EMERGING RESEARCH: HUMAN AFRICAN TRYPANOSOMIASIS

Abstracts from the human African trypanosomiasis scientific research meeting, 1-3 February 2022

Organised by the HAT Platform, DNDi and London Centre for Neglected Tropical Disease Research

PLATEFORME REGIONALE DE RECHERCHE CLINIQUE THA
TRYPANOSOMIASE HUMAINE AFRICAINE
HUMAN AFRICAN TRYPANOSOMIASIS
HAT REGIONAL PLATFORM FOR CLINICAL RESEARCH

DNDi
Drugs for Neglected Diseases *initiative*

LONDON CENTRE FOR NEGLECTED TROPICAL DISEASE RESEARCH

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Introduction

From 1 – 3 February 2022, the London Centre for Neglected Tropical Disease Research, DNDi and the HAT Platform will host a series of scientific research roundtable meetings on human African trypanosomiasis. The meeting has received an interesting and comprehensive set of research abstracts that give a good overview of both existing research and future directions.

In this booklet, we present 14 abstracts that represent research subjects in endemic countries and the broader projects of several major international partners. Most research, as might be expected, comes from Democratic Republic of the Congo (DRC), the most endemic country, but we also introduce research from Central African Republic, Chad, Burkina Faso, and South Sudan.

Two seroprevalence surveys in DRC and South Sudan provide up to date information from areas where information was previously scarce. This is complemented with recent information from a focus of re-emergence in Central African Republic.

Two abstracts remind us that the One Health concept, which involves veterinary and entomological research, is essential to understanding vector distribution and the animal reservoir.

One abstract presents a new method of qPCR-based diagnosis and another analyses the important issue of cost as a barrier to access to diagnosis and treatment.

Two partners present social science research, exploring community involvement and the perspectives of the health workers. Members of the Liverpool School of Tropical Medicine give an overview of vector control history and perspectives, while Warwick University introduces new opportunities to fine-tune HAT elimination modelling, which is nicely complemented by a specific example from a Swiss TPH student, which models the impact of a new drug in DRC. DNDi presents their drug development programme, and the Institute of Tropical Medicine of Antwerp offers their strategy to support elimination in DRC.

I expect that these presentations will be of interest to you and will feed into the three round tables planned between the 1st and 3rd of February, which will bring together HAT specialists and others from different fields of medical research.

On behalf of the organising committee (Kathryn Forbes, Florent Mbo, and Olaf Valverde Mordt), I am confident that you will enjoy watching the short 8–15-minute videos that have been prepared by the authors available on the RSTMH YouTube channel.

Olaf Valverde Mordt

Team Leader & Medical Manager, DNDi

L'introduction

Du 1er au 3 février 2022, le London Centre for Neglected Tropical Disease Research, DNDi et la plateforme THA organiseront une réunion virtuelle de recherche sur la trypanosomiase humaine africaine. La réunion a reçu un ensemble intéressant et complet de sujets qui donnent un bon aperçu à la fois de la recherche existante et des orientations futures.

Dans ce livret, nous présentons 14 résumés qui représentent des sujets de recherche dans les pays endémiques et les projets plus larges de plusieurs grands partenaires internationaux. La plupart des recherches, comme on pouvait s'y attendre, proviennent de la République Démocratique du Congo (RDC), le pays le plus endémique, mais nous introduisons également des recherches de la République Centrafricaine, du Tchad, du Burkina Faso et du Soudan du Sud.

Deux enquêtes de séroprévalence en RDC et au Soudan du Sud fournissent des informations à jour sur des zones où les informations étaient auparavant rares. Ceci est complété par des informations récentes provenant d'un foyer de réémergence en République Centrafricaine.

Deux abstracts rappellent que le concept One Health, qui implique des recherches vétérinaires et entomologiques, est essentiel pour comprendre la distribution des vecteurs et le réservoir animal.

Un résumé présente une nouvelle méthode de diagnostic basée sur la qPCR et un autre analyse la question importante du coût en tant qu'obstacle à l'accès au diagnostic et au traitement.

Deux partenaires présentent des recherches en sciences sociales, explorant la participation communautaire et les perspectives des agents de santé. Les membres de la Liverpool School of Tropical Medicine donnent un aperçu de l'histoire et des perspectives de la lutte antivectorielle, tandis que l'Université de Warwick présente de nouvelles opportunités pour affiner la modélisation de l'élimination de la THA, qui est bien complétée par un exemple spécifique d'un étudiant de Swiss TPH, qui modélise l'impact d'un nouveau médicament en RDC. DNDi présente son programme de développement de médicaments et l'Institut de Médecine Tropicale d'Anvers propose sa stratégie pour soutenir l'élimination en RDC.

J'espère que ces présentations vous intéresseront et alimenteront les trois tables rondes prévues entre le 1er et le 3 février, qui réuniront des spécialistes de la THA et d'autres issus de différents domaines de la recherche médicale.

Au nom du comité organisateur (Kathryn Forbes, Florent Mbo et Olaf Valverde Mordt), je suis convaincu que vous allez apprécier les courtes vidéos de 8 à 15 minutes préparées par les auteurs.

Olaf Valverde Mordt

Olaf Valverde Mordt Chef d'Equipe et Manager Médical, DNDi

Impact of fexinidazole on gHAT transmission: Modelling the impact of fexinidazole use on gHAT transmission in the Democratic Republic of the Congo

Gambiense human African trypanosomiasis is a deadly disease that has been declining in incidence since the start of the century, primarily due to increased screening, diagnosis and treatment of infected people. The World Health Organization (WHO) is aiming to reach interruption of transmission by 2030. The main treatment regimen currently in use requires a lumbar puncture as part of the diagnostic process to determine disease stage, and hospital admission for intravenous drug administration.

Fexinidazole is a new oral treatment for stage 1 and non-severe stage 2 human African trypanosomiasis. WHO has recently incorporated fexinidazole into its treatment guidelines for human African trypanosomiasis. The treatment does not require hospital admission or a lumbar puncture for all patients, which is likely to ease access for patients; however, it requires concomitant food intake, which is likely to reduce adherence. We use a mathematical model calibrated to case and screening data from Mushie territory, in the Democratic Republic of the Congo, to explore the potential negative impact of poor compliance to an oral treatment on transmission dynamics, and potential gains to be made from increases in the rate at which patients seek treatment.

We find that reductions in compliance in treatment of stage 1 cases are projected to result in the largest increase in further transmission of the disease, with failing to cure stage 2 cases posing a smaller concern. Reductions in compliance may be offset by increases in the rate at which cases are passively detected. Efforts should therefore be made to ensure good adherence for stage 1 patients to treatment with fexinidazole and to improve access to care. Future work in the area is needed to better quantify drug adherence to fexinidazole in the field, and to monitor any changes in the rate at which cases are passively found upon the introduction of fexinidazole.

Das Aatreyee

(PhD student, Swiss TPH, Basel, Switzerland)

Ethnographic study on Human African Trypanosomiasis (HAT) in Democratic Republic of the Congo (DRC) Applying an ecological model to understand contributory factors to community engagement in HAT control in DRC

Background:

The Democratic Republic of the Congo (DRC), which was once known as having the biggest number of Human African Trypanosomiasis (HAT) cases, has seen its share of cases reduced significantly thanks to more effective drugs, regular mass screening, and simple screening tools. While this is good news for the objective of eliminating HAT as a public health issue it also presents the risk of HAT control activities reducing, especially in terms of community engagement.

Methods:

This study has applied an ecological model framework to understand how various factors interact at different levels (individual, community, and societal) to shape local communities' knowledge, perceptions, and behaviors concerning HAT activities in the context of low endemicity. A qualitative study was conducted, using an ethnographic approach involving community members and frontline health providers from 14 communities across 6 provinces in Western and Central DRC, and policymakers were consulted at provincial and national levels.

Results:

The findings show that local communities living in HAT endemic areas are knowledgeable about HAT, including the causes, the symptoms, and the treatment. Community members' practices and behavior relating to HAT (screening and treatment) are influenced at: (i) *individual level* by level of knowledge about HAT, personal beliefs (including traditional beliefs), age, the proximity to the disease, their perception of the risk, and their gender; (ii) *community level* by the quality of, cost of and access to health services (distance); the family's assets (financial and social) and beliefs; the community's perception about HAT patients (stigma); the local leadership; and HAT related education activities; (iii) at the *societal level*, by the social representation of HAT; the endemicity context; the culture and social norms; the economic and livelihood situation, as well as HAT policies and program on community engagement.

Conclusion:

The study has proposed concrete recommendations on how to achieve community engagement, including the development of an adapted Education, Information and Communication strategy (EIC) for HAT.

Charlie Kabanga

(Freelance Research & Evaluation Consultant, London, UK)

Are there still HAT cases in Dingila? Results of HAT screening in Dingila (Bas Uélé province, DRC) six years after all screening activities had ceased

Background:

Ganga-Dingila health zone, Bas-Uélé province, Democratic Republic of the Congo reported decreasing numbers of Human African Trypanosomiasis (HAT) cases until 2015. Médecins Sans Frontières stopped operating in the area in 2015, when all HAT screening was stopped and therefore no further cases were reported. In 2021 we sought to explore the prevalence of HAT in the area to inform the need for additional control activities as we aim to move toward elimination of HAT transmission.

Methods:

Based on historical data and feedback of the health zone management team, we selected health areas and villages with the highest HAT prevalence in 2013/2014 and dispatched a fully equipped expert team of the national sleeping sickness program (PNLTHA) to perform active screening (rapid diagnostic testing-RDT and confirmatory testing) and provide treatment (if needed). In addition, passive screening (RDT) was organized. Sero-suspects of passive screening were revisited for confirmatory testing by the PNLTHA team at the end of active screening. Field confirmatory testing followed the simplified algorithm (i.e. microscopy of lymph node aspirate if palpable lymph nodes, followed by examination of blood by the mini Anion Exchange Centrifugation Technique (mAECT)), but we also collected dried blood spots (DBS) and a sample stored with DNA/RNA shield for further serological and molecular analyses.

Results:

Results: A total of 2430 persons were screened between 02/12/2021 – 14/12/2021, most (n=2364) through active screening, in 18 villages in eight health areas. Two scheduled villages could not be reached due to poor road conditions. The male/female ratio in active screening was 1.02, 48.4% were younger than 15 years. Thirty-two (1.35%) persons had a positive RDT, but none was parasitologically confirmed (after 8 exams of lymph node aspirate, and 32 by mAECT). Seropositivity ranged between 0% in children <5 years and 1.7% in those 25-45 years old. Seroprevalence in the screened villages ranged between 0 to 2.9%. Additionally, 66 persons were screened via passive screening in the health center CSR Bambesa; 6 had a positive TDR, but none was confirmed (4 lymph node aspirate and 6 blood exams by mAECT). The other passive screening sites remained dysfunctional due to general strikes of health workers. None of the sero-suspects reported HAT antecedents. Further analyses on stored samples have not yet been performed.

Conclusion:

Our results confirm (pending results of the complementary analyses) the absence of active HAT foci in Ganga-Dingila. It is however premature to conclude on the whole Bas-Uélé region, further explorations should be planned in Doruma and Ango.

Erick Mwamba Miaka

(Physician Director, PNLTHA DRC)

HAT frontline workers' elimination views: Frontline workers' views on human African trypanosomiasis training, expertise & disease elimination

Background:

Crucial to achieving elimination of human African trypanosomiasis (HAT) is frontline health workers' deployment of 'experiential knowledge' of HAT, health systems and the social environments in which the disease spreads. Unlike theoretical knowledge which may be taught in a textbook, experiential knowledge which is essential for solving health problems in context, is something which much be learnt through practice and maintained through continual exposure. In this presentation we look closely at the careers of frontline HAT workers, attending to ways HAT-related knowledge is generated and maintained within wider country systems to understand their hopes and fears for disease elimination.

Methods:

We examine two contrasting country case studies: South Sudan where HAT expertise is scattered and constantly rebuilt, and Democratic Republic of the Congo (DRC) where specialised mobile detection teams have pro-actively tested people at risk for almost a century. Through interviews conducted between 2012 and 2018, we explore the ways in which HAT workers understand, maintain, and adjust their skills amidst global- and national-level challenges.

Findings:

DRC provided more stable opportunities to develop careers in HAT because of its strong, vertical programme compared to South Sudan where health systems planning is short-term and more reliant on international organisations. However, in both contexts, HAT workers have spent decades rebuilding human resources infrastructures after previous failed attempts at elimination and through major political changes. HAT control is seen as a long-term and collective struggle involving generations of HAT workers built through participation in HAT control programmes.

More recently, participation in research trials has provided career opportunities to stay in HAT at both frontline and coordination levels and a shared sense of belonging to a global HAT community. With the decrease in cases and global drive towards elimination, the nature of HAT labour has changed: work in HAT treatment wards is less overwhelming but screening teams feel pressure to identify cases, both as something to show for extended time away from families and a desire to contribute towards global research trials to improve HAT technologies. De-skilling is a threat for health workers whose HAT exposure diminishes as cases fade and elimination strategies re-configure the learning environment. Many see the training and networking opportunities that come with vertical programmes being diluted through programme initiatives to decentralise and integrate HAT testing and treatment which have yet to prove their effectiveness and robustness. Furthermore, declining trust in government by populations in DRC and high levels of armed conflict in South Sudan has hampered community engagement making it difficult to maintain local vigilance for HAT and understand disease transmission patterns. The global decrease in HAT case numbers brings hope but most informants also expressed a deeply ingrained fear that many patients may not be accessing services.

Conclusions:

Based on a sense developed over decades of work in HAT of what has been done well and the herculean effort it takes to rebuild structures when they have been lost, our informants stress the need to both extend HAT training to more health workers while simultaneously valuing and reinforcing expert knowledge hubs. These frontline workers also invite us to consider more carefully the value of practical field expertise built up in teams and networks.

Jean-Benoît Falisse

(Lecturer, Centre of African Studies, University of Edinburgh)

Jennifer Palmer

(Co-Director, Health in Humanitarian Crisis Centre and HAT researcher, London School of Hygiene and Tropical Medicine)

A manuscript based on this abstract is currently under review at the journal, Global Public Health. It has been written also by our co-authors: Alain Mpanya, Elizeous Surur and Pete Kingsley. If the paper is accepted in time for the release of presentations, we will make it available to attendees.

An atlas to support the progressive control of tsetse-transmitted animal trypanosomosis in Burkina Faso

Background:

African animal trypanosomosis (AAT), transmitted by tsetse flies, is arguably the main disease constraint to integrated crop-livestock agriculture in sub-Saharan Africa, and African Heads of State and Government have adopted a resolution to rid the continent of this scourge. In order to sustainably reduce or eliminate the burden of AAT, a progressive and evidence-based approach is needed, which must hinge on harmonized, spatially-explicit information on the occurrence of AAT and its vectors.

Methods:

A digital repository containing tsetse and AAT data collected in Burkina Faso between 1990 and 2019 was assembled. Data were collected either in the framework of control activities or for research purposes. Data were systematically verified, harmonized, georeferenced and integrated into a database (PostgreSQL). Entomological data on tsetse were mapped at the level of individual monitoring trap. When this was not possible, mapping done was at the level of site or location. Epidemiological data on AAT were mapped at the level of location/village.

Results:

Entomological data showed that presence of four tsetse species in Burkina Faso. *Glossina tachinoides* was the most widespread and abundant species (56.35% of the catches), present from the eastern to the western part of the country. *Glossina palpalis gambiensis* was the second most abundant species (35.56%), and it was mainly found in the West. *Glossina morsitans submorsitans* was found at lower densities (6.51%), with a patchy distribution in the southern parts of the country. One only cluster of *G. medicorum* was detected (less than 0.25%), located in the Southwest. For the AAT component, data for 54,948 animal blood samples were assembled from 218 geographic locations. The samples were tested with a variety of diagnostic methods. AAT was found in all surveyed departments, including the tsetse-free areas in the North. *Trypanosoma vivax* and *T. congolense* infections were the dominant species 6.11±21.56% and 5.19±18.97% respectively), and to a lesser extend *T. brucei* infections (0.00±0.10%).

Conclusion:

The atlas provides a synoptic view of the available information on tsetse and AAT distribution in Burkina Faso. Data are very scanty for most of the tsetse-free areas in the northern part of the country. Despite this limitation, this study generated a robust tool to aid the targeting of future surveillance and control activities. The development of the atlas also strengthened the collaboration between the different institutions involved in tsetse and AAT research and control in Burkina Faso, which will be crucial for future updates and the sustainability of the initiative.

Lassane Percoma

(PhD Student, Rural Development Engineer, Nazi Boni University, Burkina Faso)

Advances and next steps in the modelling of gHAT

This presentation will provide a whistle-stop tour of the advances made in modelling of gHAT since 2015, showing how methodological advancements and access to increasing amounts of gHAT data have been brought together to produce insights on infection trends, drivers of transmission and forecasting the probability of reaching the 2030 elimination goal. I will discuss how factoring in costs through health economic evaluation can be used to suggest resource-efficient strategies to further reduce disease burden, but highlight the potential conflict between the aims of being cost-effective and achieving elimination of transmission by 2030 with high probability.

I will give a brief demonstration of the HAT Modelling and Economic Predictions for Policy project's online graphical user interface, designed to communicate large amounts of data in an easy-to-use and interactive format to non-modellers. The interface will be available for participants of the meeting to try themselves. The demonstration will show how a one-size-fits all approach is unlikely to be appropriate for the gHAT end-game, but that the range of diagnostic, treatment and vector control tools currently available or in the pipeline is likely sufficient if they can be strategically operationalised and supported by necessary funding and political will.

Finally, I will overview the next steps for modelling aimed at continuing to support decision-making across different geographies and providing assessment of progress towards and achievement of elimination of transmission using different data types.

Graphical user interface:
https://hatmepp.warwick.ac.uk/projections/v1/

Publications:
State-of-the-art fitting https://journals.plos.org/ploscompbiol/article?id=10.1371/journal. pcbi.1008532

Projections for DRC
https://www.medrxiv.org/content/10.1101/2020.07.03.20145847v2

Health economic evaluation for DRC
https://www.medrxiv.org/content/10.1101/2020.08.25.20181982v2

Health economics of elimination
https://www.medrxiv.org/content/10.1101/2021.02.10.20181974v2

Projections for Chad
https://www.medrxiv.org/content/10.1101/2021.09.22.21263989v1

Asymptomatic infection modelling
https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1009367

Measuring elimination of transmission using routine data:
https://academic.oup.com/cid/ article/72/Supplement_3/S146/6255739

Kat Rock

(Leader, HAT Modelling and Economic Predictions for Policy Project, Warwick University, UK)

Vector control and sleeping sickness: Contributions of tsetse control to HAT elimination goals

Vector control strategies to interrupt transmission of trypanosomiasis involve the use of insecticides. In the 1960-1980s insecticides were sprayed from aircrafts or by ground operators in large-scale campaigns (e.g., Botswana, Nigeria, Zimbabwe). These techniques achieved good control or even eliminated tsetse populations but they were expensive (~$450-550/km^2, and ~$250-350/km^2, respectively), logistically demanding and often dependent on governmental and/or external support for implementation. In the 1980s, the development of odour-baited targets impregnated with insecticide offered a new and more economical (~$250-300/km^2) approach.

This method was used primarily against savanna tsetse, important vectors of animal African trypanosomiasis (AAT) and the relatively rare Rhodesian form of Human African Trypanosomiasis (r-HAT). Also in the 1980s, the use of insecticide-treated cattle (ITC) was developed as an affordable (~$50-120/km^2) One Health approach, and to control the transmission of AAT and r-HAT in areas where cattle are abundant; ITC controls not only tsetse but also the vectors of important tick-borne diseases such as East Coast Fever. More recently, analyses of tsetse behaviour resulted in the development of the insecticide-impregnated "Tiny Targets": the first control tool specifically designed against tsetse of the riverine group, vectors of the most common human disease, the Gambian form of HAT (g-HAT). Control strategies, based on Tiny Targets are relatively affordable (~$75-125/km^2), community-friendly, and they require minimal external support.

Field trials demonstrated that the deployment of Tiny Targets can reduce tsetse populations by ~90% and epidemiological models indicated that this level of control will interrupt transmission. Adding vector control to case-detection and treatment would hasten local elimination of HAT transmission. The implementation of Tiny Targets in five endemic countries showed similar trends: a sustained ~80-90% reduction in tsetse abundance across all foci. Currently, this approach is protecting around 100,000 km^2, and around 3,000,000 people in countries such as Cameroon, Chad, Côte d'Ivoire, Guinea, DRC and Uganda.

Inaki Tirados

(Medical Entomologist, Liverpool School of Tropical Medicine, UK)

Andrew Hope

(Programme Manager, Liverpool School of Tropical Medicine, UK)

New simplified HAT treatments: DNDi Development of NECT, fexinidazole and acoziborole to support HAT elimination drive

At its creation in 2003, DNDi set up a program to develop new drugs for sleeping sickness, needed due to the toxicity or complex administration requirements of the drugs available at the time. A nifurtimox and eflornithine combination therapy (NECT) was jointly developed with Epicentre and MSF and made available in 2009. This first step of adding an oral drug simplified the previously available treatment with Eflornithine alone by reducing the number of intravenous administrations required, and although it still required hospitalization of patients for treatment, NECT quickly became the reference treatment for advanced HAT.

The first oral only treatment was fexinidazole, taken once a day for 10 days with food, which became available for extended use in 2020. It is now the first line treatment for early and advanced disease stages, although NECT remains the first choice for patients with severe central nervous system infection or for children below 20 kg weight. Training on the new treatment guidelines in endemic areas of Sub-Saharan Africa, together with other activities facilitating access to fexinidazole and awareness about HAT are ongoing.

The latest development, still in clinical development, is acoziborole, taken as a single oral dose, which has shown very promising results in a recently completed pivotal trial. It may be the key to simplifying disease elimination by bringing a very simple treatment into peripheral health systems. In preparation for this, there will be two further clinical trials, one for children from 1 year of age and another for people with serological reactivity to the parasites, instead of the present requirement to confirm serological screening with a formal diagnosis by microscopic observation of trypanosomes in at least one of the patient's body fluids. Acoziborole is expected to be available for general use among parasitologically confirmed adult cases from 2024. The target approval date for use in children and serologically reactive individuals is 2026.

We add here the references of the pivotal clinical trials (NECT + Fexinidazole) which are openly available

1. Priotto G, Kasparian S, Mutombo W, et al. Nifurtimox-eflornithine combination therapy for second-stage African Trypanosoma brucei gambiense trypanosomiasis: a multicentre, randomised, phase III, non-inferiority trial. Lancet (London, England) 2009; 374: 56–64.
2. Mesu VKBK, Kalonji WM, Bardonneau C, et al. Oral fexinidazole for late-stage African Trypanosoma brucei gambiense trypanosomiasis: a pivotal multicentre, randomised, non-inferiority trial. Lancet 2018. DOI:10.1016/S0140-6736(17)32758-7.

Olaf Valverde

(Team Leader & Medical Manager, DNDi, Geneva, Switzerland)

Sandra Rembry

(Clinical Project Leader, DNDi, Geneva, Switzerland)

Novel TBR qPCRs for Trypanozoon and *T.b. gambiense*: Single nucleotide polymorphisms and copy-number variations in the Trypanosoma brucei repeat (TBR) sequence

Recently published research

The Trypanosoma brucei repeat (TBR) is a tandem repeat sequence present on the Trypanozoon minichromosomes. Here, we report that the TBR sequence is not as homogenous as previously believed. BLAST analysis of the available T. brucei genomes reveals various TBR sequences of 177 bp and 176 bp in length, which can be sorted into two TBR groups based on a few key single nucleotide polymorphisms. Conventional and quantitative PCR with primers matched to consensus sequences that target either TBR group show substantial copy-number variations in the TBR repertoire within a collection of 77 Trypanozoon strains. We developed the qTBR, a novel PCR consisting of three primers and two probes, to simultaneously amplify target sequences from each of the two TBR groups into one single qPCR reaction. This dual probe setup offers increased analytical sensitivity for the molecular detection of all Trypanozoon taxa, in particular for T. b. gambiense and T. evansi, when compared to existing TBR PCRs. By combining the qTBR with 18S rDNA amplification as an internal standard, the relative copy-number of each TBR target sequence can be calculated and plotted, allowing for further classification of strains into TBR genotypes associated with East, West or Central Africa. Thus, the qTBR takes advantage of the single-nucleotide polymorphisms and copy number variations in the TBR sequences to enhance amplification and genotyping of all Trypanozoon strains, making it a promising tool for prevalence studies of African trypanosomiasis in both humans and animals.

Ongoing research

Sanger sequencing of cloned TBR sequences from 8 Trypanozoon strains (5 T.b. gambiense and 3 non-gambiense) revealed even higher polymorphisms in the TBR region. We evaluated the prevalence of 18 SNPs found only in gambiense strains on a collection of more than 200 Trypanozoon strains using genotyping qPCRs. One SNP (G37C) specifically identifies T.b. gambiense strains originating from the Democratic Republic of the Congo with almost comparable sensitivity as the original TBR-qPCR, yet curiously, the same SNP is not or limitedly present in T. b. gambiense strains originating from West Africa (Côte d'Ivoire). Interestingly, West African gambiense strains appear to contain different gambiense specific SNPs, according to Sanger sequencing, yet the surrounding nucleotide region proved impossible to generate primer sets or probes to robustly amplify these SNPs. While the discovery of gambiense specific TBR sequences seems promising, the format is not easily translatable to qPCR and likely requires next-generation amplicon-sequencing to be succesfull. Still, the promise of both sensitive as specific detection makes TBR a promising target as a marker for Trypanozoon and T.b. gambiense in particular.

Article

Single nucleotide polymorphisms and copy-number variations in the *Trypanosoma brucei* repeat (TBR) sequence can be used to enhance amplification and genotyping of *Trypanozoon* strains

Nick Van Reet

(Senior Researcher, Trypanosoma Unit,
Institute of Tropical Medicine, Antwerp, Belgium)

Investigations on the animal reservoir of human African trypanosomiasis in active foci in Chad: implications for control strategies. Identification of potential reservoirs of Trypanosoma brucei gambiense in domestic animals from HAT foci in Chad.

Background:

Human African trypanosomiasis (HAT) has been targeted for zero transmission to humans by 2030. Animal reservoirs of gambiense-HAT could jeopardize these elimination goals. This study was undertaken to identify of potential reservoirs of Trypanosoma brucei gambiense in domestic animals from HAT foci in Chad.

Methods:

Blood samples were collected from 443 goats, 339 sheep, 228 dogs, 98 pigs, 155 donkeys and 131 horses. Rapid diagnostic test (RDT) and capillary tube centrifugation (CTC) were performed to search for trypanosomes. DNA was extracted from the buffy coat, and trypanosomes of the subgenus *Trypanozoon* as well as *T. b. gambiense* were identified by PCR.

Results:

Of 1394 blood samples, 13.20% were positive by RDT and 6.88% by CTC. PCR revealed 234 animals (16.78%) with trypanosomes belonging to *Trypanozoon*, including 21 (1.5%) *T. b. gambiense*. This trypanosome was found in all investigated animal species and all HAT foci. The difference is significant between villages and the number of animals harboring *T. b. gambiense* DNA.

Conclusion:

This study revealed that pigs, dogs, sheep, goats, donkeys and horses are potential reservoir hosts of T. b. gambiense in Chad. The identification of *T. b. gambiense* in all animal species of all HAT foci suggests that these animals should be considered when designing new control strategies for sustainable elimination of HAT. Investigations aiming to decrypt their specific role in each epidemiological setting are important to achieve zero transmission of HAT.

References:

- Trypanosome infections in naturally infected horses and donkeys of three active sleeping sickness foci in the south of Chad. Parasites & Vectors, 13:323. https://doi.org/10.1186/s13071-020-04192-1.
- Molecular identification of *Trypanosoma brucei gambiense* in naturally infected pigs, dogs and small ruminants highlights domestic animals as potential reservoirs for sleeping sickness in Chad. *Parasite*, 27: 63 (2020). https://doi.org/10.1051/parasite/2020061

Joel Vourchakbe

(Teacher Researcher, Faculty of Science and Technology, University of Doba, Chad)

Support to the HAT elimination agenda in DRC. First step on the way to interruption of gHAT transmission in DRC

In the following years, the National Control Program of Human African Trypanosomiasis of DRC (PNLTHA) will be supported to implement a country wide comprehensive strategy, based on depleting the HAT parasite reservoir in humans and reducing the density of the tsetse fly vector. The *Belgian Government* and the *Bill & Melinda Gates foundation* will be the main donors. The *Institute of Tropical Medicine, Antwerp* (ITM) will ensure the coordination, with the *Liverpool School of Tropical Medicine* and the Belgian development agency *Enabel* as its most important implementation partners.

Active case finding through voluntary screening by mobile teams of the population at risk, will continue to play an important role in the years to come. We foresee four different active surveillance modalities: i) routine active screening according to the current WHO strategy, ii) surveillance of historic foci, iii) probing of blind spots, and iv) reactive screening in the villages of origin of HAT cases detected through passive screening, i.e. patients visiting the fixed health facilities. The passive case finding approach will be integrated in the primary health care system. Priority will be given to health zones reporting most cases in the previous years. Targeted vector control with *Tiny Targets* will be applied through a vertical, riverine deployment approach and a community-based approach. Field validation of new diagnostic tools will be conducted. Action research to improve the impact of the different approaches and to optimize available diagnostic and vector control tools will be high on the agenda.

Available digital tools will be fine-tuned for better data collection and their application will be extended. A major challenge is to improve the data management and real-time data assessment. The quality assurance system will be further developed, beyond pictures and videos applied to check serological testing by mobile teams. Dried blood spots and other samples will be checked at regional laboratories, including for external quality assurance of passive screening. Updated Standard Operation Procedures will be made available at a wider scale.

We will prepare a transformative screen-and-treat strategy, anticipating the availability of Acoziborole by 2025. The overall goal is the interruption of HAT transmission.

Anja De Weggheleire

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Paul Verle

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Assessment of costs for patients as a result of HAT: Assessment of medical and non-medical costs for patients as a result of screening, diagnosis and treatment of sleeping sickness in the DRC

Objective:

The reduction of Human African Trypanosomiasis (HAT) cases indicates that we are on the right path to eliminating HAT as a public health issue and sustainable eradication of the disease by 2030. This will require a continued commitment to disease control activities. More user-friendly screening tests and improved treatments have been developed. This allows for a shift from mass screening to control and monitoring of the disease, all integrated into the primary health care system. However, previous studies have shown that financial barriers are one of the reasons people do not get tested. Little information is available on out-of-pocket expenses related to case detection. This study aims to bridge this gap by estimating the medical and non-medical costs incurred during the different stages of HAT case detection and management, namely; serological testing, parasitological testing, disease staging and treatment – and how these costs influence perception and participation in these activities.

Methods :

This study uses both qualitative and quantitative methods. First, group discussions and semi-structured interviews with individuals who have been in contact with HAT screening activities are held in order to identify individuals' costs and how this may influence their behavior. Second, a survey was conducted on a random sample of 400 people who, in the past 12 months, had contact with HAT screening activities in order to estimate medical and non-medical costs related to HAT and to assess how these costs influenced behavior toward HAT control.

Findings :

The study estimates the costs associated with HAT control, indicates the scale of these costs even when HAT testing and treatment are provided free of charge, and how this influences behavior and participation.

Rian Snijders

(PhD student, Health Economist, Institute of Tropical Medicine, Antwerp, Belgium)

Evaluation des dépenses pour les patients dues au THA : Evaluation des dépenses médicales et non-médicales pour les patients dues au dépistage, au diagnostic et au traitement de la maladie de sommeil en RDC

Objectif :

La diminution des cas de trypanosomiase humaine africaine (THA) indique que nous sommes sur la bonne voie pour l'élimination de la THA en tant que problème de santé publique et l'élimination durable de la maladie d'ici 2030. Il faudra pour cela maintenir l'engagement en faveur des activités de lutte contre la maladie. Des tests de dépistage plus faciles à utiliser et des traitements améliorés ont été mis au point. Cela permet de passer du dépistage de masse au contrôle et à la surveillance de la maladie, intégrés dans le système de soins de santé primaires. Toutefois, des études antérieures ont montré que les obstacles financiers sont l'une des raisons pour lesquelles les gens ne se font pas dépister. Il existe peu d'informations sur les dépenses personnelles liées à la détection des cas. Cette étude vise à combler cette lacune en estimant les coûts médicaux et non médicaux encourus au cours des différentes étapes de la détection et de la gestion des cas de THA – à savoir, les tests sérologiques, les tests parasitologiques, le stade de la maladie et le traitement – et comment ces dépenses influencent la perception et la participation à ces activités.

Méthodes :

Cette étude utilise des méthodes qualitatives et quantitatives. Tout d'abord, des discussions de groupe et des entretiens semi-structurés avec des personnes ayant été en contact avec des activités de dépistage de la THA sont menés afin d'identifier les dépenses des personnes et la manière dont cela peut influencer leur comportement. Ensuite, une enquête était menée sur un échantillon aléatoire de 400 personnes qui, au cours des 12 derniers mois, ont été en contact avec des activités de dépistage de la THA, afin d'estimer les dépenses médicales et non médicales liées à la THA et d'évaluer comment ces coûts ont influencé le comportement vis-à-vis du contrôle de la THA.

Résultats :

L'étude estime les dépenses liées au contrôle de la THA, indique l'importance de ces dépenses même lorsque les tests de dépistage et le traitement de la THA sont fournis gratuitement et comment cela influence le comportement et la participation.

Conclusion :

La surveillance de la THA intégrée au système de soins de santé sera essentielle pour parvenir à une élimination durable de la maladie. Cette étude permet d'informer les décideurs politiques et de soutenir les adaptations contextuelles pour améliorer la couverture des approches innovantes de contrôle de la maladie.

Rian Snijders

(PhD student, Health Economist, Institute of Tropical Medicine, Antwerp, Belgium)

Re-emergence of Human African Trypanosomiasis (HAT) in Bangassou, Central African Republic

Background:

The World Health Organization set an objective of eradicating Human African Trypanosomiasis (HAT) in 2030. The prevalence of this tropical disease left to case management has been significantly reduced in recent decades, but there are pockets of infection that remain, especially in inaccessible or conflict-affected areas, and may be subject to re-emergence.

Materials and Methods:

We conducted a retrospective 34-month study (January 2016 to October 2018) at the Hôpital Régional Universitaire de Bangassou (HRUB) [Regional University Hospital of Bangassou] in order to determine the epidemiological status of this condition.

Findings:

During the period of the study, out of a total of 2312 patients hospitalized at HRUB, 21 were admitted for a confirmed HAT infection. The mean age of patients was 27 years ± 18 years with extremes of three months and 75 years old. Predominant among the clinical signs were sleep disorders (95.2%), behavior disorders (66.6%), and itchiness (19%). Trypanosoma was isolated in the CSF of all patients. Cytorachy varied 20-2000 cells/mm^3 with an average of 464,14 *[sic]* elements/mm^3. Five subjects had previously traveled to Haut-Mbomou, one of the prefectures that harbors the three active HAT outbreaks. Four other cases had never left the city of Bangassou, hence the strong hypothesis of local transmission and a re-emergence of HAT in this previous focal point of infection.

Conclusion:

The active parasitological survey coupled with an on-going entomological survey for tsetse flies in and around Bangassou will allow for confirmation of this hypothesis.

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Pascal Mbelesso

(Deputy Dean of Health Sciences, University of Bangui, CAR)

Réémergence de la trypanosomose humaine africaine à Bangassou, République Centrafricaine

Introduction:

L'Organisation Mondiale de la Santé a fixé comme objectif d'éliminer la trypanosomose humaine africaine (THA) en 2030. La prévalence de cette maladie tropicale négligée à prise en charge des cas a été considérablement réduite au cours des dernières décennies, mais de poches infectieuses subsistent, surtout dans les zones inaccessibles ou ayant des conflits et peuvent faire l'objet d'une réémergence.

Matériel et méthodes:

Nous avons réalisé une étude rétrospective de 34 mois (janvier 2016 à octobre 2018) à l'Hôpital Régional et Universitaire de Bangassou (HRUB) afin de déterminer la situation épidémiologique de cette affection.

Results:

Durant la période d'étude, sur un total de 2312 patients hospitalisés à l'HRUB, 21 ont été admis pour une infection à THA confirmée.

L'âge moyen des patients était de 27ans ± 18 ans avec des extrêmes de trois mois et 75 ans. Les signes cliniques étaient dominés par les troubles du sommeil (95,2%), les troubles de comportement (66,6%), et le prurit (19%). Le trypanosome a été isolé dans le LCR de tous les malades. La cytorachie variait 20-2000 cellules/mm3 avec une moyenne de 464,14 éléments/mm3. Cinq sujets avaient précédemment effectué des déplacements vers le Haut-Mbomou, l'une des préfectures qui abrite les trois foyers actifs de la THA. Les 4 autres cas n'ont jamais quitté la ville de Bangassou, d'où la forte hypothèse d'une transmission locale et donc d'une réémergence de la THA dans ce foyer historique.

Conclusion:

La prospection parasitologique active couplée à une enquête entomologique en cours, pour la recherche des glossines dans et autour de Bangassou permettra de confirmer cette hypothèse.

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HAT Elimination: Contribution of stationary health facilities in eliminating HAT

Background:

By following Jamot's proposed [method], it appears that for several years now, the most effective way to battle Human African Trypanosomiasis (HAT) has been the use of mobile teams. This control strategy has proven to be so effective that in 2011 the WHO had estimated that the elimination of HAT as a public health issue was feasible in two thousand and twenty.

These mobile teams of Jamot's are currently expensive compared to stationary health structures. Hence, almost all of the technical and financial partners want to support them. Faced with this paradigm, the question we ask ourselves is: what will be the substantial contribution of stationary health facilities in eliminating HAT? Therefore, we wanted to conduct a study to assess the contribution of these stationary structures in the elimination of Human African Trypanosomiasis (HAT)

Our study focused on twenty-seven of the health care structures of the Provincial Coordination of the fight against HAT from the East Kasai region in the Democratic Republic of Congo (DRC) The study covers the period from two thousand to two thousand and nineteen.

Objective:

Our objective is to determine the level of contribution coming from stationary health care structures in the objective of eliminating HAT endorsed by the World Health Organization (WHO) and to propose a paradigm that can reduce the cost.

Methods:

To fully assess the level of stationary structures' contribution in eliminating HAT compared to mobile units, we proceeded with the literature review technique. We looked at ten years of annual reports (from 2010 to 2019) from mobile units of the Provincial Coordination of the fight against HAT from the East Kasai region. The data collected was on the total population studied, the number of patients diagnosed according to the stage of the disease, and the percentage related to it. The variables were collected according to the type of control structure. To determine this contribution, we used the proportions (percentage) of patients diagnosed according to the circumstances of their diagnosis and the stage of the disease (by stationary health care structures or mobile units).

Findings:

After comparing the proportion of patients diagnosed by mobile units and stationary health facilities, it appears that the mobile units produced more stage 1 cases than stationary structures, that is, about 80% and 20% respectively. This difference was shown by F.Mbo in his thesis: ***Towards a reinforcement of passive screening and its contribution in the fight against Human African Trypanosomiasis*** in which he showed that ore than 70% of cases detected in passive screening from 2001 to 2005 were at the advanced or neurological stage of sleeping sickness.

Despite this apparent difference, the contribution of stationary structures in eradication remains irrefutable.

Patrice Kabangu

(National Case Management supervisor, PNLTHA DRC)

Elimination de la THA: Contribution des formations sanitaires fixes dans l'elimination de la THA

Introduction:

En parcourant le postulat de Jamot, il apparait que depuis plusieurs années le moyen le plus efficace pour lutter contre la trypanosomiase Humaine Africaine (THA) était le recours aux équipes mobiles. Cette approche de lutte avait montré son efficacité qui a fait qu'en 2011, l'OMS avait estimé que l'élimination de La THA comme problème de santé publique était envisageable en deux mille vingt. Ces équipes mobiles de Jamot sont considérées comme onéreuses actuellement comparativement aux structures sanitaires fixes. D'où la quasi-totalité des partenaires techniques et financiers souhaitent appuyer ces dernières. Devant ce paradigme, la question que nous nous posons est celle de savoir, quelle sera la contribution substantielle des formations sanitaires fixes dans l'l'élimination de la THA. Ainsi, nous avons voulu mener une étude afin d'évaluer la contribution de ces structures fixes dans l'élimination de la trypanosomiase Humaine Africaine comparativement aux équipes mobiles. Notre étude a porté sur vingt-sept structures sanitaires de la Coordination Provinciale de lutte contre la THA du Kasaï oriental en République Démocratique du Congo (RDC) dont vingt-trois structures sanitaires fixes et quatre équipes mobiles. Cette étude concerne la période allant de deux mille dix à deux mille dix-neuf.

Objectif:

Notre objectif est de déterminer le niveau de contribution des structures sanitaires fixes dans l'objectif de l'élimination de la THA prôné par l'Organisation Mondiale de la Santé (OMS) et de proposer un paradigme qui pourra permettre de réduire le coût.

Méthodologie:

Pour bien évaluer le niveau de contribution des structures fixes dans l'élimination de la THA comparativement aux unités mobiles, nous avons procédé à la technique de revue documentaire. Nous avons consulté les rapports annuels de dix années (de 2010 à 2019) des unités mobiles de la Coordination Provinciale de lutte contre la THA du Kasaï oriental. Les données récoltées concernaient la population totale examinée, le nombre des malades diagnostiqués selon le stade de la maladie, et le pourcentage s'y rapportant. Les variables ont été collectées selon le type des structures de lutte. Pour apprécier cette contribution, nous nous sommes basées sur les proportions (pourcentage) des malades diagnostiqués selon les circonstances de diagnostic et le stade de la maladie (par les structures sanitaires fixes ou unités mobiles).

Résultat:

Après la comparaison des proportions des malades diagnostiqués par les unités mobiles et les formations sanitaires fixes, il ressort que les unités mobiles produisent plus des cas au stade 1 que les structures fixes soit environ respectivement 80 et 20%. Cette différence était démontrée par F.Mbo dans sa thèse : *Vers un renforcement du dépistage passif et sa contribution à la lutte contre la trypanosomiase humaine africaine* où il a démontré que Plus de 70% de cas détectés en passif chaque année de 2001 à 2005 ont été au stade avancé ou neurologique de la maladie du sommeil. En dépit de cette apparente différence, la contribution des structures fixes dans l'élimination reste irréfutable.

Patrice Kabangu

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LONDON CENTRE FOR NEGLECTED TROPICAL DISEASE RESEARCH

About the London Centre for Neglected Tropical Disease Research

The London Centre for Neglected Tropical Disease Research (LCNTDR) is an innovative research collaboration that brings together leading experts to conduct cutting-edge research to build the evidence base around the design, implementation and evaluation of neglected tropical disease (NTD) control and elimination programmes. LCNTDR facilitates coordination of NTD research activities between its members, with its priority being to enhance efforts to control some of the most neglected diseases worldwide.

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About the HAT Platform

The HAT platform aims to build and strengthen research methodologies and clinical trial capacity in HAT – endemic countries, so that new diagnostics and treatments for this fatal disease can be rapidly and effectively evaluated, registered, and made available to patients.

Learn more about the HAT Platform at:
https://dndi.org/global-networks/hat-platform/

DNDi
Drugs for Neglected Diseases *initiative*

About DNDi

A not-for-profit research and development organization, DNDi works to deliver new treatments for neglected patients, those living with Chagas disease, sleeping sickness (human African trypanosomiasis), leishmaniasis, filarial infections, mycetoma, paediatric HIV, and hepatitis C. DNDi is also coordinating a clinical trial to find treatments for mild-to-moderate COVID-19 cases in Africa. Since its inception in 2003, DNDi has delivered nine new treatments to date, including new drug combinations for visceral leishmaniasis (kala-azar), two fixed-dose antimalarials, and DNDi's first successfully developed new chemical entity, fexinidazole, approved in 2018 for the treatment of both stages of sleeping sickness. DNDi recently launched its new 2021-2028 Strategic Plan.

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