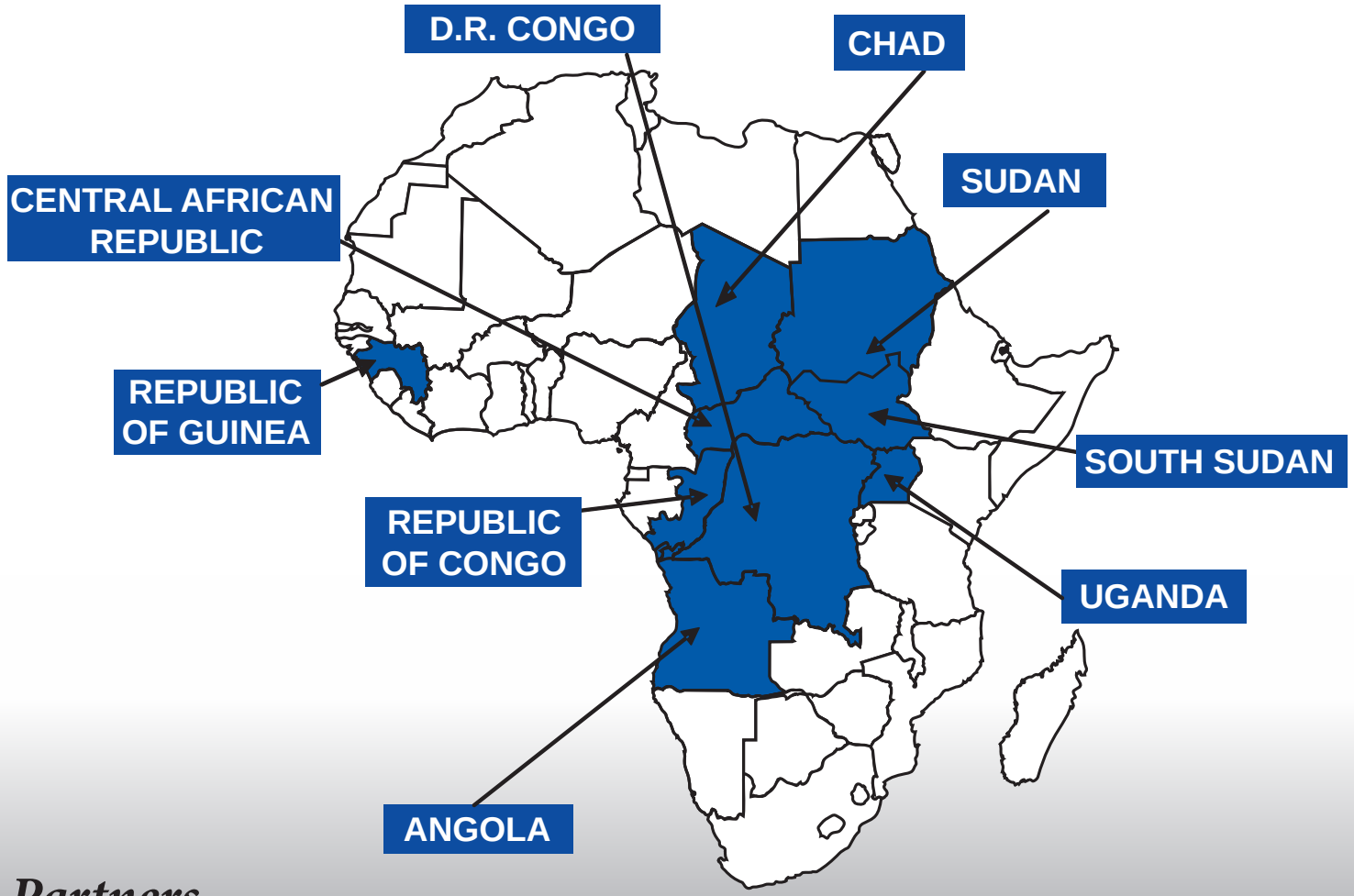
HAT Platform

REGIONAL PLATFORM FOR CLINICAL RESEARCH

NEWSLETTER N° 17, June 2016

SLEEPING SICKNESS NATIONAL CONTROL PROGRAMS : MEMBER COUNTRIES



Partners

Others partners

International and national research groups : ITMA, INRB, CDC, TRC-KARI, etc.

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Our thanks to Violaine Dallenbach and Louise Burrows for proofreading of the newsletter

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Editorial

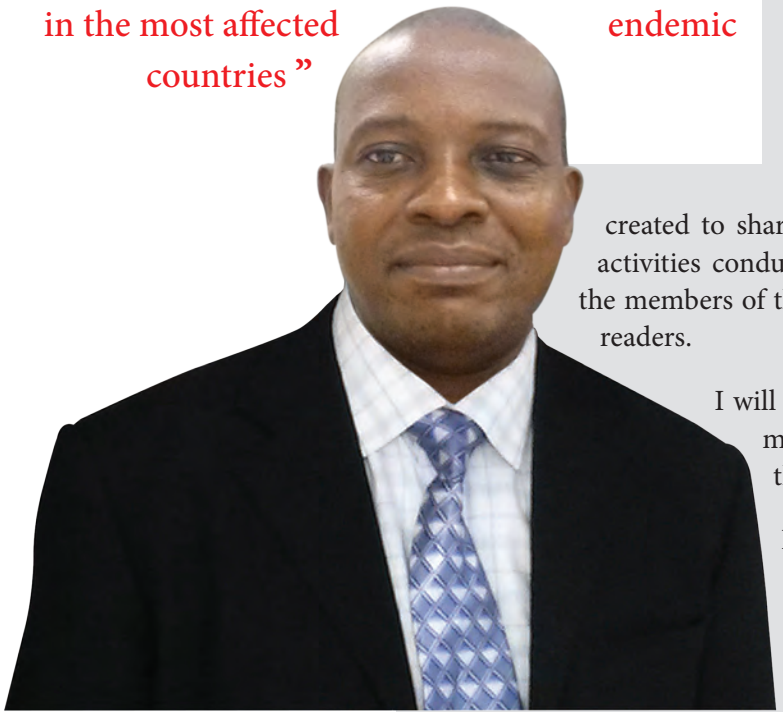
Presentating the new coordinator

Dear members of the HAT Platform and dear readers, my name is Dr. Florent Mbo Kuikumbi, the new coordinator of the HAT Platform.

To start with, I would like to pay a warm tribute to Dr. Augustin Ebeja, first coordinator of the HAT Platform, for his outstanding work since the Platform's creation in 2005.

Before joining the HAT Platform, I worked for 12 years as a provincial coordinating physician for the DRC National HAT Control Programme. I also worked as a coordinating investigator and co-investigator for clinical trials and operational research studies on human African trypanosomiasis.

> "The regional HAT Platform focuses on strengthening clinical or operational research capacity in human African trypanosomiasis in the most affected endemic countries"



The regional HAT Platform focuses on strengthening clinical or operational research capacity in human African trypanosomiasis in the most affected endemic countries, and its objective is to provide the population of these countries with diagnostic tools (simple, sensitive and adapted) and therapeutic tools (effective and adapted to both stages of the disease).

The HAT Platform Newsletter was created to share information on control and research activities conducted in the different countries with all the members of the HAT Platform, our partners and our readers.

I will work closely with all focal points of the member countries and all the partners of the HAT Platform.

I wish our HAT Platform every success.

Dr. Florent Mbo Kuikumbi

Report on the regional HAT Platform steering committee meeting, N'Djamena, 13 September 2015

Members of the HAT Platform steering committee during the meeting, 13 September 2015, N'Djamena, Chad

The steering committee, which oversees the smooth running of the Platform, met on September 3, 2015 in N'Djamena, Chad, in a parallel meeting to the 33rd International Scientific Council on Trypanosomiasis Research and Control (ISCTRC). All the representatives of endemic member countries were present, i.e. Angola, Central African Republic, Democratic Republic of the Congo, Republic of the Congo, Sudan, South Sudan, Guinea and Uganda. Six of our partners attended the meeting (IRD, Edinburgh University, WHO, MSF, DND*i*, and FIND).

The meeting's agenda is described below.

- **Review of the first semester of activities 2015**
  - Distribution of Newsletter N° 16
  - HAT training in the Dinamadji district, Chad
  - Supervisory training in Congo Brazzaville
  - HAT Platform support for the investigator meeting and workshop to plan the activities of the DRC national HAT control Platform
  - Recruitment of the new HAT Platform coordinator
- **Planned activities in the second semester 2015:**
  - Preparation and finalization of Newsletter N° 17
  - Organization of HAT training in South Sudan
  - Organization of the Platform steering committee meeting in N'Djamena
  - Organization of the HAT Platform participation in the 33rd ISCTRC in N'Djamena
  - Support of the scientific meeting of the DRC national HAT control programme (28-29 September, 2015)

- Collection of the remaining records, training reports and supervisory trainning reports (Chad, Congo Brazzaville)
- Preparation of a HAT training project in Angola in 2016 to be submitted to the Gulbenkian foundation to apply for funding
- Visits to review the HAT Platform activities with the member countries over the past three months
- Preparation of the annual action plan 2016
- Coordinator training (clinical trials and other training courses, provided in English in one English-speaking country)
- Post-training support of Dr Mariame Camara in Guinea

The member countries presented their country's epidemiological situation as well as their activities and their needs in terms of clinical research, including strengthening research methodologies.

The following recommendations were made:

1. Finalize the HAT Platform's status. A 3-month period was granted to the coordinator to reply.

2. Member countries expressed the need to harmonize and standardize the HAT screening algorithm at the initiative or under the leadership of the World Health Organization.

3. Strengthen the recommendations of the previous meeting:

   – Designate a person to ensure that these recommendations are implemented

   – Define the terms of reference and plan the roles

4. Advocate that the partners provide support to Angola, currently suffering under budgetary restrictions.

Mariette Dethoua, Ayak Chol and Florent Mbo

Members of the HAT Platform steering committee during meeting, 13 September 2015, N'Djamena, Chad

This conference was held in N'Djamena on September 14-18, 2015, in the large hall of the Palais des Congrès, under the patronage of His Excellency the Prime Minister of the Republic of Chad, in conjunction with the African Union, and under the coordination of the Inter-African Bureau for Animal Resources.

Participation in the 33rd Conference of the International Scientific Council on Trypanosomiasis Research and Control (ISCTRC)

a) Summary of the conference

- The country reports highlighted the renewed interest and growing commitment from African governments to tsetse fly and trypanosomiasis control.
- Significant progress has been achieved in the quantification of tsetse infestation and disease prevelance.
- The tools and methods developed by the scientific community are widely used by the affected countries.
- Impressive results in vector control have been reported in the countries where tsetse control measures are implemented, particularly Zanzibar, Botswana, Kenya, Ghana, Mali, Ethiopia, Uganda, Burkina Faso and Senegal.
- The participants insisted that these advantages will last only if more robust and concerted measures between the countries are implemented.
- The WHO laid out a roadmap for the elimination of human African trypanosomiasis due to *Trypanosoma brucei gambiense* by 2020, and for the elimination of disease transmission by 2030.
- A report from FIND (Foundation for Innovative New Diagnostics) outlines the progress made in the development of a test for second-stage human African trypanosomiasis, based on the presence of the neopterin biomarker in cerebrospinal fluid, and which could be used both to stage the disease and to confirm its cure.
- Several endemic countries implemented strategies and passive screening tools integrated within their healthcare systems, to diagnose the disease in villages where populations are at risk, thereby improving control of the disease.
- The participants described the progress achieved in tsetse and HAT control following the implementation of public-private partnerships.

- The R&D reports from the private sector and international Organizations (FAO, IAEA, ICIPE, etc.) show that these entities have become increasingly sensitive to the needs of affected countries. Rapid diagnostic tests, medicinal products and other technologies have reached various stages of their development.
- The participants also explained that drug resistance remains a problem in the management of animal African trypanosomiasis, but they also praised the investments made by the partners to solve this problem.
- The need to strengthen regulatory controls on import and use of trypanocides was highlighted.

b) Participation of HAT Platform members in the 33rd ISCTRC:

Presentation by Dr. Veerle Lejon on the research activities of RID (*Research Institute for Development*, France).

1. Increased vector control

The study comparing two areas (with and without vector control) showed that the combination of vector control and medical control reduces the transmission of gambiense trypanosomiasis and is helping accelerate the process towards the elimination of the disease (Courtin et al. 2015).

2. Diagnosis and monitoring strategies

This project focuses on trypanolysis used as a marker for contact with *T.b. gambiense*. Trypanolysis positivity in CATT-positive subjects was proportional to the prevalence of the disease in the foci.

This study suggests that trypanolysis can be used for the management of individual cases and to define control strategies.

In terms of passive surveillance, a project is being conducted in collaboration with the World Health Organization on the integration of HAT monitoring and control within the health services of several countries (Burkina Faso, Guinea, DRC, Mali and Niger). In this project, peripheral health centers refer suspected cases (clinical suspicion) to the referral health centers, which perform a serological screening test before referring the patient to a diagnostic and treatment center, and a trypanolysis center.

3. Epidemiological data

Researchers examined cases of spontaneous recovery and asymptomatic carriers in human African trypanosomiasis. Based on their experience in the field in West Africa, on the follow-up of patients who refused treatment for 10 years in Ivory Coast, and on the follow-up of trypanolysis-positive suspected cases (over 10 years in Ivory Coast and 2 years in Guinea), the researchers have come to the conclusion that infection outcomes are more complex than it seemed. They also described the natural course of the infection, showing that HAT is not always fatal and that certain individuals are able to control the infection without become ill.

They emphasized the role of untreated asymptomatic carriers and on their impact on transmission or possible resurgence of HAT infection.

Florent Mbo




iLED microscope camera

Microscopic imaging enables diagnosis validation in clinical trials

Presentation at the 33rd ISCTRC on 15 September 2015, in N'Djamena, Chad, by Sophie Delhomme, Antoine Tarral, Josès Dinanga, Wilfried Mutombo, Digas Ngolo, Patient Pati Pyana, Pascal Carpentier, Olaf Valverde Mordt, and Nathalie Strub Wourgaft

An iLED microscope camera takes photos and mini-videos to document and archive HAT diagnosis and follow-up, as it is impossible to store fresh slides preparations. To save and store these photos and videos, we use the electronic library application PowerFolder.

To validate the HAT diagnosis, we use photos of the parasite identified on a slide after staining, and the Fuchs-Rosenthal chamber to count WBSc in CSF. Short 2-5 second videos, showing a trypanosome in a fresh preparation (CTC, mAECT, MSC, lymph node on a slide) are also used.

How are documents stored?

The documents are saved on an SD memory card. Each one contains a set of numbers and letters provided directly by the microscope:

Example for a photo:
F911BA_20140106_120808_432

Example for a video:
/2014-09-04/20140904_182440_227.h264

These codes are unique and cannot be modified, which preserves their traceability.

In the laboratory, relevant photos are taken at each patient visit during clinical trials. A register is created and maintained to match photos and videos with the corresponding patient's codes and visits. These photos and videos are then transferred to the investigator as well as to the registry. For each patient and each visit, the investigator creates an electronic folder (e.g. 607001-V12M) and saves the photos and videos for each patient separately for each trial.

To view examples of short videos, click on the following:

Clip 1 (100X mAECT): https://www.youtube.com/watch?v=7s2zvVGyzdE&feature=youtu.be
Clip 2 (200X Fuchs-Rosenthal chamber): https://www.youtube.com/watch?v=bnsDmJISf2Q&feature=youtu.be
Clip 3: (400X lymph node aspirate): https://www.youtube.com/watch?v=EeXil-hx_Gg&feature=youtu.be

Olaf Valverde

Update on DND*i* HAT Clinical Program

There are 3 ongoing clinical trials of fexinidazole:

- FEX004: Phase II/III pivotal study on stage 2 HAT in adults (n=394). Inclusions were completed in April 2015. The primary endpoint is the cure measured at 18 months follow-up, but patients' visits continue until 24 months.
- FEX005: Adult patients with stage 1 and early stage 2 HAT (n=230). Inclusions were completed in September 2015.
- FEX006: Children 6-14 years old, all stages (n=125). Inclusions were completed in January 2016.

The primary endpoint for the last two trials is measured 12 months after the end of treatment and follow-up is maintained until 18 months.

The submission of the fexinidazole regulatory file, including data from all three trials, is expected early 2017, even though the last follow-up visit is scheduled for mid-2017. The submission process will start with the European Medicines Agency, and once their scientific opinion has been received, an application for marketing authorization will be filed with the national authorities of endemic countries, starting with the Democratic Republic of the Congo.

As in 2014, the clinical trials require substantial screening work to include 153 patients with stage 2 HAT. DND*i* funded the active screening activities, which enabled 9 mobile teams to screen 409,730 individuals, and the clinical trial sites and surrounding health structures to screen a further 62,047.

A new fexinidazole trial is in its advanced planning stage:

- FEX009: Effectiveness and safety of fexinidazole administered to adult and paediatric inpatients and outpatients, in an open cohort (n= 174). Expected to start in July 2016.

The biggest difference between this trial and the previous ones is that some of the patients will be treated at home. This will allow us to determine the feasibility of outpatient management for those whose clinical status does not require hospitalization. Other patients that were excluded from the previous trials will be included: pregnant and breastfeeding women, undernourished patients or patients with concomitant diseases. However, these new population groups will remain hospitalized throughout the treatment period. The treatment will be provided in a new packaging, developed by Sanofi. Once the treatment has been authorized, this new packaging will be used by the countries' national control programmes and health systems. This study will be carried out in five sites in the DRC.

Oxaborole: SCYX-7158 (provisional name)

- OXA002 is a pivotal study on a new chemical entity, to be conducted in adults with stage 2 HAT (N= 210). The study is due to start in June 2016.

This molecule has recently successfully completed Phase I trials in human volunteers who received a single dose with three tablets of 320 mg (total intake 960 mg). The trial will take place in at least seven sites in the DRC. If a futility analysis performed on the first 20 patients shows adequate initial efficacy and safety, the study will recruit stage 1 HAT patients. The study will include children by the second half of 2017.

Olaf Valverde

Training on good clinical and laboratory practice in HAT Platform member countries

Training on human African trypanosomiasis in the Dinamadji health district, Chad

A training workshop for health personnel involved in HAT control was held in the Danamadji health district in Chad on 19-21 August 2015, with the financial support of the HAT Platform. This training followed the resurgence of new cases in the Maro *sub-prefecture*, where 23 new cases were diagnosed over the past three years (1 case in 2013, 5 cases in 2014 and 17 cases identified by active screening in February 2015). The objective of this workshop was to strengthen the capacities of healthcare personnel in the Danamadji health district for the management of human African trypanosomiasis. The participants were physicians, nurses and laboratory technicians working in health facilities in the district's area of HAT transmission. Out of the 22 registered participants, 20 attended the training workshop.

The main topics included:

- HAT epidemiological situation in Chad
- HAT epidemiology
- HAT management
- HAT control strategy
- Vector control
- National HAT control policy in Chad

Formative supervision on human African trypanosomiasis in the Republic of the Congo

The National HAT Control Programme conducted supervisory training visits to monitor the activities of health workers in peripheral screening and treatment centres. All screening and treatment centres currently operational in the Republic of the Congo were concerned:

- Cuvette: Loukoléla, Mossaka
- Plateaux: Gamboma, Mpouya
- Pool: Ngabé, Mindouli, Brazzaville (basis of the programme)
- Bouenza, Madingou, Nkayi, Loudima

The primary objective was to evaluate the technical capabilities and attitudes of the health workers in the integrated health centres /treatment centres located in areas of sleeping sickness transmission.

The methodology used was based on:

- Interviews with the health workers to answer a number of questions listed in the supervision plan
- Review of data collection media (registers, datasheets, etc.) by the supervisors
- Visits to the depots for medicinal products and laboratory supplies

During these supervision visits, the capacities of the health personnel in the integrated health centres /treatment centres were strengthened in terms of diagnosis, treatment, case notification and reporting, and the completion of report forms and epidemiological surveillance forms. Diagnostic and treatment tools were evaluated.

In view of the findings, the programme may organise training/refresher courses for workers in health centres on basic HAT control methods, to increase the latter's integration. This decentralization effort will be supported by regular supervisions.

Clinical training on human African trypanosomiasis in South Sudan

A training course on the diagnosis and management of human African trypanosomiasis, organised by the National HAT Control Programme of South Sudan, was held on 23-25 November 2015, under the leadership of the World Health Organization and with the support of the HAT Platform. The WHO participated in this training via their NTD focal point in South Sudan, who gave a presentation on data collection tools.

A total of 36 people attended this training course, including physicians, nurses and laboratory technicians working in trypanosomiasis endemic areas, in the counties and in the main treatment centres (Juba university hospital, Yei hospital, and Nimule treatment centre). This training was also supported by two facilitators of the DRC National HAT Control Programme: Patrice Kabangu, responsible for HAT management, and Jean Kwete, head of the laboratory and Platform coordinator.

The objective of the training was to improve the diagnosis and management of human African trypanosomiasis. The methodology included plenary sessions and practical workshops.

The results are given below:

- The participants were sensitized to detecting suspect clinical cases of human African trypanosomiasis, refering suspect clinical or serological cases to facilities for confirmation, and managing HAT cases correctly.

- The use of data collection and reporting tools, and the basic ideas of health education for the population and communication techniques were explained to them.

- Demonstrations on how to insert a venous catheter and how to use sensitive diagnostic techniques were performed and then practised by a few participants.

At the end of the training course, recommendations were given that two technicians from South Sudan follow a practical training course on HAT with their partners at the national HAT Control Programme within a mobile unit in the Democratic Republic of the Congo, to enhance their practical knowledge and help them acquire skills, which they could then take back to South Sudan to supervise and provide continuing education to the programme's personnel.

Peka Mallaye, Stephane Ngampo, Richard Lako and

Florent Mbo



Presentation of the Dubreka centre, Guinea

The *Centre hypno-léproserie de Dubréka*, commonly referred to as Trypano or Macompo by the town's inhabitants, is located 50 km from Conakry, within the prefecture of Dubreka. It is a highly renowned centre which dates from colonial times.

The *Centre hypno-léproserie de Dubréka* is a referral centre for the management of tropical diseases, such as leprosy, tuberculosis, human African trypanosomiasis (HAT) and onchocercosis.

In 2014 and 2015, the centre treated 61 patients in spite of the ongoing Ebola epidemic on the Guinean coast at the time.

The centre's personnel includes one physician, three laboratory technicians and two nurses, all trained in the management of tropical diseases. It also has visiting trainee nurses.

The centre is divided into twelve buildings, with two offices for the physicians, two consulting rooms, two laboratories, including one for molecular biology fully equipped by FIND, eight hospital wards, four of which were recently refurbished, a pharmacy, a meeting and training room, and further buildings for ex-leprosy patients. The centre may become a clinical research centre.

Mariame Camara

Une vue du Centre de Dubréka

Meeting of fexinidazole investigators, July 2015

A meeting with the investigators of the fexinidazole clinical study sites was held in Kinshasa on 7-8 July 2015. The meeting was opened by the director of the DRC National HAT Control Programme.

The following topics were addressed:

- Review of the pivotal study on oxaborole SCYX-7158
- Progress report on studies FEX04, FEX05 and FEX006
- Audit of some of the sites
- Management procedures for the study products
- Use of an iLED microscope camera
- Follow-up visits of patients included in the clinical studies
- Financial consideration: how to improve fluidity, financial report and use of funds for local purchases
- Management of serious adverse effects

Exchanges on the feasibility of the pivotal study on SCYX-7158 included the follow-up of outpatient and inpatient treatment, and the use of community workers to monitor or report adverse effects. A team was created to discuss patients' inclusion criteria (out- and inpatients).

Investigators were given a reminder on the management of study supplies, and on the importance of following procedure, from ordering supplies to their ultimate distribution. The importance of an iLED microscope camera to document diagnostic and follow-up examinations was also explained. Particular attention was given to the management of patients during clinical study follow-up visits, and to the risk of losing them to follow-up. Solutions were suggested to improve patients' compliance with follow-up,

such as taking their exact address, explaining the importance of lumbar puncture, and establishing good communication between the healthcare team and the patients.

The last two sessions were dedicated to the documents relating to the use of funds, and to exchanges on the serious adverse effects reported by the study sites.

Patrice Kabangu, Digas Ngolo and Florent Mbo

Meeting of the scientific committee of the DRC National HAT Control Program, September 2015

Scientific committee members the sleeping sickness national control program, PNLTHA DRC

The scientific committee of the National HAT Control Programme of the Democratic Republic of the Congo (PNLTHA) met on 28-30 September 2015 in Kinshasa, on the premises of the World Health Organization, with the participation of sleeping sickness experts from the National HAT Control Programme and the Ministry of Health of the DRC, WHO, DND*i*, FIND, the HAT Platform, IRD, INRB, MSF, the faculty of medicine of the University of Kinshasa, etc. The objectives of the meeting included:

1. Making recommendations on the revision of the HAT control policy in the DRC, based on scientific evidence and the current situation of HAT in the country.
2. Defining the basis of a strategic HAT control plan in the DRC, given the HAT elimination goal of 2020, set by the WHO.

Working groups presented seven topics during this meeting:

1. Community involvement
2. Vector control
3. Diagnostic tools and screening procedures
4. Treatment and post-treatment follow-up
5. Integration
6. Monitoring
7. Follow-up of seropositive individuals

Experts during the scientific committee meeting of the DRC National HAT Control Programme

After several plenary discussions, the following recommendations were made:

1. Community involvement

a. Circulate the message on HAT elimination to all stakeholders (community, political and administrative authorities, experts, etc.)

b. Develop the Information, Education and Communication (IEC) campaign on HAT, using proven health promotion methods (belief models relating to health or other topics).

c. Focus on the combination of interpersonal communications with workers close to the communities and with mass media (radio), which is their main source of information.

d. Recycle mobile units on the importance of good participation.

2. Vector control

a. Establish a systematic vector control programme

b. Revision of information on vector control:

- Tsetse fly distribution based on the species, but only those that are HAT vectors, i.e. *G. palpalis* and *G. fuscipes* (remote sensing, GIS, field tests)
- Evaluation of control tools based on species, biotope and budget, and considering traps and screens impregnated with insecticide, etc.

c. The least expensive and most suitable tools are the small screens: US$80/km² in Uganda. The screen itself costs US$1, but its deployment is expensive, even though one person can lay 50 per day.

In the DRC:

a. Vector control must target the most active foci based on available budget and logistics considerations.

b. Vector control campaigns should be each 3 years + an undetermined period using barriers.

3. Diagnostic tools and screening procedures

Screening

Active screening (AS) and passive screening (PS) are complementary measures to detect and treat cases as early as possible and reduce the human reservoir. In all epidemiological settings, AS and PS must be synergistic and the planning of one does not exclude the presence of the other.

Active screening

The village, chosen for its epidemiological status, is the geographical unit used to plan the activities of the mobile units.

The National HAT Control Programme must explore the possibility of using new alternative approaches for active screening, not only to expand the coverage of the population at risk, but also to make it more effective.

CATT is still considered as the serological screening tool best suited to active screening.

Passive screening

Rapid screening tests are recommended for screening the population seen at fixed general healthcare facilities,resenting signs of sleeping sickness.

Parasitological diagnosis

Concentration methods, such as CTC or mAECT, are recommended for detecting the presence of parasites in the patient's blood. They are more suitable than fresh blood or dried blood spot techniques.

4. Treatment and post-treatment follow-up

The decision to treat a patient must always be based on a parasitological confirmation.

Rapid diagnostic tests (RDTs) using serum are used for screening and a positive result does not constitute a treatment indication.

The detection of trypanosomes in the cerebrospinal fluid must be performed by modified simple centrifugation (MSC). A traumatic lumbar puncture is not reliable and must be repeated!

Recommended treatment

There is no evidence so far supporting a change in the current regimen based on pentamidine for 7 days for stage 1 HAT, and on NECT (nifurtimox for 10 days and 7 days for eflornithine) for stage 2 HAT.

If a recurrence occurs following NECT treatment, a compassionate treatment is initiated because there is currently no single and standardised treatment recommendation. In case of relapse with the current treatment NECT, the National HAT Control Program must provide both options below:

1. NECT as a long treatment (eflornithine for 14 days, 4 times/day + nifurtimox for 10 days): efficacy estimated at 98% but with toxicity.

2. Melarsoprol: significant toxicity (ensure availability).

5. Integration

There is no unique and standardised recipe to promote integration, so it must be adapted to the regions.

6. Monitoring

Revise the approaches used for active and passive monitoring, to make them simpler and more flexible.

7. Follow-up of seropositive patients

Current knowledge on seropositivity is insufficient. More extensive research is required to improve our understanding of the epidemiological role of seropositive patients (asymptomatic carriers) and self-cure cases.

We hope that other national programs will use these recommendations to revise their national policy. For further details, please refer to the DRC National HAT Control Program.

Marleen Boelart and Crispin Lumbala

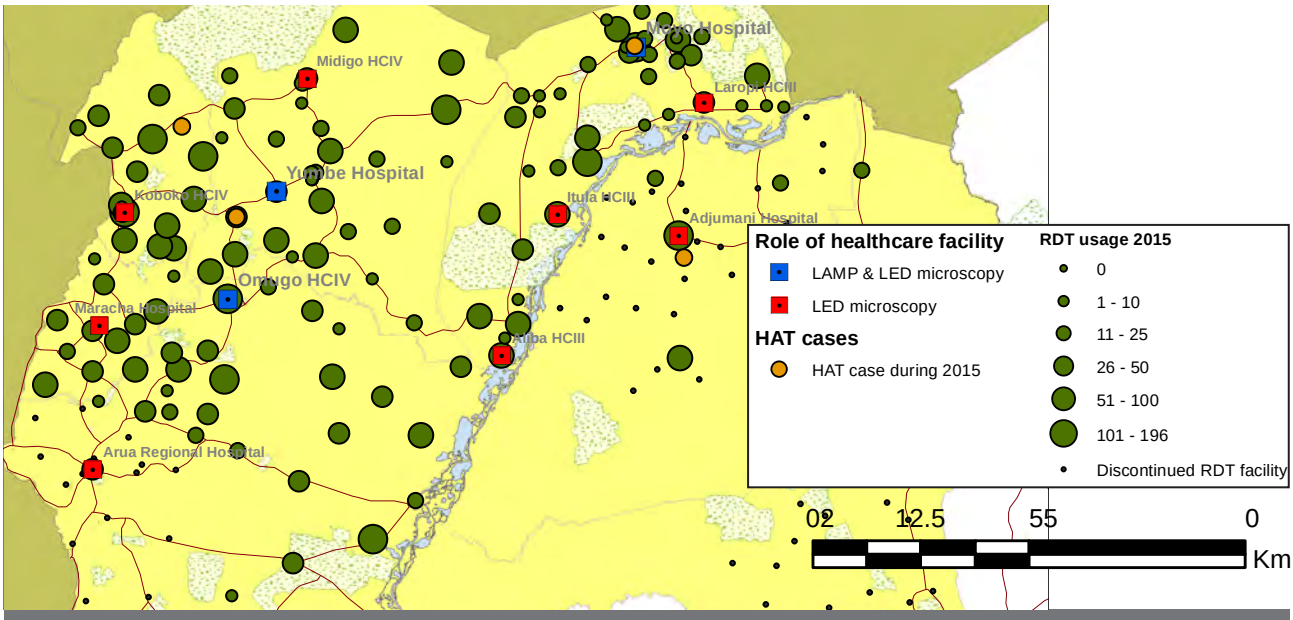
New HAT screening strategy developed by FIND in Uganda and in the Democratic Republic of the Congo

A. PROJECT UPDATE IN UGANDA

Accelerating elimination of gambiense human African trypanosomiasis: the last mile

ISSEP (Intensified Sleeping Sickness Elimination Programme) is a joint initiative of the Government of Uganda, FIND and WHO. The programme covers the seven districts where *T.b. gambiense* HAT is found in Uganda, an area of 16,460 km^2 in the northwest of the country with 2.22 million inhabitants. Over the past two years, the programme has significantly increased access to HAT diagnostics in affected districts, supplying rapid diagnostic tests to 200 rural and urban health facilities, thereby enabling initial diagnosis close to home. Confirmatory diagnosis has been scaled up in the form of nine LED fluorescence microscopy (FM) centres, as well as three facilities equipped with molecular LAMP test capabilities, for further analysis on fresh blood or dried blood spots for suspect cases with negative microscopy.

Under ISSEP, RDT-positive patients and those with clinical signs strongly suggestive of HAT are referred to the nearest of the nine facilities equipped with LED FM. If a suspect remains negative by microscopy, a blood sample is taken and dried on filter paper. It is then transported by the programme's motorcyclists for analysis to the nearest of the three LAMP facilities (unless microscopy was already performed in one of those three facilities). Lamp-positive patients are considered as strong suspects and further tests by



Healthcare facilities implementing ISSEP in north western Uganda. The light green circles represent facilities that were excluded in July 2014.

microscopy must be performed, as demonstration of parasites is currently required to confirm HAT cases.

ISSEP was initiated in August 2013, and by June 2014, 5,748 people had been tested for HAT using rapid diagnostic tests (RDTs). Out of 200 suspected cases identified, 6 were confirmed as HAT cases. The data showed that the endemic region was shrinking, and in July 2014 the programme area was reduced to 125 facilities performing RDTs, centred on areas reporting positive RDTs. Between July 2014 and September 2015, an additional 8,368 patients were tested for HAT with RDTs, and out of 180 suspects identified, 6 more cases were confirmed. Only three HAT cases were detected between January and September 2015 – a clear indication that *T.b. gambiense* sleeping sickness in Uganda is continuing to decline. Meanwhile, the Government of Uganda is carrying out targeted active screening in villages where the most recent cases were found. The ISSEP model is proving to be a great success in accelerating the elimination of sleeping sickness, by identifying the very few remaining cases.

B. PROJECT UPDATE IN KONGO CENTRAL, DRC

Driving elimination of human African trypanosomiasis in a challenging transboundary region

The Democratic Republic of the Congo (DRC) has the greatest number of HAT cases globally and accounted for 84.5% of all cases reported in 2014 (n=3,206). Kongo Central (formerly Bas Congo) is one of the smallest HAT-endemic provinces in the DRC, and its HAT focus is isolated from the other foci in the country. Over the past 10 years, only a relatively small number of HAT cases have been reported annually, making it a good candidate for HAT elimination through intensified control. The outer limits of this HAT focus extend into the neighbouring countries of Angola and the Republic of the Congo, making cross-border collaboration critical to achieving the goal of elimination.

Twenty-three out of 31 health zones in Kongo Central province, an area of approximately 33,800 km^2, are endemic for HAT, with more than 4.5 million people at risk of infection. In recent years, disease surveillance in this vast province has consisted of active screening using CATT by a single mobile team and passive screening in only 36 health facilities. The terrain of the province has numerous rivers and is difficult to navigate, meaning that the mobile team cannot access the most endemic villages, and health facilities that offer screening are often far from the population at risk. Achieving HAT elimination in Kongo Central requires a cost-effective strategy to deliver screening services as close as possible to the villages, and harmonization of activities with neighbouring Angola and the Republic of the Congo.

The arrival of new diagnostic tools co-developed by FIND and other partners has radically enhanced HAT screening in Kongo Central. HAT RDTs and training have been provided to 597 health facilities, which are now conducting the first stage of screening. To confirm the disease in HAT suspects, 23 of these 597 facilities have been upgraded and equipped to perform parasitology tests, including LED fluorescence microscopy (FM), and five of these have been equipped to perform LAMP tests as well. Upgrading of health facilities was initiated in 2014, while implementation of the strategy started in July 2015. By the end of October 2015, all 597 facilities were participating. From July through November 2015, 3,609 RDTs were performed, and out of 119 positives, 10 were confirmed as HAT cases. Seven of the 10 cases were initially screened at facilities that were not previously testing for HAT, and one of the cases was from Angola. Importantly, seven of the ten diagnosed cases were in stage 1 or early stage 2, which is safer and easier to treat than the late stage when the brain is affected.

Joseph Ndungu and Sylvain Bieler

How to write scientific articles

Scientists are expected to report their findings and share their results by publishing research articles in scientific journals. However, writing a good scientific article is not easy, even for experienced scientists. Although every manuscript is different, most articles follow a certain structure and knowing this structure facilitates the job. On 1 October 2015, Veerle Lejon, research director at IRD (*Institut de Recherche pour le Développement*), gave a seminar on article writing at INRB (*Institut National de Recherche Biomédicale*) in Kinshasa. The key points of the seminar are outlined below.

An important first step when writing an article is to define the central take-home message. Everything you write should be centred on this message. Next, create an outline based on keywords. Give the reasons why the study was done and make a list of methods used. List the results, keeping in mind that they should support the central message. Finally, list your conclusions, the novelties and limitations of the study as well as its implications in current practice. Check if you have all the necessary data at hand, all reference articles and your draft tables and figures. You are now ready to start the real writing!

You must now organize the ideas in your draft as a text, following the IMRAD structure (**I**ntroduction, **M**aterials and Methods, **R**esults **a**nd **D**iscussion), which is used by most journals. Each of these sections plays a specific role and has its own substructure.

The introduction must be brief (300-500 words) and provide all the information needed to understand the article. It introduces the literature from general to specific and explains why the topic is important. It summarises the problem or open research questions and explains the gap in current research, and what is new in the present research. At the end of the introduction, the research hypothesis and/or study objectives are given.

The materials and methods section explains how the experiments were done so that colleagues can evaluate the work and even replicate it. This section is usually organized chronologically or by type of procedure. The main challenge is to find a balance between detail and a maximum length of about 800 words.

The results section presents the study results without interpretation, as text, numbers, tables and figures. It follows the same sequence as the materials and methods section. It is not necessary to give all results, which would divert the reader's attention from the main message. However, all results related to the main message - supporting or contradicting the initial research hypothesis - should be provided.

The discussion contains the interpretations, opinions, and implications of the study. It should provide answers to the initial questions given in the introduction, and explain the gap in current research, and what is new in the present research. Results should be explained without repetitions, avoiding side issues not related to the take-home message. The discussion starts with a description of the main results in one or two sentences. Then, the importance and significance of the results should be discussed, providing alternative explanations and including any doubts. The international research context is at the heart of the discussion, comparing and contrasting observed results with those given in other publications, explaining unexpected results, and giving the strengths and weaknesses of the study with equal attention to both. The discussion ends with the take-home message, followed by a paragraph on the applications, recommendations, and implications for the different stakeholders, and a list of the research perspectives.

References are the source of the information used in the manuscript. What you write should be original, you may only copy wordings or sentences from other articles on condition that you name the original article. For these reasons, the easiest is to insert the quotations during the initial writing process. Generally, quotations and references are presented either as a numbered list or by alphabetical order based on the first author name and publication year. The format depends on the journal and is described in the author guidelines.

Once these sections have been finalized, the bulk of the writing is done. It is now time to start revising the article and checking if its message is well-defined, if each paragraph represents a single idea, if sentences are clear, and to remove redundant words. Proof-read the document as often as necessary until you feel that nothing can be improved anymore. Make sure that all quotes and references are listed correctly. Now you can start circulating the manuscript among your co-authors. If you are an inexperienced writer, do not wait until you have completed the writing and have your text corrected section by section by your supervisor to gain time.

The last two important tasks include finding a good title which will attract the attention of potential readers. The title must be short and include no more than about 10 key words that refer to the content of the article. The second task is to create an abstract, i.e. a condensed version of the article, that will induce the reader to read on, and the editor of the selected journal to consider your manuscript. Abstracts are usually 250 to 300 words long, and can be structured or unstructured depending on the journal. When making the first draft of the abstract, copy sentences from your text describing the main objectives, methodology, results and conclusions, limiting yourself to two or three sentences for each item. The first sentence should describe the research hypothesis. Next, delete all non-essential words and sentences. The abstract is very important and therefore should never be written in a hurry.

Once all these sections are completed and revised, your manuscript is ready to be submitted.
Good luck!

The full presentation, intended as a manual for article writing, can be viewed at:
http://umr-intertryp.cirad.fr/content/download/4411/32981/version/1/file/Scientificwriting-15-10-01.pdf
The following sources were consulted when preparing the seminar:

- Writing Workshop: PLOS and PLOS Neglected Tropical Diseases.
  http://journals.plos.org/plosntds/s/commitment-to-capacity
- San Francisco edit newsletters: www.sfedit.net
- Docherty & Smith. The case for structuring the discussion of scientific papers. BMJ 1999;318:1224–5.
- Kallestinova E.D. How to Write Your First Research Paper. Yale Journal of Biology and Medicine 84 (2011), pp.181-190.

Dr. Veerle Lejon
Director of research, RID, France

Recent scientific publications read for you

1. Simo G, Rayaisse JB. Challenges facing the elimination of sleeping sickness in west and central Africa: sustainable control of animal trypanosomiasis as an indispensable approach to achieve the goal. *Parasit Vectors*. 2015 Dec16;8(1):640

Summary

African trypanosomiases are infectious diseases caused by trypanosomes. Whereas the elimination of human African trypanosomiasis (HAT) is expected by 2020, animal African trypanosomiasis (AAT) remains an important threat for livestock production in some affected areas. In West and Central Africa, parasites causing trypanosomiases have been shown to coexist in some cases in the same tsetse fly or same animal. Therefore, the control of these separate diseases must be treated as a general trypanosomiasis control, or "one health" concept where the coordination of control operations will be beneficial for both diseases. In this context, implementing control activities on AAT will help to sustain HAT control. It will also have a positive impact on animal health and economic development in the regions. Training of inhabitants on how to implement and sustain vector control tools will promote the long-term sustainability of control operations that will lead to the elimination of HAT and AAT.

2. Rodgers J, Bradley B, Kennedy PG, Sternberg JM. Central Nervous System Parasitosis and Neuroinflammation Ameliorated by Systemic IL-10 Administration in Trypanosoma brucei-Infected Mice. *PLoS Negl Trop Dis.* 2015 Oct 27;9(10)

Summary

The invasion of the central nervous system (CNS) by African trypanosomes represents a critical step in the pathogenesis of human African trypanosomiasis. Clinical evidence on both stages of the disease and experimental mouse infections have shown that a systemic inflammatory response is associated with a predisposition to CNS invasion.

Using the *Trypanosoma brucei brucei* GVR35 experimental infection model, the authors demonstrated that systemic delivery of the anti-inflammatory cytokine IL-10 lowers plasma IFN-γ and TNF-α concentrations and CNS parasite levels, and improves the neuroinflammatory process and clinical symptoms of disease. The results provide evidence that CNS invasion may be susceptible to immunological attenuation.

Florent Mbo

Other recent scientific publications

1. Bonnet J, Boudot C, Courtioux B. Overview of the Diagnostic Methods Used in the Field for Human African Trypanosomiasis: What Could Change in the Next Years? *Biomed Res Int.* 2015;2015:583262
2. Burri C, Yeramian PD, Allen JL, Merolle A, Serge KK, Mpanya A, Lutumba P, Mesu VK, Bilenge CM, Lubaki JP, Mpoto AM, Thompson M, Mu- nungu BF, Manuel F, Josenando T, Bernhard SC, Olson CA, Blum J, Tidwell RR, Pohlig G. Efficacy, Safety, and Dose of Pafuramidine, a New Oral Drug for Treatment of First Stage Sleeping Sickness, in a Phase 2a Clinical Study and Phase 2b Randomized Clinical Studies. *PLoS Negl Trop Dis.* 2016 Feb 16;10(2)
3. Cecchi G, Paone M, Argilés Herrero R, Vreysen MJ, Mattioli RC. Developing a continental atlas of the distribution and trypanosomal infection of tsetse flies (Glossina species). *Parasit Vectors.* 2015 May 22;8:284

4. Jones DC, Foth BJ, Urbaniak MD, Patterson S, Ong HB, Berriman M, Fairlamb AH. Genomic and Proteomic Studies on the Mode of Action of Oxaboroles against the African Trypanosome. *PLoS Negl Trop Dis*. 2015 Dec 18;9(12)

5. Kaiser M, Mäser P, Tadoori LP, Ioset JR, Brun R. Antiprotozoal Activity Profiling of Approved Drugs: A Starting Point toward Drug Repositioning. *PLoS One*. 2015 Aug 13;10(8)

6. Kato CD, Alibu VP, Nanteza A, Mugasa CM, Matovu E. Interleukin (IL)-6 and IL-10 Are Up Regulated in Late Stage Trypanosoma brucei rhodesiense Sleeping Sickness. *PLoS Negl Trop Dis*. 2015 Jun 19;9(6)

7. Kato CD, Nanteza A, Mugasa C, Edyelu A, Matovu E, Alibu VP. Clinical profiles, disease outcome and co-morbidities among T. b. rhodesiense sleeping sickness patients in Uganda. *PLoS One*. 2015 Feb 26;10(2)

8. Kato CD, Matovu E, Mugasa CM, Nanteza A, Alibu VP. The role of cytokines in the pathogenesis and staging of Trypanosoma brucei rhodesiense sleeping sickness. *Allergy Asthma Clin Immunol*. 2016 Jan 22;12:4.

9. Lamour SD, Gomez-Romero M, Vorkas PA, Alibu VP, Saric J, Holmes E, Sternberg JM. Discovery of Infection Associated Metabolic Markers in Human African Trypanosomiasis. *PLoS Negl Trop Dis*. 2015 Oct 27;9(10)

10. Lumbala C, Simarro PP, Cecchi G, Paone M, Franco JR, Kande Betu Ku Mesu V, Makabuza J, Diarra A, Chansy S, Priotto G, Mattioli RC, Jannin JG. Human African trypanosomiasis in the Democratic Republic of the Congo: disease distribution and risk. *Int J Health Geogr*. 2015 Jun 6;14:20

11. Mukadi P, Lejon V, Barbé B, Gillet P, Nyembo C, Lukuka A, Likwela J, Lumbala C, Mbaruku J, Vander Veken W, Mumba D, Lutumba P, Muyembe JJ, Jacobs J. Performance of Microscopy for the Diagnosis of Malaria and Human African Trypanosomiasis by Diagnostic Laboratories in the Democratic Republic of the Congo: Results of a Nation-Wide External Quality Assessment. *PLoS One*. 2016 Jan 20;11(1)

12. Musaya J, Matovu E, Nyirenda M, Chisi J. Role of cytokines in Trypanosoma brucei-induced anaemia: A review of the literature. *Malawi Med J*. 2015 Jun;27(2):45-50

13. Nzou SM, Fujii Y, Miura M, Mwau M, Mwangi AW, Itoh M, Salam MA, Hamano S, Hirayama K, Kaneko S. Development of multiplex serological assay for the detection of human African trypanosomiasis. *Parasitol Int*. 2016 Apr;65(2):121-7

14. Pohlig G, Bernhard SC, Blum J, Burri C, Mpanya A, Lubaki JP, Mpoto AM, Munungu BF, N'tombe PM, Deo GK, Mutantu PN, Kuikumbi FM, Mintwo AF, Munungi AK, Dala A, Macharia S, Bilenge CM, Mesu VK, Franco JR, Dituvanga ND, Tidwell RR, Olson CA. Efficacy and Safety of Pafuramidine versus Pentamidine Maleate for Treatment of First Stage Sleeping Sickness in a Randomized, Comparator-Controlled, International Phase 3 Clinical Trial. *PLoS Negl Trop Dis*. 2016 Feb 16;10(2)

15. Simarro PP, Cecchi G, Franco JR, Paone M, Diarra A, Priotto G, Mattioli RC, Jannin JG. Mo- nitoring the Progress towards the Elimination of Gambiense Human African Trypanosomiasis. *PLoS Negl Trop Dis*. 2015 Jun 9;9(6)

16. Steinmann P, Stone CM, Sutherland CS, Tanner M, Tediosi F. Contemporary and emerging strategies for eliminating human African trypanosomiasis due to Trypanosoma brucei gambiense: review. *Trop Med Int Health*. 2015 Jun;20(6):707-18

17. Sternberg JM, Gierliński M, Biéler S, Ferguson MA, Ndung'u JM. Evaluation of the diagnostic accuracy of prototype rapid tests for human African trypanosomiasis. *PLoS Negl Trop Dis*. 2014 Dec 18;8(12)

Aita Signorell

Obituary

Reine Gressiti (Batangafo, Central African Republic)

Reine worked as a nurse in the fexinidazole study team in Batangafo, a highly endemic area for trypanosomiasis in the Central African Republic. The investigator, Dr. Francis Regongbenga, wrote the following eulogy for her:

While your family, your whole nation and all the Organizations for which you worked, including DND*i*, still needed you, your life was taken away as you were saving another life.

May you rest in peace.

Dosithe Mafuta: 37 years dedicated to the control of sleeping sickness in the DRC

Our head of the Kwamouth mobile team Mafuta passed away on 21 August 2015 from a long illness at the Bandundu General Hospital.

I spent many good times with Dosithe Mafuta. I appreciated his outstanding managerial sense during the management team meetings of the Kwamouth rural health area, and especially during the mobile team work in the field and major actions in the Kwamouth health area. Mafuta rendered enormous services to the population of this health area. It is difficult to forget a loved one who taught us what sleeping sickness is, and who was considered a true expert. We shall always remember our head of the mobile team.

Dosithe Mafuta was born in 1957. As soon as he obtained his nursing degree, he joined the M'poo Trypanosomiasis Screening, Treatment and Control Centre in 1978 (Sia health zone). Three years later, he was transferred to work as a nurse with the Semendwa mobile team. After a few years, he was transferred again to work as a microscopy nurse with the Masimanimba mobile team. In 1995, he was promoted head of the Masimanimba mobile team, where he excelled. In 2004, the management of the National HAT Control Programme appointed him as head of the Kwamouth mobile team.

As head of the mobile team, he contributed to the practical training of the provinces' coordinating physicians, physicians in charge of an area, medical biologists, laboratory technicians, and registered nurses in endemic health areas, some of whom now hold managerial positions within the DRC National HAT Control Programme, where HAT is hyperendemic. In 2006, when several health areas were endemic for HAT and ignored by the management teams, Dosithe suggested that HAT activities should be included in our monthly and annual surveillance activities in the Kwamouth rural health area. Beyond the HAT activities, during the mobile team field work, Dosithe Mafuta was also vaccinating children in hard to reach villages, not covered by the health area. May he rest in peace.

Digas Ngolo Tete, Fexinidazole Coordinating Investigator

Visits and Meetings


Visit of the Coordinator to the DNDi regional office in Nairobi, October 2015


Visit of the Coordinator to KARI, October 2015

Participation of the HAT Platform at the conference on HAT, University of Juba, South Sudan, November 2015


Participation in the 21st session of JAF-APOC, 16-17 December 2015, Kampala, Uganda, and informal meeting with the DNDi Geneva delegation, the director of the onchocerciasis program in the DRC and the Cameroonian delegation

Birth Notices

Births in the families of fexinidazole coordinators and investigators working in DND*i* sites:

Annaelle Lumeya, daughter of Dr Lumeya, investigator, DRC

Digrace Ngolo Ofraël, son of Dr Digas Ngolo, coordinator of fexinidazole clinical trial, DRC

Pavel Badibanga, son of Badibanga, laboratory supervisor, fexinidazole coordination

Mike Exaucé Mayala, son of Dr Tim Mayala, co-investigator, DRC

4TH JOINT SCIENTIFIC MEETING HAT PLATFORM-EANETT

Human African trypanosomiasis elimination:
The same objective for research and control.

CONAKRY, GUINEA, 20-22 SEPTEMBER 2016

Deadline for registration and submission of abstracts for oral and poster presentations:
June 30, 2016

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