كل حمل ثلاثة قناطير قال وانما يجيئون
على الوصايف والرياح التي اوطانهم فقط وانما الثغر العبد كالج فعلى المطايا قال
ان خدعه ورجعنا معه الي حضرة ملكه فاراد ان يتخذ بيتا كقعد سلطانه
بحكم السنا بحللا بالكلس لغرابيه بارصهم فاطرفه اواسحاق الطويحي منساقه من
الشكل استفرغ فيها اجادته وكان صناع البدن واصغر علمها من الكس والعالى
عليه بالاصابع الممقده مغناث من ابق المثنائي ووقعت من السلطان موقع الاستغراب
لفقدان صناعه السابار منهم ووصله بانتي عشر الفان منساقيل النبر منونه
عليها الي ما كان له من الابن والحل العبد والصلات السنه وكان بين هذا
السلطان منساقوسى وبين ملك المغرب تعهد من بني مرين السلطان الحسن
سوراصلة ومغناوات سفرت بينهما الاعلام من رحلات الدولتين واستجاب
صاحب المغرب من صناع وطنه وتخف مما ملكه ما يحدث عنده الناس زمانا
على ما يذكر عند مؤرخه بعث بها مع علي بن غانم امير المعقل واعيان من رجال
دولته ونوارت تلك الوصاية اعطاهما كما تساي واتصلت ايام منساقوسى
هذا خمس وعشرون سنة ولما شاهدك وفي امره ما لي من تعهد منساقوسى
ومعنى مغنا عند هم تحيد وهلك لاربع سنين من ولايته وولي امرهم من بعدك
منساقوسى من ابي بكر وهو اخو موسى واتصلت ايامه اربع وعشرين سنة
في هذا فولى من بعدك ابنه فسان سليمان وهلك لتسعة اشهر من ولايته
فولى عليهم من بعدك ماري جاطة ومنساقوسى واتصلت ايامه
اربعه عشر عامًا وكان شرف وال عليهم بما ساهم من النكال والعشرف وافتاد
الغرم واتخف ملك المغرب لعمده السلطان اباسامه بن السلطان الحسن بن
بالهدية المذكورة سنة ثنتين وستين وكان فيها الحويان العظيم المهديك
السنغري بارص المغرب المعروف بالزرارة يتحدث الناس بما اجمعه منه
من معترف الليلي والشاه في خيلانه ونعوته ذهرا واحبر في القاضية الثقة
ابو عبد الله محمد بن واسول من اهل بجلماسه وكان وطن بارص كوكوم من بلادهم
واستعملوه في خطه القضاها لقبية ثمان سنين وست وسبعين وسبعين واخبرني
عن فلوهم بالكثر مما كتبه وذكروني عن هذا السلطان جاطة انه امسك ملكهم
والف ذخيرتهم وكاد ان ينقض منساقوسى سلطانه قال ولقد انتهى الحال بهم في سرقة
وسد بره ان باع حجر النعنا الذي كان في جملة الذخيرين بخراينهم وهو حجر يزن
عشرين قطا لا مفعول من المعدن من غير علاجها لصناعة ولا تصفية بالنار
كانوا يرونه من القيس الذخير والغراب لندور مثله في المعدن فعرضه جاطة
هذا الملك المشرف على تجار مصر المترددين الي بلده وابنا عوه منه بالبحر الامان

Thomas Mastermann Winterbottom



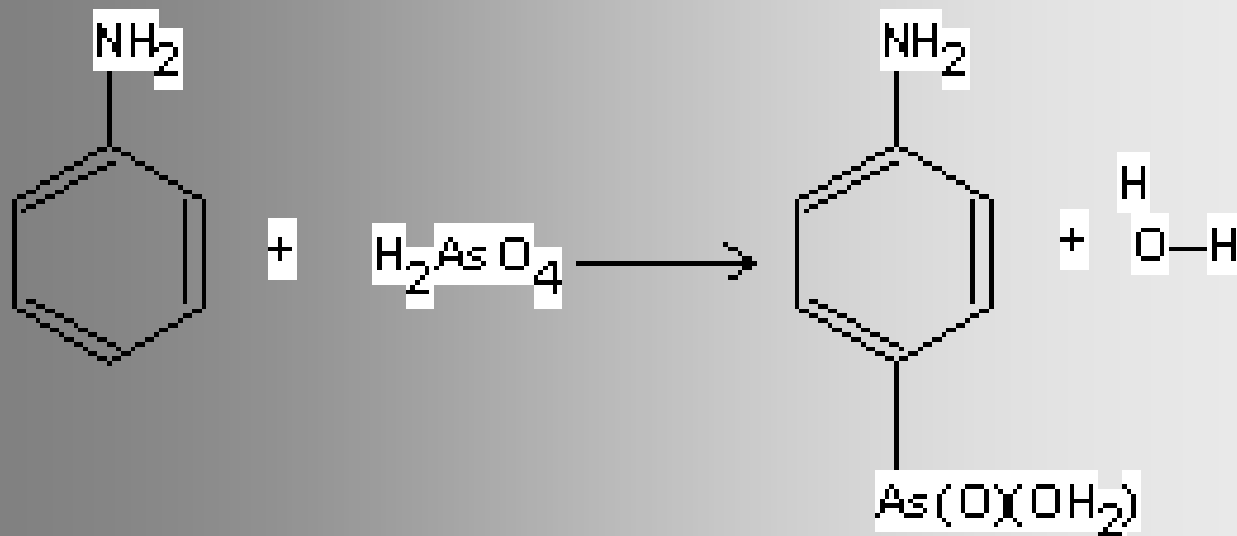
An account of the native Africans in the neighbourhood of Sierra Leone, to which is added an account of the present state of medicine among them - 1803



"The Africans are very subject to a species of lethargy, which they are much afraid of, as it proves fatal in every instance. The Timmanees call it marree, or 'nluoi, and the Bullems nagonlôe, or kadura; it is called by the Soosoo, Kee Kollee Kondee, or sleepy sickness, and by the Mandingoes seenoyuncaree, a word of similar import. This disease is very frequent in the Foo-la country, and it is, said to be much more common in the interior parts of the country than upon the sea coast. Children are very rare among free people, though it is asserted that the slaves from Benna commonly have a ravenous appetite, eating twice the quantity of food before the disease has continued some time, the appetite declines, and the patient is carried off in a few days. In some rare instances the patient is carried off in a few days before the commencement of this complaint, though probably, dependent upon the disease, however, appear to consider these tumours as a symptom, and quit of them as soon as they observe any such appearances. The disease is treated by the application of blisters and of setons has been employed but with little success, usually proves fatal within three or four months. The natives make use of a plant called in Soosoo, finka, are boiled for some time in water and is covered over with cotton clothes, a process which never fails to give relief, and is persisted in for 'a considerable length of time, and is given in the complaint.

Small glandular tumours are sometimes observed in the neck a little before the commencement of this complaint, though probably, depending rather upon accidental circumstances, than upon the disease itself. Slave traders, however, appear to consider these tumours as a symptom, indicating a disposition to lethargy, and they either never buy such slaves, or get quit of them as soon as they observe any such appearances.

1863



De l'action de la
chaleur sur
l'arséniate d'aniline
et de la formation
d'un anilide de
l'acide arsénique



Antoine Béchamp



Premiers laboratoires



Photo Courbouin - Cliché de la Dépêche coloniale illustrée. In G. Martin, Leboeuf, Roubaud. Rapport de la Mission d'Etudes de la maladie du sommeil au Congo français. 1906-1908. Masson et Cie 1909. Paris



(Photo Courbouin).

(Cliché de la *Dépêche coloniale illustrée*)

Fig. 65. — Une scène de fétichisme dans un village éprouvé par la maladie du sommeil.

H.W. Thomas : Use of the of the Béchamp's anilide to cure sleeping sickness

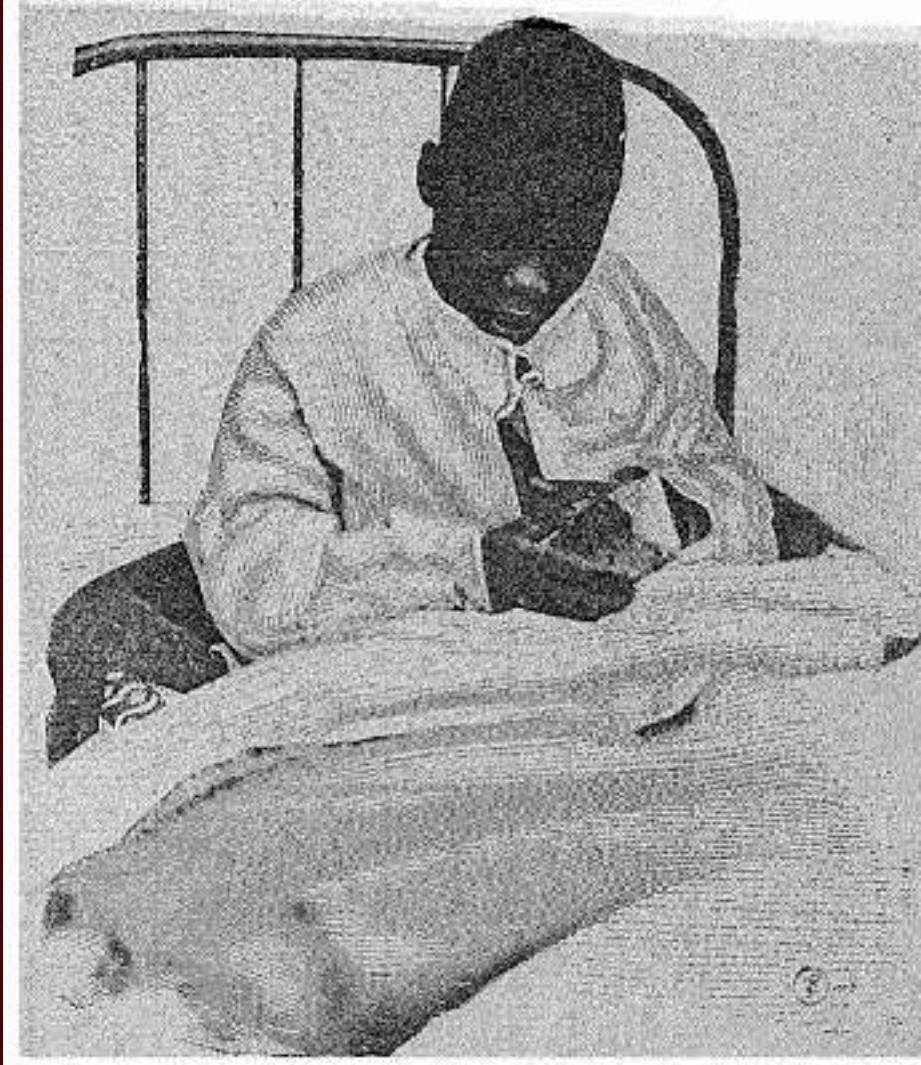
«magic bullets»

...treatment of trypanosomiasis and other protozoal diseases and produced trypan red, which was, as his Japanese assistant Shiga showed, effective against trypanosomes.

He also established, with A. Bertheim, the correct structural formula of atoxyl



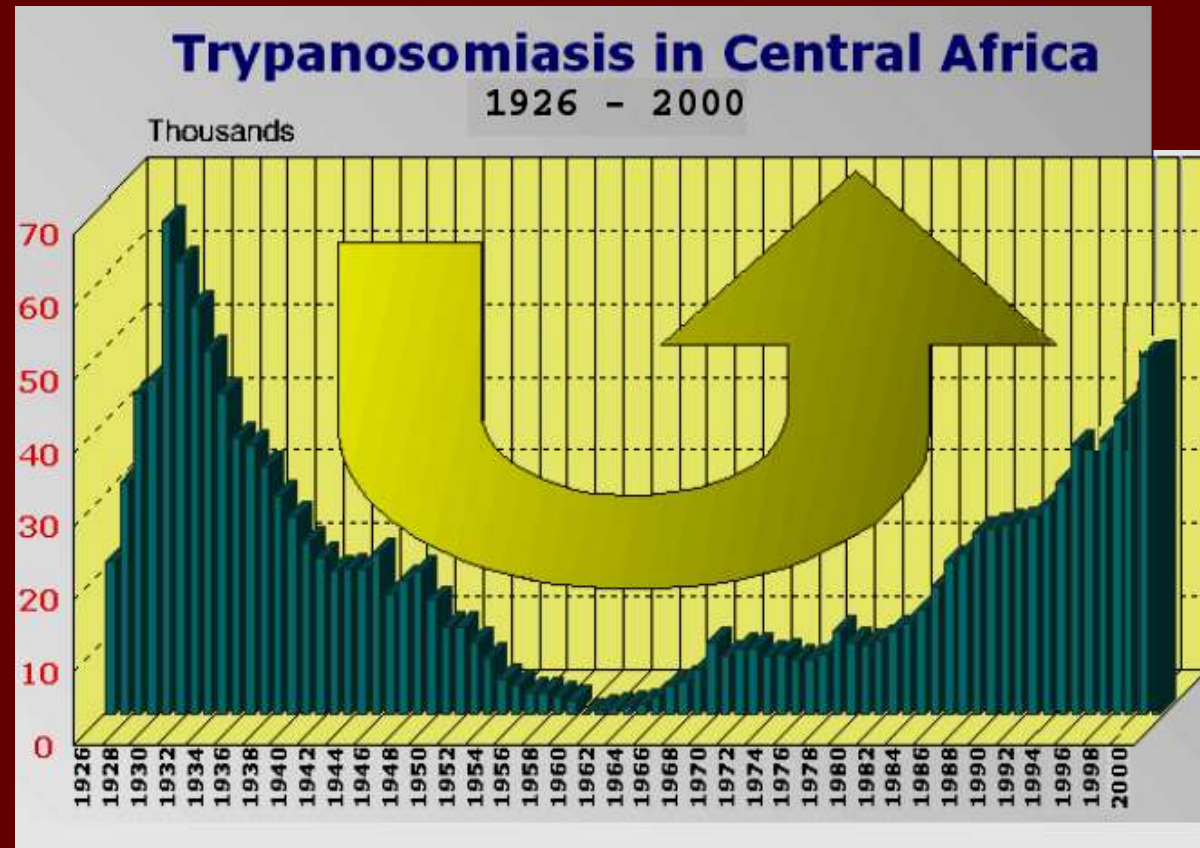
Paul Ehrlich 1854-1914



First patients treated
in London - 1903

1965

The disease is eliminated as a public health problem



networks

The WHO SS treatment and drug resistance network

A coherent approach of the concept of access to treatment

Drug development
Clinical trials
Drug delivery
Safe administration
Treatment centers rehabilitated
surveillance of TT and resistance
Early diagnosis
field activities
Training



Where is the hospital?



21 3 2002

HUMAN AFRICAN TRYPANOSOMIASIS



**No electricity, no water, no technician, no drugs...
Closed.....**

HUMAN AFRICAN TRYPANOSOMIASIS



HUMAN AFRICAN TRYPANOSOMIASIS



HUMAN AFRICAN TRYPANOSOMIASIS

CLINICAL SIGNS



Fever
Pruritus
Headaches
Muscular pains

Cervical
Adenopathies



Low predictivity

HUMAN AFRICAN TRYPANOSOMIASIS

Screening



HUMAN AFRICAN TRYPANOSOMIASIS

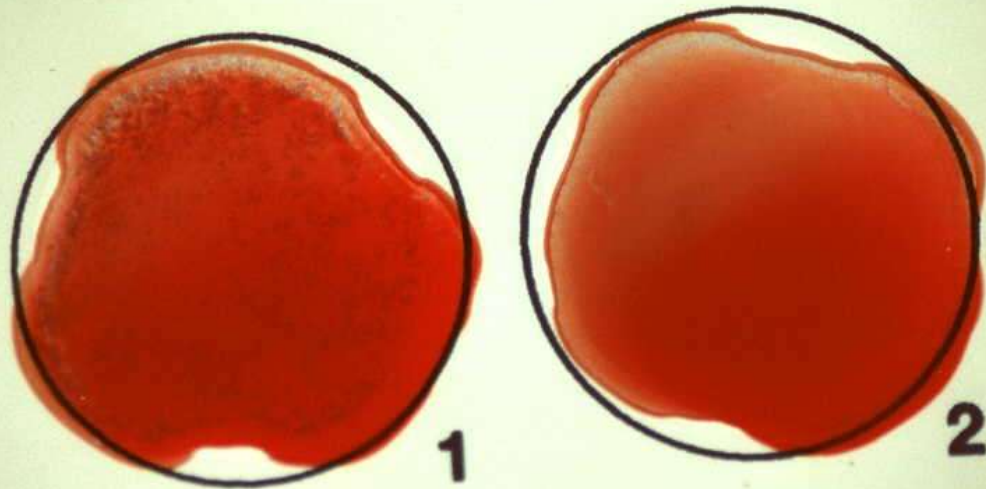


Screening tests

CATT

Card Agglutination Trypanosomiasis Test

Not enough specific



1977:

N. Van Meirvenne & E. Magnus

HUMAN AFRICAN TRYPANOSOMIASIS

DIAGNOSTIC



HUMAN AFRICAN TRYPANOSOMIASIS

**Gland Juice
examination**

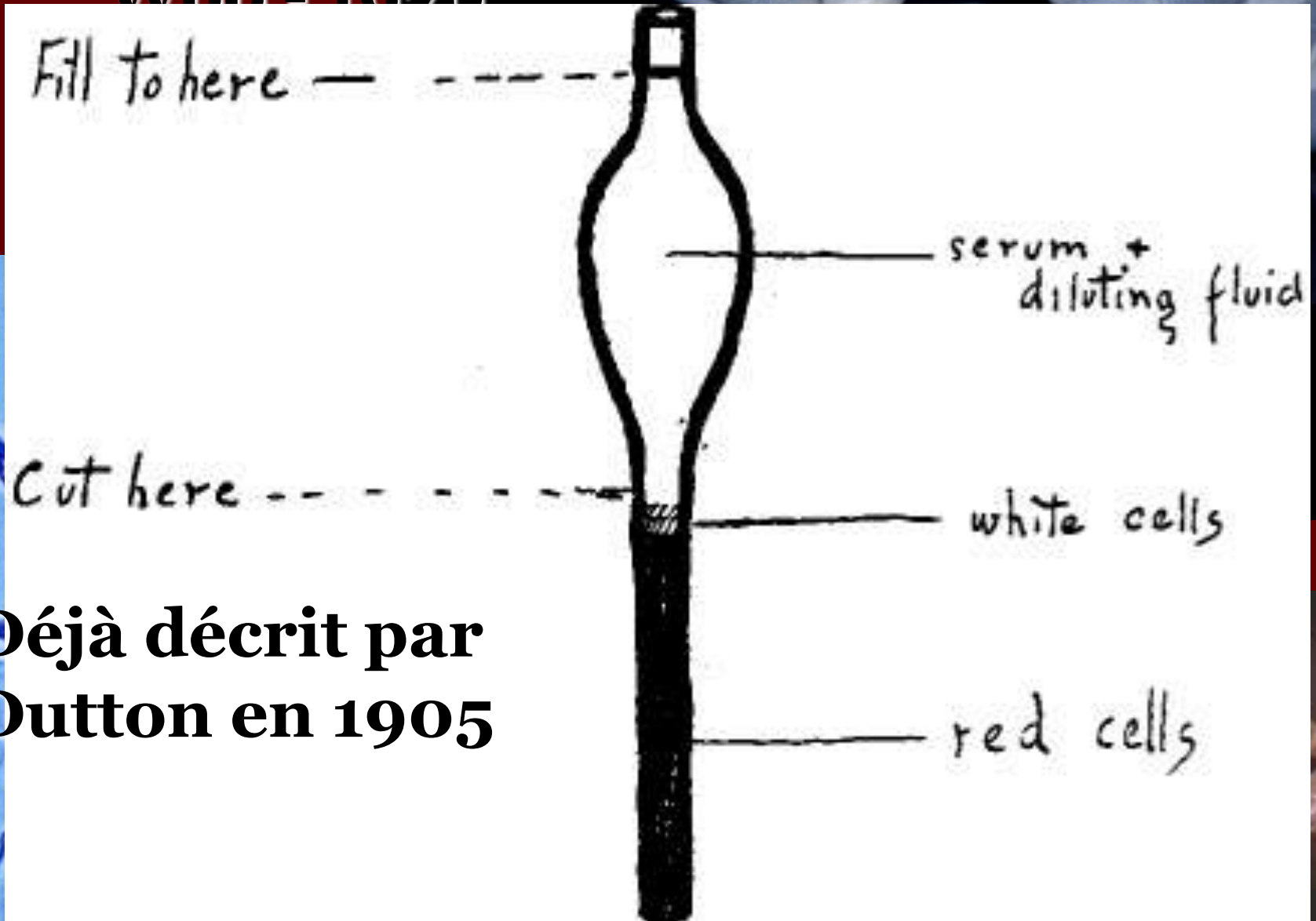
DIAGNOSTIC



Low sensitivity

HUMAN

Woo - 1970



**Déjà décrit par
Dutton en 1905**

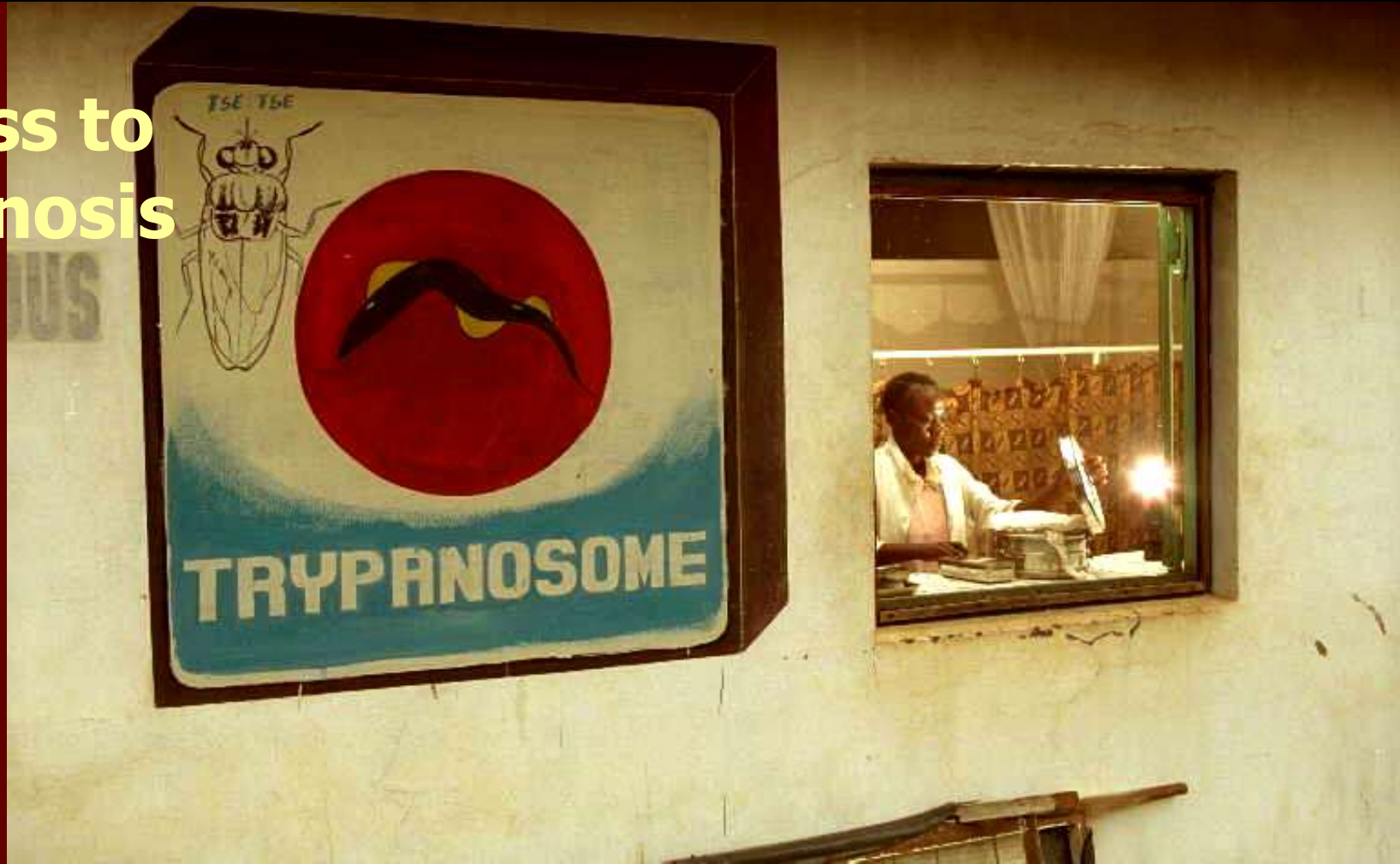
DIAGNOSTIC

Lanham - 1968

**Mini - anion
exchange column**

HUMAN AFRICAN TRYPANOSOMIASIS

Access to diagnosis



- Access to early diagnosis
- Access to systematic screening
- Access to diagnosis centre
- Access to efficient tests

HUMAN AFRICAN TRYPANOSOMIASIS

STAGING

CSF examination

Criteria > 5 cells/mm³



HUMAN AFRICAN TRYPANOSOMIASIS



HUMAN AFRICAN TRYPANOSOMIASIS

T.b. gambiense



T.b. rhodesiense



Pentamidine

Suramin

Melarsoprol

Eflornithine



HUMAN AFRICAN TRYPANOSOMIASIS

Treatment

T.b gambiense

Pentamidine

200 mg/vial

daily or every other day intramuscular injection, 7 injections, 4mg/Kg/day

adverse reactions (hypotension, diabetis, hypersalivation, nephrotoxicity)

idine Isethionate BP 200 mg

er for intravenous infusion
muscular injection



Development 1938-1944

HUMAN AFRICAN TRYPANOSOMIASIS

T.b. rhodesiense

Suramin (1920)
vials, 1g

single weekly intra-muscular injection, for 6 weeks, 20mg/Kg
some adverse reactions (nausea, vomiting, urticaria - rarely, renal damage and exfoliative dermatitis)



HUMAN AFRICAN TRYPANOSOMIASIS

Melarsoprol

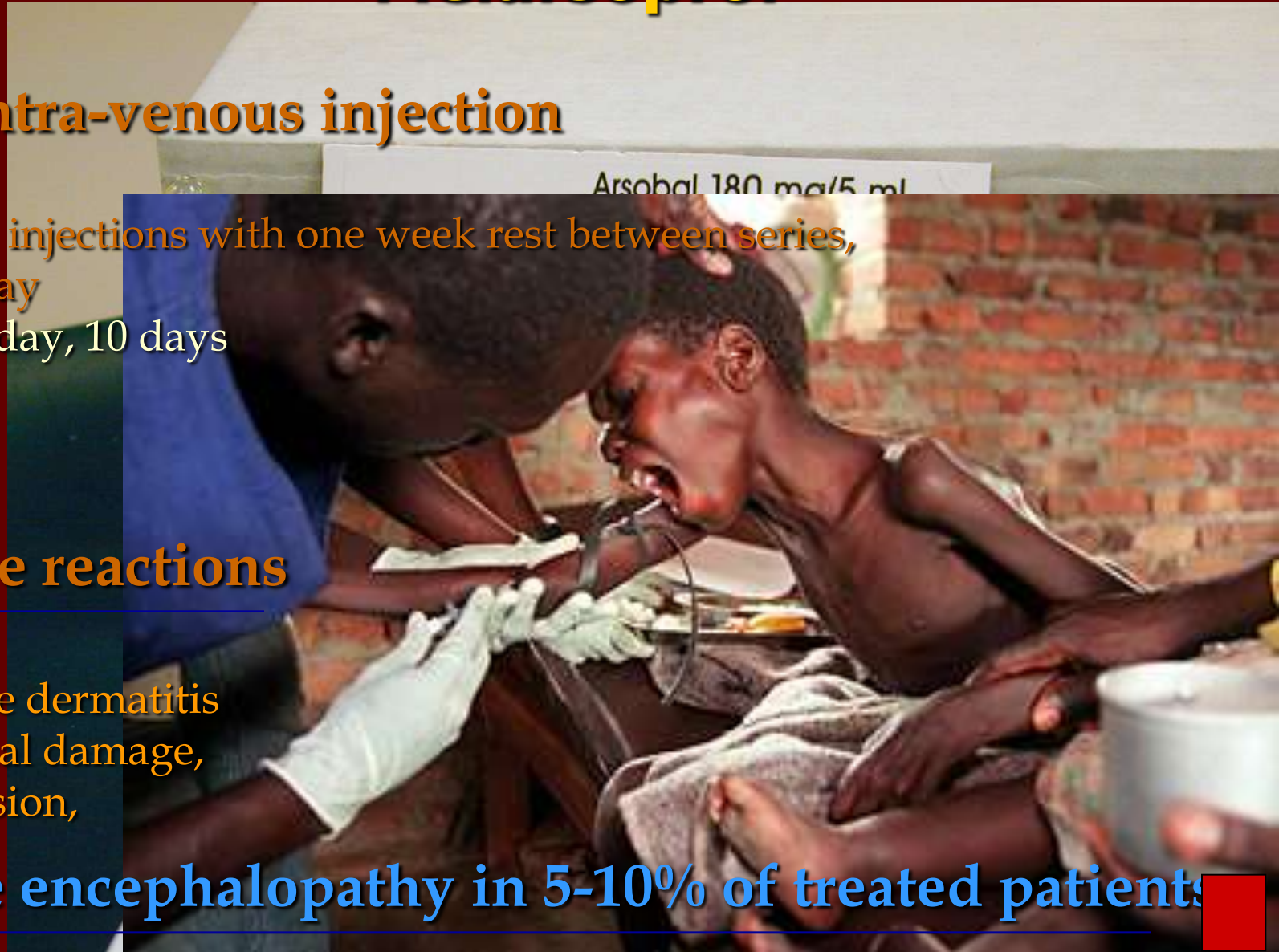
strictly intra-venous injection

- 3 series of 3 injections with one week rest between series, 3,6mg/kg/day
- 2,2mg/kg/day, 10 days

adverse reactions

exfoliative dermatitis
myocardial damage,
hypertension,

reactive encephalopathy in 5-10% of treated patients



HUMAN AFRICAN TRYPANOSOMIASIS



HUMAN AFRICAN TRYPANOSOMIASIS

Miracle drug curing sleeping sickness

London Observer Service

Dramatic success is being achieved in the battle against one of Africa's oldest scourges, sleeping sickness.

Patients in the last stages of the disease and facing certain death have been saved by a new drug known as DFMO, now under trial in several African countries.

The cures achieved have been so rapid and spectacular that DFMO is being called "the resurrection drug": Two years after treatment, patients for whom there seemed no hope are leading normal lives and show no further symptoms of the disease.

DFMO has also proved successful in treating one of the most common causes of death among AIDS patients, *Pneumocystis carinii* pneumonia. The drug does not cure AIDS but has been shown to be effective in prolonging life for patients whose pneu-

monia infection had defeated other drug treatments.

The latest results of the trials of DFMO were reported at a recent meeting at the World Health Organization's headquarters in Geneva by the Special Program for Research and Training in Tropical Diseases, which has financed much of the research. The program is funded by the WHO, the World Bank, the U.N. Development Program and a number of donor countries, including the U.S. and Britain.

Sleeping sickness is a parasitic disease carried by the tsetse fly and is endemic in 36 countries across the center of Africa. Fifty million people are at risk, and increasing numbers have been contracting the disease. About 100 new cases are reported each year, although this is certainly a considerable number.

P

the joints and a range of other symptoms including the extreme lassitude which gives the disease its name. Victims left untreated show mental deterioration, incontinence and seizure, and ultimately die.

The cause of the disease is a microscopic parasite, called a trypanosome, transferred to the bloodstream by the tsetse fly. There are a variety of different trypanosomes, responsible for two distinct human diseases and one affecting animals.

Trypanosomes are quick-change artists, escaping destruction by the human immune system through their remarkable

ability to alter their surface covering, or "coat." No sooner has the immune system identified a trypanosome's coat and mobilized antibodies to deal with it than the parasite changes to a new coat and escapes.

For the same reason, vaccines against trypanosomes do not offer much hope. Protection against a parasite with such a bewildering range of disguises — more than 100 coats, all different — cannot be provided by any imaginable vaccine in present medical knowledge.

Existing drugs can kill the parasites, but may also kill the patients.

Administration:

400mg / Kg / day

1 perfusion each 6 hours, during 14 days

1 perfusion each 6 hours, during 7 days



HUMAN AFRICAN TRYPANOSOMIASIS

Nifurtimox (Lampit®) Tablets 120mg
*(has been used in *T.b.gambiense*)*

• **per os, 5 to 7 mg/Kg/day, 3 time/day, 14 to 21 days**

adverse reactions (toxic effects involving central and peripheral nervous system)

but not registered for sleeping sickness





Fighting ostracism....

HUMAN AFRICAN TRYPANOSOMIASIS

Access to treatment facilities

- Distance and transportation
- Equipment
- Trained medical staff
- Follow-up



HUMAN AFRICAN TRYPANOSOMIASIS

Access to a safe and efficient treatment

- Drug delivery
- Treatment failure and resistance
- Adverse effects management
- Administration schedule
- Safer drugs



Drug supply

WHO



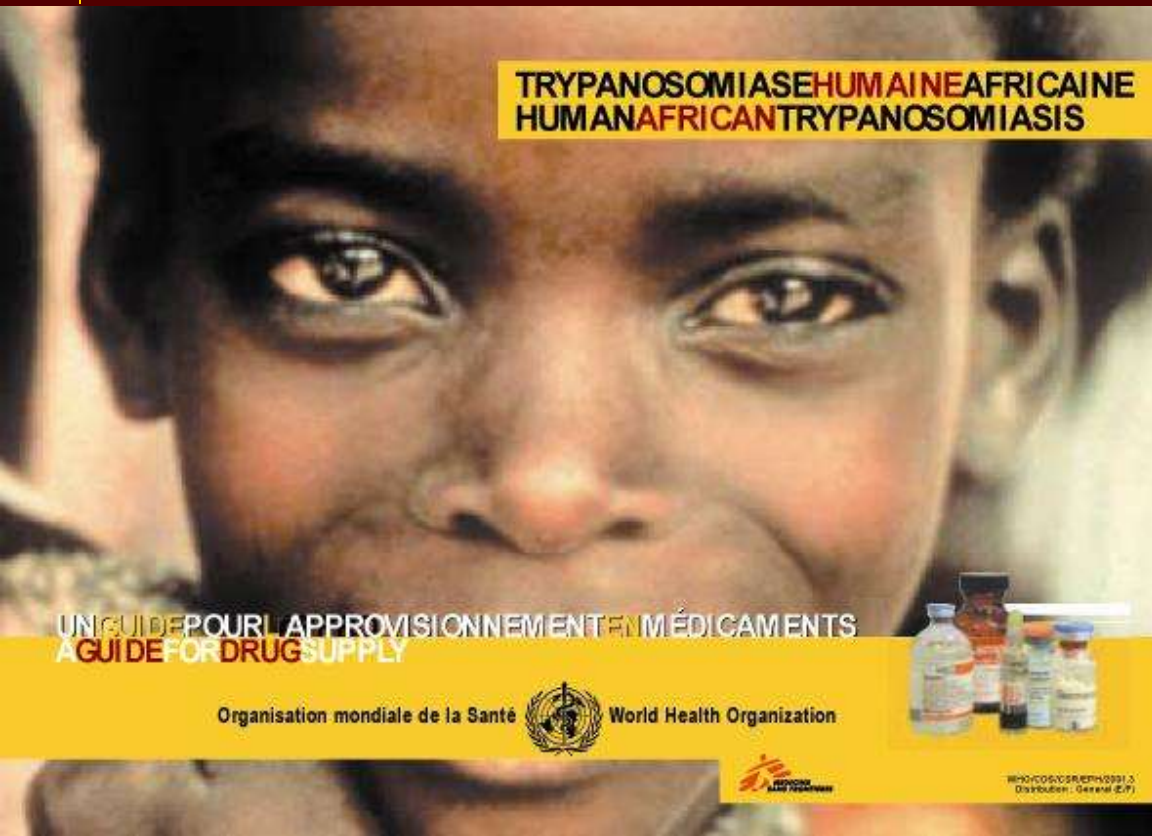
MSF



Countries



Patients



Management of drugs
Reporting
Drugs forecast

Act on the disease neglect

Act on strategies and policy



Implement systems to:

Enable populations to meet health capacities

Enable existing health capacities to absorb new tasks

Ensure health care delivery closer to the populations

reaching populations



Strengthening programmes towards sustainability

From fragmented epidemiological knowledge to a complete vision



Revival of weak programmes

*Creating conditions for
involvement of donors*



From effective drug delivery to effective access to treatment

Administer the drug as quickly as possible after diagnosis



Synergizing links between Control, Surveillance and Research



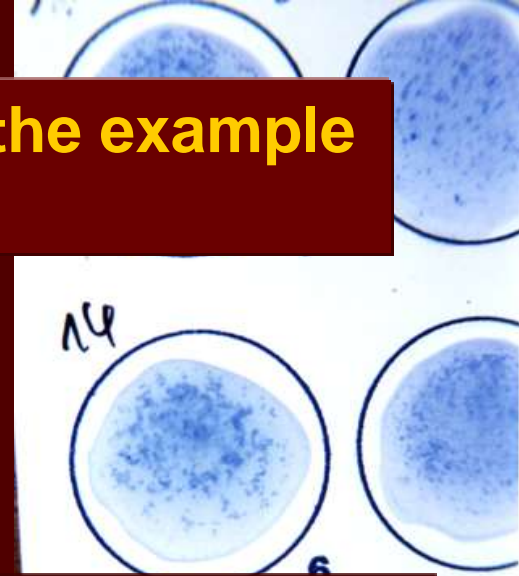
Research activities carried out or supported through the WHO SS treatment and drug resistance network

Initiate new research initiatives

Offer the best conditions to research teams in the field

DNDi and African DNDi established

Opening ways for new initiatives - the example of diagnostic tools



A new initiative to develop new diagnostic tools is being prepared

A working group has been established with CPE, TDR, IMT, a manufacturer and others. A PDT will be established.

3 actions are identified:

- short term: Latex IgM
- Medium term: Dipstick
- Long term: Development of synthetic peptides antigens

Looking at socio-economic aspects

Refining and Extending DALY Calculations for *T. b. rhodesiense* and *T. b. gambiense*



Millions of DALYS

HIV	70
Malaria	32
Respiratory diseases	33
Diarrheal diseases	32
Measles	18
Tuberculosis	16.5
Trypanosomiasis	10-16



Strengthening credibility

Developing more actions with more partners

The example of Bayer

- Suramin donation
- Nifurtimox for compassionate use
- Nifurtimox label extension

Nifurtimox for Chagas disease



Bringing in more partners

DiaMed Diagnostic

The example of the ITFDE

Civil society involvement

Hope Unity Harmony Hope Unity Harmony Hope Unity Harmony

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Please help them

