



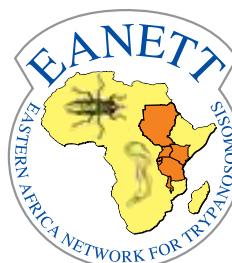
HAT

REGIONAL PLATFORM FOR CLINICAL RESEARCH

Platform

NEWSLETTER N° 20
November 2019

Special Edition



5th Joint Scientific Meeting

**“ Research and control activities
challenges in keeping HAT
below the elimination threshold
beyond 2020 ”.**

3-4 October 2018, Kampala, Uganda

DNDi

Drugs for Neglected Diseases initiative
Initiative Médicaments contre les Maladies Négligées



FIND
Because diagnosis matters

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*Our thanks to Violaine Dallenbach, Sandrine
Lo Lacono, Julie Archer and Louise Burrows for
proofreading of the newsletter*

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EDITORIAL



Dear Readers,

The 20th HAT Platform Newsletter is a special edition focusing on the activities of the 5th Joint HAT Platform-EANETT Scientific Meeting held from 3rd to 4th October 2018 in Kampala, Uganda, on the sidelines of 11th DNDi partners' meeting. The theme of the scientific meeting was "Challenges faced by research and control activities to maintain HAT below the elimination threshold by 2020". The meeting was attended by over 100 participants involved in HAT control, working in research institutions or in the health sector in endemic and non-endemic countries (Angola, Burkina Faso, Central African Republic, Republic of the Congo, Democratic Republic of the Congo, Cameroon, Guinea, Equatorial Guinea, Sudan, South Sudan, Chad, Kenya, Tanzania, Switzerland, United Kingdom, France, and United States of America).

A total of 58 abstracts were submitted, of which 56 were selected, 34 for oral presentations and 22 as posters. Due to funding limitations, only 33 oral presentations and 13 posters were presented. These oral presentations and poster sessions were preceded by a session on HAT elimination, an address by the World Health Organization (WHO) entitled "How to keep HAT below the elimination threshold after 2020", and a presentation on the results of the clinical trials on fexinidazole, the first all-oral treatment for sleeping sickness. Some of these presentations are summarised in this issue. Full presentations can be obtained by contacting the HAT Platform coordinator. WHO advocates integrated management of NTDs, and in this special edition, we also discuss drug development for other NTDs, such as onchocerciasis, and the extension of HAT trial activities to other HAT member countries. Onchocerciasis is an NTD that occurs in Africa and is co-endemic with HAT in most HAT foci. We believe that NTD research should focus on the elimination of NTDs as a public health problem in Africa.

Happy reading to all.

Dr. Florent Mbo Kuikumbi

Summary of the 5th Joint Scientific Meeting HAT Platform-EANETT, 3-4 October 2018, Kampala, Uganda

Opening ceremony



Prof. Charles Waiswa, Executive Director of the Coordinating Office for the Control of Trypanosomiasis in Uganda



Dr Florent MBO, HAT Platform coordinator, DRC



Prof. Grace Murilla, chair of EANETT, Kenya

The opening ceremony began with the welcome address of the master of ceremonies, Prof. Enock Matovu, to all the participants. The HAT Platform Coordinator then thanked Uganda's Ministry of Health for its contribution to trypanosomiasis control in the country, and Makerere University for hosting this meeting in Kampala. The HAT Platform Coordinator also thanked DNDi, which funded this scientific meeting, and other partners, such as FIND, IMT Antwerp, Swiss TPH, IRD, and other research institutions under the leadership of WHO, for their technical and material support to organise this conference. The EANETT (East African Network for HAT Control) Coordinator praised this partnership, which allows researchers from different backgrounds to discuss the results of their research projects.

On behalf of the internal and external members of the Committee, the Chair of the Scientific Committee thanked all the outstanding HAT experts and the participants attending the meeting. The theme of the meeting was "Challenges faced by research and control activities to maintain HAT below the elimination threshold by 2020". A total of 58 abstracts were submitted, of which 56 were selected, 34 for oral presentations and 22 as posters. Due to funding limitations, only 33 oral presentations and 13 posters were presented. The scientific meeting was divided into four sessions:

1. Roundtable on the elimination of human African trypanosomiasis
2. Epidemiology, operational research and socioeconomic issues associated with HAT elimination
3. Research on new diagnostic and therapeutic options
4. Vector control and genetic and genomic aspects of HAT elimination

Description of the sessions

Session I: Roundtable on the elimination of sleeping sickness: disease progression and new treatment prospects



Dr José Ramon Franco, Representative of WHO HAT team, Switzerland

The WHO representative gave an overview of the current HAT situation and discussed how to maintain the disease below the elimination threshold after 2020. He presented the objective which are to eliminate HAT as a public health problem by 2020, and to stop the transmission of *gambiense* HAT (gHAT) by 2030. This progression towards elimination is measured by primary indicators (i.e. number of cases reported every year and size of the risk area reporting less than one case per 10,000 people per year), and secondary indicators assessing the quality and intensity of activities.

These secondary indicators are:

- Geographical distribution of the disease
- Populations with different levels of risk
- The proportion of at-risk populations covered by control and surveillance activities

The epidemiological situation shows a reduction in the number of cases down to 1447 in 2017, i.e. below the elimination target set at 2000 cases by 2020.

Gambiense HAT accounted for 98% of all reported cases, and *rhodesiense* HAT for 2%. The areas at risk reporting one or more cases per 10,000 people examined per year are decreasing for both forms of the disease. Active screening coverage was improved.

In terms of passive surveillance, the number of health facilities able to diagnose the disease rose from 732 in 2013 to 1370 in 2017, and the number of health facilities able to treat the disease increased from 530 in 2013 to 686 in 2017.

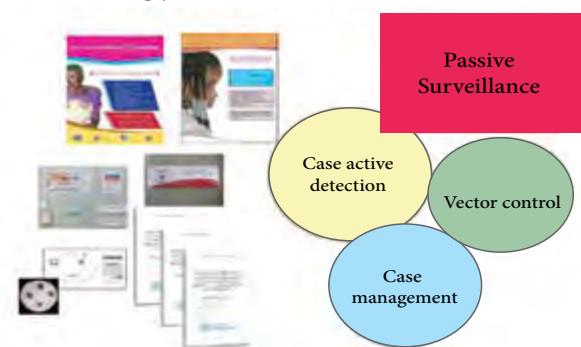
However, this downward trend in the number of cases hides some degree of under-detection for the following reasons:

In certain regions, the epidemiological situation is unknown due to accessibility issues (geographic or safety);

Other regions are not covered by surveillance and control activities due to a lack of financial resources and management or organisational problems (national programs, community, etc.).

In 2016 and 2017, 17 endemic countries were still reporting HAT cases: Angola, Cameroon, Central African Republic, Chad, Republic of the Congo, Ivory Coast, Democratic Republic of the Congo, Equatorial Guinea, Gabon, Guinea, Malawi, Nigeria, Sudan South, Uganda, Tanzania, Zambia and Zimbabwe. Countries are required to submit their validation dossier to WHO. A country may be considered as having eliminated HAT as a public health problem once surveillance and control activities detected less than one case per 10,000 people examined per year in all health districts over the past 5 years.

Strategy of HAT elimination





Dr Nathalie Strub-Wourgaft, Director of NTD/DNDi, Switzerland



Dr Antoine Tarral, Head of HAT team / DNDi, Switzerland

The second speaker in this session presented DNDi's NTD projects in Africa. She pointed out that over 90% of the global NTD burden is concentrated in Africa. She reviewed DNDi's clinical trial program, and explained the different development phases of the new chemical entities for the following NTDs:

- *Gambiense* and *rhodesiense* human African trypanosomiasis
- Cutaneous and visceral leishmaniasis
- Chagas disease
- Filarial diseases, and particularly onchocerciasis
- Mycetoma

The different sites of clinical trials on NTDs in Africa were shown (DRC, Uganda, Kenya, Guinea, Malawi and Ethiopia). DNDi uses and builds research capacity through clinical research platforms on HAT, leishmaniasis, Chagas disease and filarial diseases, which play a key role in defining patient needs and target product profiles, building local capacity, conducting Phase II and III clinical trials, facilitating the registration of new treatments, accelerating the implementation of new treatments, and ensuring that the treatments reach the patients.

The third speaker reviewed the achievements of DNDi's HAT research program and the progress towards disease elimination. He presented the three treatments currently developed or being developed by DNDi for HAT control and elimination:

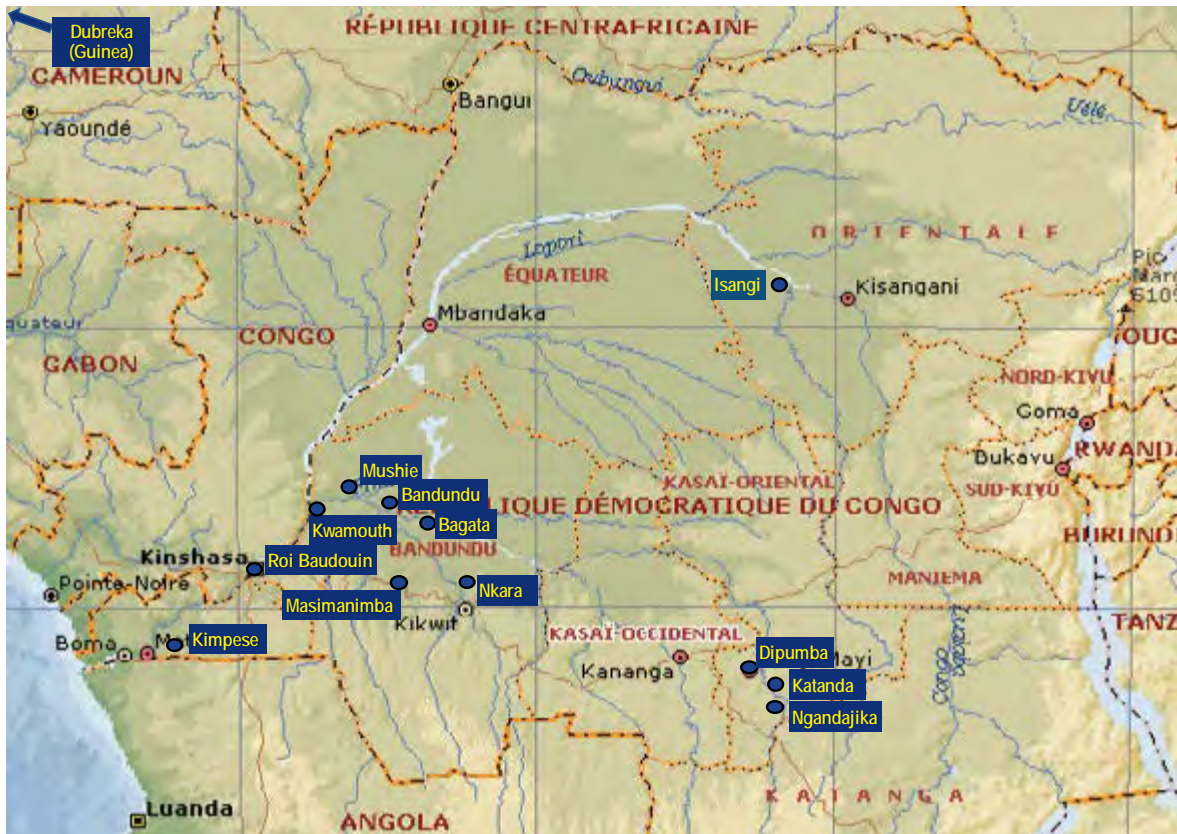
- NECT, to which DNDi continues to support access in endemic countries

- Fexinidazole, with 91.2% efficacy in Phase II/III studies, was approved by the European Medicines Agency in November 2018 and registered in the DRC in December of the same year. Fexinidazole is the first all-oral treatment.
- Acoziborole, a promising oral therapy currently evaluated in Phase II and III clinical trials, for which recruitment is expected to end in 2019.

The challenges associated with Phase II and III of clinical trials include:

- The selection of sites based on the epidemiology of the disease
- Facilities
 - Patients' ward
 - Laboratory, pharmacy, investigators office
 - Telecommunication, electricity, cold chain
 - Water, hygiene measures and waste management
 - Staff training on Good Clinical Practice, nursing, laboratory procedures, data transfer
- Equipment
 - Microscopy with camera (video)
 - HAT diagnosis, biochemistry, haematology, digitized ECG and collection of samples for PK/ PD assays

Map of the clinical trial sites (FEX-004, FEX-005, FEX-006, FEX-009 and OXA-002)



Support was given to case detection:

- Active case detection
 - Support to the ten National Sleeping Sickness Control Program (NSSCP) mobile teams
 - 1 million people examined
 - 110 HAT cases detected
- Passive case detection
 - Ten study sites in hospitals
 - Further peripheral-level centres have been added since 2018
 - Nine are able to carry out parasitology and serology tests
 - Only two perform serology tests, then collect the trypanolysis samples to be sent to INRB

- Reactive active screening of previously identified serological suspects
- Additional active detection of NSSCP cases with the collaboration of IMT

An update was given on patient recruitment on 31 August 2018 for the FEXI009 clinical trial (91 patients, of which 24 were treated as outpatients), and for the OXA002 clinical trial (124 stage 2 patients with > 20 leukocytes per microliter).

The speaker concluded by saying that the sustainable elimination of the disease requires new tools. Surveillance and control efforts (mobile teams, passive case detection centres, sentinel surveillance sites) must be supported to prevent a re-emergence of the disease.

The fourth presentation focused on the results of the fexinidazole clinical trial.

The plan for the Phase II/III clinical development of fexinidazole was discussed with the European Medicine Agency (Article 58) during two meetings of the scientific advice committee (2011 and 2014).

Study number	design	population	Dose	N	Country
FEX004	OL ⁽ⁱ⁾ , randomised, non-inferiority, vs NECT	Adults inpatients Stage 2 g-HAT	Day 1-4: 1800mg/day qd - Day 4-10: 1200mg/day QD	394	DRC ⁽ⁱⁱ⁾ , CAR ⁽ⁱⁱⁱ⁾
FEX005	OL, cohort	Adults inpatients Stage 1, early stage 2 g-HAT	Same as FEX004	230	DRC ^(iv)
FEX006	OL, cohort	Children $\geq 6-14$ years All stages, g-HAT, inpatients	> 35kg: same as FEX004 ≥ 20 kg to < 35kg 1200mg/day, QD 4days 600mg/day, QD 6 days	125	DRC ^(iv)
FEX009	OL, cohort	All the above, in- or outpatients	As above	91	DRC and Guinea

A total of 710 patients treated with fexinidazole

(i) Sponsor blinded (ii) Democratic of Republic of Congo (iii) Central African Republic (iv) same sites as FEX004

Design of three clinical trials on fexinidazole

FEX004 pivotal study	<p>Open-label for the site but blinded for the sponsor (including data management)</p> <p>Based on a binary endpoint: success or failure measured at 18 months follow-up. Failure is defined as:</p> <ul style="list-style-type: none"> – Trypanosome in any body fluid after EOH, or – WBCs > 20/μl in CSF, or – Rescue treatment, or – Death, or – Lost to follow-up <p>Non-inferiority test with a 13% acceptability margin</p> <p>Primary analysis on mITT (excluding patients who fled due to civil war and consequently LTFU)</p>
FEX005	Adults – Stage 1 working hypothesis: success rate greater than 80%
FEX006	Children - Working hypothesis: success rate greater than an unacceptable rate of 80% and compatible with a 92% target rate

Study population

		FEX004 (a)		FEX005 (b)		FEX006 (b)	All Fexi
		NECT	Fexinidazole				
N	ITT	130	264	230	125		619
	mITT	127	262				
LTFU	ITT	3	4	0	0		4
	mITT	0	2				
Treatment discontinuation (N)		0	2	0	0		2
Gender (%)							
	Male	61.5	61	50	53.6		55.4
	Female	38.5	39	50	46.4		44.6
Age (years)							
	Mean	35.32	34.48	34.38	10.86		29.68
	Min-Max	15 - 68	15 - 71	15 - 73	6 - 15		6 - 73

(a) 18 months follow-up - (b) 12 months follow-up

Primary efficacy analysis

	FEX004	FEX005	FEX006
N	(394) mITT 389 262 fexi - 127 NECT	230	125
Efficacy based on (success rate**)	(S.R.= 91.2% (fexi)vs 97.6%(NECT)	S.R. = 98.7% [96.2%- 99,7%]	97.6% [93.1%- 99.5%]
	Difference (effectsize) = -6.61% C.I. of difference = [-11.2%;-1.61%]	p <0 .0001 (H ₀ : S.R.≤ 80%)	p <0 .0001 (H ₀ : S.R.≤ 80%)
	P=0.0029* (H ₀ : Δ _{S,R} ≤ -13%)		

*Note: the two-sided p-value presented here is from a Blackwelder test (with a non-inferiority margin of -13%). It should be compared to 0.0294 (two-sided). The confidence interval is adjusted for multiplicity of testing.

**Success is defined as the absence of failure.

Success rate based on the number of WBCs and the presence of tryps in CSF at baseline

EP population, n = 608*, fexinidazole group, 3 studies pooled [95% C.I.]

CSF parameter	Absence of trypanosomes	Presence of trypanosomes	Overall success rate
WBC ≤ 5	99.6% (253/254), [98.2%, 99.9%]	100% (2/2), [33.3%, 100%]	98.1% (255/256), [98.2%, 99.9%]
6 ≤ WBC ≤ 20	100% (59/59), [95.8%, 100%]	100% (3/3) [46.4%, 100%]	100% (62/62), [96.0%, 100%]
21 ≤ WBC ≤ 100	98.6% (72/73), [85.5%, 97.3%]	97% (32/33), [86.7%, 99.7%]	98.1% (104/106), [94.1%, 99.6%]
WBC > 100	91.7% (22/24), [75.9%, 98.2%]	88.1% (140/159), [82.3%, 92.4%]	88.5% (162/183), [83.3%, 92.5%]
Overall success rate	99.0% (406/410), [97.7%, 99.7%]	89.8% (177/197), [85.1%, 93.5%]	96.0% (583/607), [94.3%, 97.4%]

*One patient was not included in this table due to missing data

Effect of WBC count (Log_e WBCs): p < 0.0001

N.B. WBCs > 20 = late stage 2 (adults and children)

Effect of tryps: p < 0.0001

A cut-off point at 100 WBCs differentiates higher and lower success rates.

Effect of tryps in addition to WBCs: not significant
due to the correlation between tryps and WBCs

Link between high WBC count and clinical symptoms in all fexinidazole studies

Symptom	WBC ≤ 100 69.7%	101 ≤ WBC ≤ 400 16.5%	WBC > 400 13.8%	P -value association	Occurrence rate
			% (n/N)		
Headache	63.5 (273/430)	71.6 (73/102)	75.3 (64/85)	0.0531	66.5 (N = 616)
Weight loss	38.5 (165/429)	61.8 (63/102)	57.6 (49/85)	<0.0001	45 (N = 616)
Asthenia	27.0 (116/429)	60.8 (62/102)	67.1 (57/85)	<0.0001	38.1 (N = 616)
Pruritus	25.6 (110/430)	52.0 (53/102)	81.2 (69/85)	<0.0001	37.6 (N = 617)
Sleepiness	16.3 (70/429)	70.6 (72/102)	78.8 (67/85)	<0.0001	33.9 (N = 616)
Fever	28.4 (122/429)	47.1 (48/102)	34.1 (29/85)	0.0014	32.3 (N = 616)
Anorexia	15.3 (66/430)	19.6 (10/102)	12.9 (11/85)	0.4266	15.7 (N = 617)
Insomnia	16.3 (70/430)	34.3 (35/102)	43.5 (37/85)	<0.0001	23.2 (N = 617)
Tremor	7.4 (32/430)	34.3 (35/102)	51.8 (44/85)	<0.0001	18.0 (N = 617)
Walking disability	3.3 (14/430)	20.6 (21/102)	30.6 (26/85)	<0.0001	9.9 (N = 617)
Nausea	9.5 (41/430)	8.8 (9/102)	5.9 (5/85)	0.5578	(N = 617)
Language disability	1.4 (6/429)	14.7 (15/102)	21.2 (18/85)	<0.0001	(N = 616)

P-values are linked to the null hypothesis of equality of success rate in the presence and absence of each symptom. The occurrence rate is the percentage of

patients presenting the symptom at entry into the set of patients treated with fexinidazole that were evaluated.

Management of failures

ITT set of patients	Fexinidazole N (%)	NECT N (%)	Cumulated relapses fexinidazole N (%)	Cumulated relapses NECT N (%)	Excess relapse rates
Randomized	264	130	0	0	
Relapse at M3	0	0(0%)	0	0	0%
Relapse at M6	3(1.14%)	0(0%)	3(1.14%)	0(0%)	1.14%
Relapse at M12	7(2.65%)	0(0%)	10(3.79%)	0(0%)	3.79%
Relapse at M18	3(1.14%)	0(0%)	13(4.92%)	0(0%)	4.92%
Relapse at M24	2(0.76%)	0(0%)	15(5.68%)	0(0%)	5.68%

Abbreviations: CSF, cerebrospinal fluid; ITT, intention-to-treat; LTFU, lost-to-follow-up; M, month; NECT, nifurtimox-eflornithine combination therapy; WBC, white blood cells

14 out of the 15 patients received NECT, and 7 were cured, 5 were lost-to-follow-up, and 2 only had a

6-month follow-up. NECT treatment was associated with a high success rate.

Safety summary

	DNDiFEX004 NECT (N=130)	DNDiFEX004 Fexinidazole (N=264)	DNDiFEX005 Fexinidazole (N=230)	DNDiFEX006 Fexinidazole (N=125)	All Fexinidazole (N=619)
TEAEs	121 (93%) [607]	247 (94%) [1525]	214 (93%) [1258]	116 (93%) [583]	577 (93%) [3366]
Serious TEAEs	13 (10%) [22]	31 (12%) [51]	20 (9%) [32]	10 (8%) [14]	61 (10%) [97]
Severe TEAEs	23 (18%) [27]	52 (20%) [68]	23 (10%) [31]	22 (18%) [25]	97 (16%) [124]
Deaths	2 (2%) [2] *	9 (3%) [11] *	4 (2%) [7]	1 (<1%) [2]	12 (2%) [17]
Possibly Related	103 (79%) [345]	215 (81%) [923]	195 (85%) [859]	103 (82%) [353]	513 (83%) [2135]
Permanent treatment discontinuation	0	2 (<1%) [2]	0	0	2 (<1%) [2]

Format is number of subjects (percent of subjects) [number of events]
TEAEs=Adverse events occurred during the treatment

* No statistical difference between NECT and fexinidazole on relative risk of death $p>0.05$

Patients with AEs according to organ system by decreasing frequency (ITT)

	DNDi/FEX004 NECT (N=130)	DNDi/FEX004 Fexinidazole (N=264)	DNDi/FEX005 Fexinidazole (N=230)	DNDi/FEX006 Fexinidazole (N=125)	All Fexinidazole (N=619)
Any TEAE	121 (93%)	247 (94%)	214 (93%)	116 (93%)	577 (93%)
Gastrointestinal disorders	64 (49%)	157 (59%)	179 (78%)	98 (78%)	434 (70%)
Nervous system disorders	64 (49%)	158 (60%)	142 (62%)	61 (49%)	361 (58%)
General disorders and administration site conditions	51 (39%)	122 (46%)	94 (41%)	51 (41%)	267 (43%)
Psychiatric disorders	23 (18%)	103 (39%)	73 (32%)	19 (15%)	195 (32%)
Musculoskeletal and connective tissue disorders	21 (16%)	58 (22%)	38 (17%)	13 (10%)	109 (18%)
Investigations	10 (8%)	7 (3%)	42 (18%)	21 (17%)	70 (11%)
Blood and lymphatic system disorders	18 (14%)	29 (11%)	13 (6%)	20 (16%)	62 (10%)
Infections and infestations	8 (6%)	22 (8%)	13 (6%)	12 (10%)	47 (8%)
Respiratory, thoracic and mediastinal disorders	11 (8%)	32 (12%)	9 (4%)	6 (5%)	47 (8%)
Vascular disorders	9 (7%)	24 (9%)	18 (8%)	1 (<1%)	43 (7%)
Skin and subcutaneous tissue disorders	8 (6%)	22 (8%)	13 (6%)	7 (6%)	42 (7%)
Eye disorders	3 (2%)	15 (6%)	16 (7%)	10 (8%)	41 (7%)
Cardiac disorders	7 (5%)	18 (7%)	17 (7%)	4 (3%)	39 (6%)
Renal and urinary disorders	7 (5%)	13 (5%)	6 (3%)	0	19 (3%)
Injury, poisoning and procedural complications	14 (11%)	15 (6%)	0	2 (2%)	17 (3%)
Reproductive system and breast disorders	1 (<1%)	5 (2%)	5 (2%)	0	10 (2%)

FEX009 study update (recruitment status until 6 May 2019)

Treated patients	Follow up at 3 months	Follow up at 6 months	Follow up at 12 months	Follow up at 18 months
139	116	100	53	35

OXA002 study update (recruitment status until 31 March 2019 and follow up until 6 May 2019)

Treated patients	Follow up at 3 months	Follow up at 6 months	Follow up at 12 months	Follow up at 18 months
208	196	167	103	68

In summary

- A total of 710 patients were treated with fexinidazole, of which results from 619 adults and children at both stages of the disease were included in the regulatory submission
- Fexinidazole met the efficacy criteria as defined in the protocol in all three studies
- The overall efficacy rate was 96%
- Fexinidazole showed a favourable safety profile and no patient discontinued treatment due to

side effects (this is also confirmed in the ongoing study)

- Fexinidazole is under review by EMA

Notes after the meeting: Fexinidazole has received a favourable scientific opinion from EMA according to the article 58 procedure on 15 november 2018 and was approved by regulatory pharmaceutical authorities from the DRC health ministry on 24 december 2018 for its use by PNLTHA as on available treatment

Impact of the Ebola outbreak on sleeping sickness in coastal Guinea: A retrospective analysis (2012-2017) from the Guinean national HAT control program

Oumou Camara et al.



PNLTHA, GUINEA

This work was conducted in coastal Guinea, the last HAT foci still very active in West Africa. The Guinean government and its partners are conducting HAT control activities to reduce the burden of this neglected tropical disease and, as directed by WHO, to eliminate it as a public health problem by 2020. Unfortunately, these control efforts were severely hampered by the Ebola outbreak that hit the country in 2014-2015. The aim of the study was to evaluate the impact of this unprecedented outbreak on HAT screening and treatment activities, and on the transmission of *T. brucei gambiense* more globally.

A retrospective analysis of the data collected by the NSSCP between 2012 and 2013 (pre-Ebola period) and 2014-2015 (Ebola outbreak) showed that HAT active screening activities were interrupted, and HAT passive screening activities dropped sharply

with the spread of the Ebola outbreak. During the outbreak, HAT patients were diagnosed at a later stage of the disease and attendance at post-treatment control visits was also severely affected. Only 59 HAT patients were diagnosed and treated during the Ebola outbreak (January 2014-October 2015), compared to 154 before the outbreak (February 2012-December 2013). This potentially high number of undiagnosed human reservoirs of trypanosomes may have contributed to increased transmission. After Guinea was declared free of Ebola, screening activities (both passive and active) resumed progressively. In 2016 and 2017, Guinea reported 107 and 140 HAT cases, respectively (almost twice as many as during the pre-Ebola period), and became the second most affected country after DRC.

A major lesson learned from the Ebola outbreak is that disruption to medical care may rapidly lead to a re-emergence of HAT in areas with high intensity transmission. The authors hope that current HAT control measures combining screening and tsetse control interventions will help Guinea to keep on target for the elimination goal.

Geographic distribution of HAT cases in the DRC from 2011 to 2017: Spatial analysis of HAT Atlas data

Shancy Shampa *et al.*



PNLTHA, RDC

The Democratic Republic of the Congo (DRC) is the country with the largest number of human African trypanosomiasis (HAT) cases in the world, with nearly 80% of all cases reported to the World Health Organization. The HAT Atlas is a major asset

to improve our knowledge of the distribution of HAT patients, georeferenced at the village level. The aim of this presentation was to use the atlas to show the

geographical distribution of patients with HAT, and identify the areas of transmission.

A descriptive spatial analysis of the case distribution from 1st January 2011 to 31st December 2017 in the geo-referenced endemic villages was carried out.

During this period 25,633 HAT cases were detected and reported by the DRC. The various maps show the cumulative number of cases and their distribution by transmission area during these 7 years. In conclusion, the creation of this database and the identification of HAT transmission areas help the national program improve its planning of control and surveillance activities.

Active research strategy to identify unconfirmed CATT-positive suspects set up by a health district team in the DRC

Matthieu Nsio *et al.*



Bagata health zone, DRC

The WHO set the goals of HAT elimination as a public health problem by 2020 and HAT eradication by 2030. However, elimination requires the deployment of control activities in endemic health districts to ensure that activities are maintained

in multipurpose health services. One of the activities that can be monitored is the follow-up of unconfirmed CATT-positive suspects by primary healthcare facilities. The objective of our work is to share our active search strategy, conducted by the health district team, of CATT-positive suspects that were not confirmed passively by multipurpose health services.

The Bagata health district team in the DRC identified 50 CATT-positive suspects between January 2017 and March 2018 in five health centres conducting CATT-based serological screening and HAT diagnosis.

An active system was implemented to find former CATT-positive suspects that had not been confirmed passively by the five health centres. These suspected cases were found, and a parasitology confirmation test was performed at the Bagata general referral hospital.

Preliminary results showed that from 50 suspected cases identified, 14 were present for the confirmation test. Of these, ten were brought to the hospital by the district team and four came on their own.

The authors believe that HAT elimination requires the combination and adaptation of several strategies. Prior to the implementation of this strategy, no HAT cases had been diagnosed in the health district facilities over a period of 3 to 6 months.

In conclusion, the authors consider that in the current period of low prevalence, targeting CATT-positive or RDT-positive suspects through repeated parasitology tests by a health district team would be a sustainable way to identify the latest remaining HAT cases. More efforts are required to make this operation cost-effective.

Quantifying HAT transmission dynamics in a peri-elimination era through mathematical modelling

Katherine Rock et al.



University of Warwick,
United Kingdom

As we enter the peri-elimination phase for *gambiense* HAT, new challenges arise to identify remaining cases effectively and maintain the progress achieved so far. As we find fewer cases, the HAT strategy must necessarily change, but it is difficult to assess the possible impact of

this change on transmission. Mathematical modelling provides a tool which can be used to infer underlying transmission dynamics from current case data, but also to predict the outcome of different interventions.

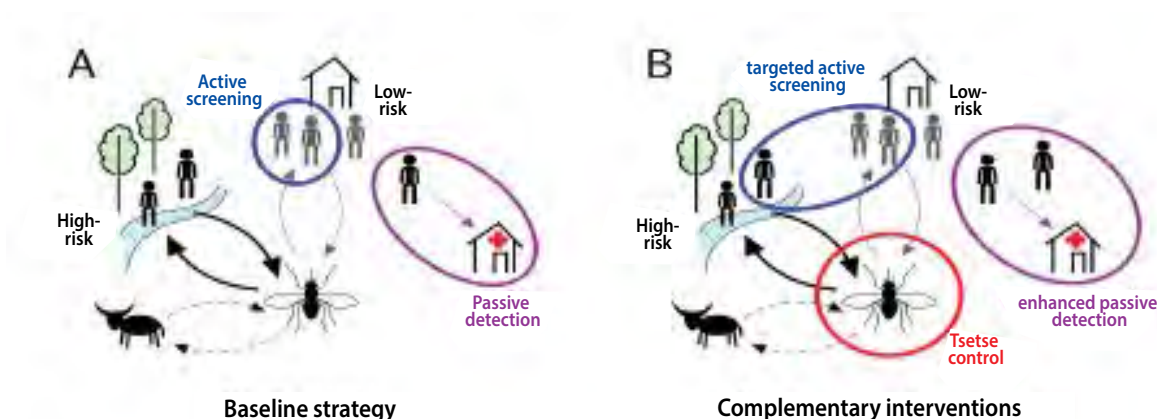
Mechanistic mathematical models which can capture transmission dynamics of *gambiense* HAT were used to predict the impact of a variety of plausible interventions on transmission and case reporting in different epidemiological settings. Strategies considered include combinations of traditional or door-to-door active screening, passive surveillance

with or without improvements to fixed health facilities, and vector control based on tiny targets.

Across different settings, the authors consistently find that tsetse control strategies, combined with continued medical interventions, reduce transmission quickly. They can avert many cases which would be expected without this intervention, although there was a lag before this would be observed in case reporting. Other improved interventions, such as improved passive surveillance or door-to-door active screening, can also be very beneficial for elimination but with likely slower progress towards the targets.

In conclusion, not all settings require tsetse interventions to reach elimination thresholds, however it could speed up the time needed to achieve them. The exact combination of interventions required to meet elimination goals will depend on determination, and future cost-effectiveness analysis will help to identify efficient strategies whilst accounting for uncertainty and risk in cessation of medical and vector interventions.

Modelling strategy impact



Risk of HAT resurgence in low-prevalence conflict areas: case of Kasai Occidental province in the DRC

Rashidi Samuel et al.



PNLTHA, DRC

Human African trypanosomiasis (HAT) is an endemo-epidemic disease specific to tropical Africa that occurs often in rural and remote areas where the health system is deficient (WHO, Epidemiol weekly report, 2004). To date, sustained efforts to

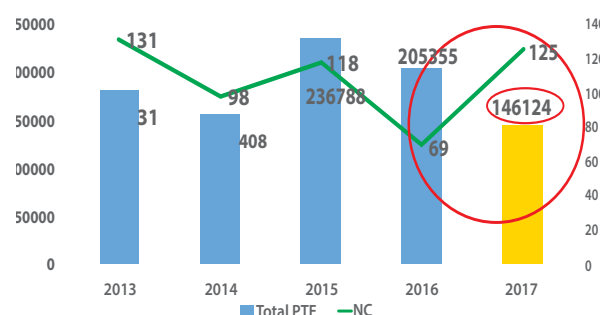
implement the main control strategies, i.e. reduction of human reservoirs through active and passive screening, monitoring patient treatment and vector control, reduced the number of cases reported annually down to a level close to the elimination target (WHO Report 2017). However, it is now recognized that cessation of control activities has most often been one of the causes of resurgence of the disease (Ekwanzala et al., The Lancet 1996). This may be due to different contributing factors such as war, tribal conflicts, etc.

The authors presented the risk of resurgence of the disease in a low prevalence conflict zone.

This is a cross-sectional descriptive study that focused on the analysis of epidemiological data from Kasai Occidental province from 2013 to 2017, and in the first half of 2018.

New cases (NC) occurred in 2017 in the same proportions as four years ago, coverage was low (59%), 169 endemic villages were visited out of 287 planned, and 87,980 people at risk were not covered. Unlike in previous years, 80% of new cases were diagnosed in the first stage of the disease in 2017, which shows active HAT transmission. This situation was also observed in the other provinces of the DRC and in Angola.

PTE and NC evolution from 2013 to 2017



Detection of sleeping sickness: syndromic perception in South Sudan

Jennifer Palmer et al.



London School of Tropical
Medicine and Hygiene,
United Kingdom

As the infection burden of sleeping sickness decreases globally, diagnosis relies increasingly on lay people's powers of observation to identify potential cases. The author presented an account of the syndromic experiences of patients

in Nimule, South Sudan. Community discourses were well known and described sleeping sickness as consisting of four interdependent symptoms: sleeping

disorders, mental confusion and hunger, which leads to dangerous anti-social behaviour, and pain in the neck and back, reflecting their knowledge of disease transmission and the diagnostic procedure. Patients and their families and friends had some perception of the onset, progression and resolution of the disease, based on what they knew of these discourses. Even though they were unaware of some pathognomic biomedical signs, they perceived other biomedically underestimated sensory signs which led them to consult screening services. Therefore, the perception of the disease by those infected involves physical, cultural and community processes.

Innovative tools and quality data to achieve the elimination of sleeping sickness

Alain Mpanya et al.



PNLTHA, DRC

Human African trypanosomiasis (HAT) is a vector-borne parasitic disease that affects poor people in rural areas of sub-Saharan Africa. About 80% of the cases occur in the DRC. Over the last decade, the number of cases dropped considerably, and the size of outbreaks declined to a

level compatible with the elimination of HAT.

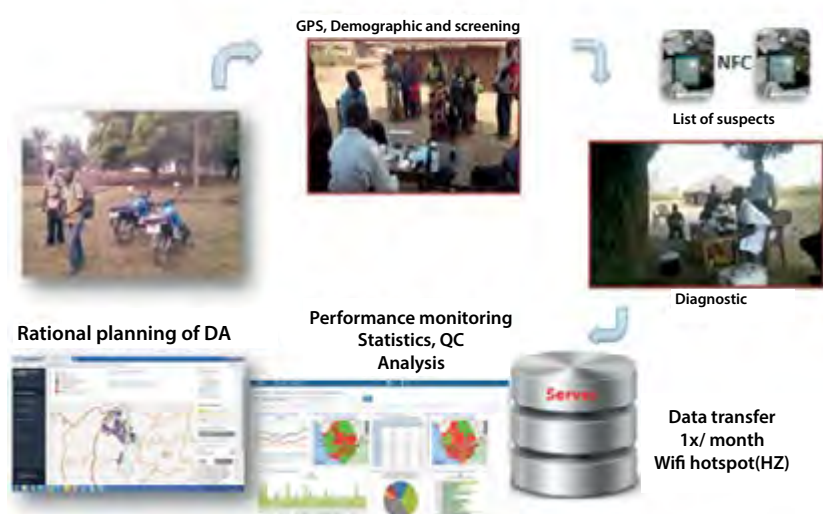
The number of cases reported annually dropped to a thousand, but millions of people are still at risk. This increases the need for reliable data to better guide mass screening campaigns.

IMT, with the support of the Bill and Melina Gates Foundation, developed a digital platform in

partnership with the NSSCP in the DRC to monitor and streamline mass screening planning activities. We developed an Android mobile app to help screening teams collect demographic and epidemiological data, as well as GPS coordinates. It also provides visual evidence (images and video) of diagnostic test results.

Since there is no source of electrical energy in the areas where HAT occurs, 12V batteries and solar panels are used. Every month when screening teams return to the station, digital data are synchronized with the web interface. The screening teams use an integrated planning tool and a route planner to find the remaining endemic villages. The digital information system is an integral concept designed to manage the elimination of HAT and potentially of other NTDs. They presented the captured data, the web interface and the dashboard with the active screening planning tool that has just been launched in three of the most endemic provinces in the DRC to accelerate the elimination of HAT.

Data collection and management



Human African trypanosomiasis (HAT), epidemiological, diagnostic, therapeutic and evolutionary aspects in children and adolescents in three healthcare sites in Guinea

Ansoumane Kourouma et al.



PNLTHA, GUINEA

Sleeping sickness is still prevalent in maritime Guinea, and every year more than 50 cases are detected by the NSSCP. Children suffering from this disease are not diagnosed in health facilities, whose staff have not been trained. The objective of this study was

to study the epidemiological, diagnostic, therapeutic and evolutionary aspects of trypanosomiasis in children and adolescents aged 0-17 years at the three treatment sites. This ambispective, descriptive, longitudinal study lasted 8 years, from 1 January 2010 to 31 December 2017. Children accounted for 29.19% of the total population.

- 92 patients were included
- Age varied between 3 months and 17 years, with an average of 10 years
- The 10-14 year age group was the most affected (33.70% of cases)
- 66.30% were males

- 61.96% were schoolchildren
- The Boffa prefecture was the most affected (38.04% of cases)
- 57.61% of the patients had been detected through passive screening
- The most common clinical signs included cervical lymphadenopathy, fever, sleep and behavioural disorders, facial oedema, pallor of integuments, asthenia, neurological disorders and pruritus
- Positive serology in 98.78% of patients
- Lymph node puncture was positive in 93.84% of the patients
- 86.96% of patients were at stage 2
- 66.36% had received the nifurtimox-eflornithine treatment combination
- 98.91% of patients were improved but 97.83% had not submitted to the four controls required to be declared cured
- None of the thirteen (13) formerly infected HAT patients had a health problem related to this disease

Intensification of vector control and passive and active screening will help eliminate HAT in Guinea by 2020.

Enhanced screening and diagnosis of gambiense HAT in north-west Uganda – Moving towards elimination

Charles Wamboga et al.



Ministry of Health, Uganda

The incidence of gambiense human African trypanosomiasis (gHAT) in Uganda has been declining, from 198 cases in 2008 to 2 cases at the end of June 2018. A strategy to accelerate elimination of the disease in north-west Uganda has been implemented since

The strategy, which helped to extend passive gHAT screening to the entire population at risk, consists of a diagnostic algorithm based on the use of rapid diagnostic tests (RDTs) to screen patients suspected of having gHAT, followed by parasitological confirmation at strategically located microscopy centres. For patients with negative parasitology, blood samples are further tested by loop-mediated isothermal amplification (LAMP).

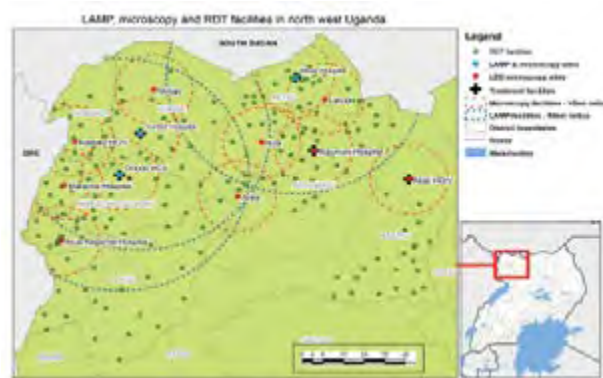
Patients suspected of gHAT infection are sent to one of the 174 health facilities in the region, thereby reducing

2013.

the distance they must travel to be diagnosed from 23 km before 2013 to 2.5 km. This network of health facilities, combined with the use of active screening, provided a rapid response to the recent challenge of the influx of South Sudanese refugees into north-west Uganda. Over 1 million refugees settled in the region, both in refugee camps and among local communities. A large number of them come from gHAT endemic areas in South Sudan. Two gHAT cases were diagnosed among refugees in 2017, by health facilities using the gHAT RDTs. One other case was diagnosed in 2018

by active screening in the refugee camps. The strategy is supported by epidemiological studies to identify areas with potential active transmission and thus guide active screening campaigns.

In conclusion, this strategy is appropriate to accelerate gHAT elimination in low-prevalence settings and shows that it is possible to integrate passive screening into existing healthcare delivery systems. However, the conflict in South Sudan may still jeopardise gHAT elimination in Uganda.

Health facilities performing HAT screening within the HAT *gambiense* belt since 2013

HAT associated with witchcraft in DRC endemic areas : Presentation of a clinical case

Helene Mahenzi et al.



Human African trypanosomiasis (HAT) is a neglected tropical disease prevalent in remote rural areas where educational attainment is often very low and attachment to cultural beliefs high. In this environment, any health problem is associated with a

bad spell, and HAT, like any other disease, is thought to be due to witchcraft.

It is in this context that the authors presented a clinical case of HAT in a girl aged 4, whose parents consulted, without success, several health facilities, traditional healers, and even revivalist churches to seek deliverance. These observations were also

reported by other authors (Hasker. E et al, Trop Med Int Health, 2011).

During her hospitalisation in a nutritional management unit of the hospital, systematic serological screening, advocated by the NSSCP, confirmed stage 2 HAT with nutritional complications. At 6-month follow-up, the patient weighed 17 kg (vs. 8 kg upon admission) after treatment with eflornithine infusion for 7 days and oral nifurtimox for 10 days administered through a nasogastric tube, and associated nutritional care.

As we move towards the HAT elimination goal by 2020 set by the WHO, public awareness must be strengthened. We believe that there are other clinical cases such as this one within our communities, which require appropriate information and guidance, and the involvement of all actors, whether traditional practitioners, community and religious leaders, or health professionals.

Enhanced passive screening for HAT in Angola: Progress towards elimination

Makana Don Paulo et al.



ICCT, ANGOLA

In December 2016, a programme was initiated in the provinces of Zaire and Cabinda in Angola to expand and intensify passive screening for HAT. These provinces form a large transboundary region with the Democratic Republic of the Congo (DRC) and the Republic of Congo. Zaire is endemic for HAT, while Cabinda had not reported cases for many years, it is infested with tsetse flies, and little medical surveillance has been conducted.

To enhance case detection, passive screening was extended to all health facilities in Zaire and to selected facilities in Cabinda. Screening for HAT was based on a hierarchical diagnostic algorithm in which patients with a positive rapid diagnostic test (RDT) were referred for confirmatory testing by microscopy at one of six health facilities. In addition, ten health facilities were able to perform mHCT, and two other facilities provided molecular testing using LAMP for

patients who were RDT positive but not confirmed as infected with HAT.

Between December 2016 and December 2017, 4,516 RDTs were performed, of which 67 (1.5%) were positive with one case identified in Zaire. Referral of RDT positives was hampered by difficulties in accessing the small number of facilities offering microscopy testing. In 2018, the programme was extended to 82 health facilities in Bengo and Uige provinces, which performed 5,959 RDTs in June 2018, of which 55 were positives, and 9 were confirmed HAT cases. Further cases were detected with the addition of mini-mobile teams to follow-up RDT positives. Reactive active screening in villages where HAT cases had been recently reported identified another 12 cases.

This programme demonstrates that enhanced passive screening can drive local elimination of HAT. Passive screening combined with small mobile teams overcomes some of the challenges of case referral. Reactive active screening in villages where HAT cases have been reported appears to be very beneficial.



From January to September 2018, 69 cases were detected in Angola, and case detection was improved by the follow-up conducted by mini-mobile teams.

Enhanced passive screening for HAT in a troubled transboundary focus in the Republic of Congo

Ossibi Bienvenu et al.



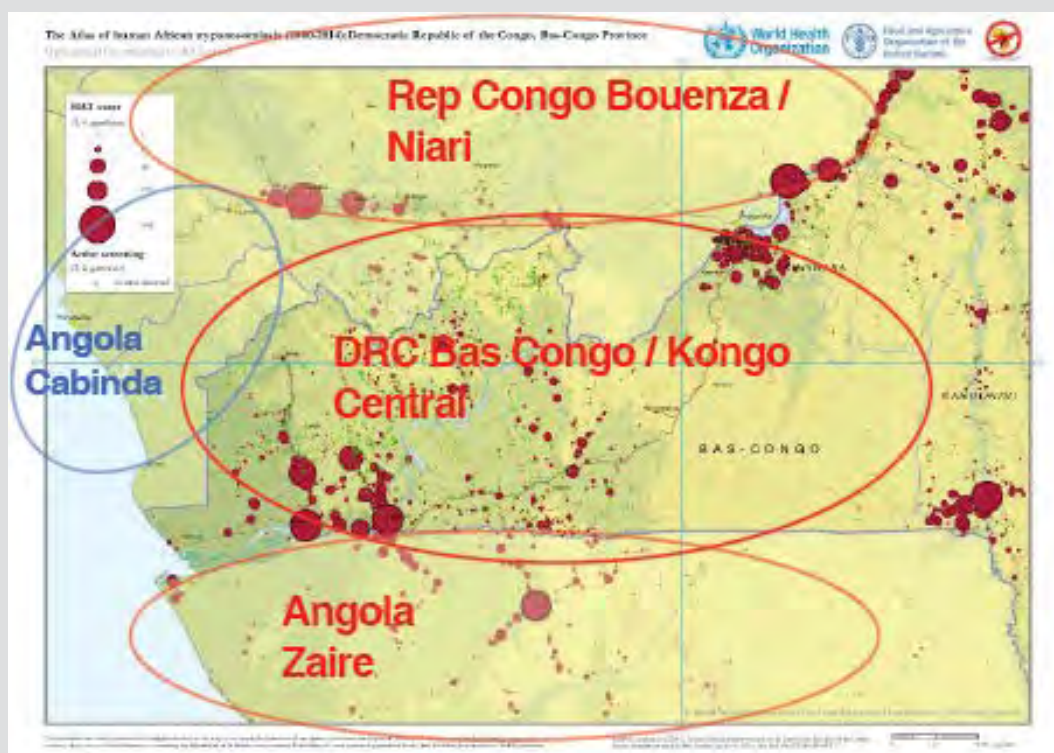
PNLTHA, CONGO

The south-west border of the Republic of the Congo forms a transboundary HAT focus with regions located in the DRC and Angola. The area includes the departments of Pool, Bouenza and Niari, but Pool has been inaccessible due to civil instability. Prior to this programme, the population's HAT diagnostic coverage was limited, with only three facilities providing HAT diagnosis. In partnership with FIND, the NSSCP of the Republic of the Congo implemented a programme to enhance of passive screening for HAT in this region.

The programme started with the characterisation and mapping of the 57 health facilities in the HAT endemic regions of these departments. The laboratories of three

facilities were then upgraded to perform microscopy using fluorescence microscopes, and one laboratory was upgraded to perform loop mediated isothermal amplification (LAMP) of DNA. All facilities in Niari and Bouenza were equipped with rapid diagnostic tests (RDTs), but 16 facilities in Pool could not be reached. RDT-positive patients are referred for confirmatory testing by microscopy. Between March and June 2018, 916 HAT RDTs were performed by 41 health facilities, yielding 17 positives, of which three were confirmed as having HAT, i.e. 0.3% of those tested were diagnosed with HAT.

Initial results of this programme demonstrated a high HAT burden in the population screened. Continuation of this programme and its extension to other foci in the Republic of the Congo, supplemented by reactive screening, may yield further valuable results to help drive HAT elimination.



Map of cross-border project on HAT elimination between the DRC, Congo and Angola

Enhanced passive screening for HAT in the Kongo Central province of the DRC - progress towards elimination after three years

Kayembe Simon *et al.*



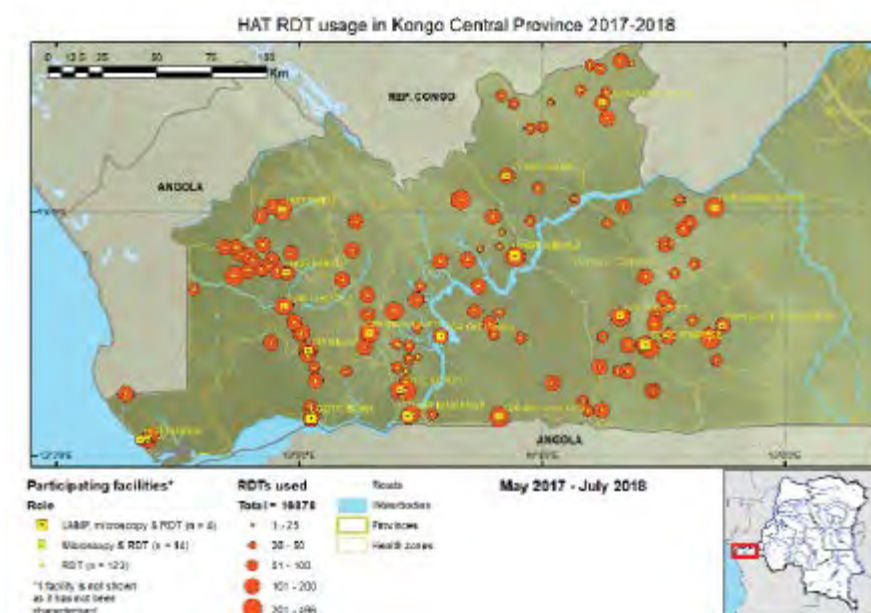
CONSULTANT FIND,
DRC

Use of HAT RDT in the Kongo Central province of the DRC: given the case distribution, the number of healthcare facilities dropped: 142 centres providing HAT TDR, 18 microscopy, and 4 LAMP and microscopy.

In August 2015, intensive screening for human African trypanosomiasis (HAT) was initiated in the Kongo Central (former Bas-Congo) province of the DRC, by extending passive screening for the disease to all 600 health facilities in HAT endemic areas of the province.

screening was used in villages where cases had been passively identified during the programme.

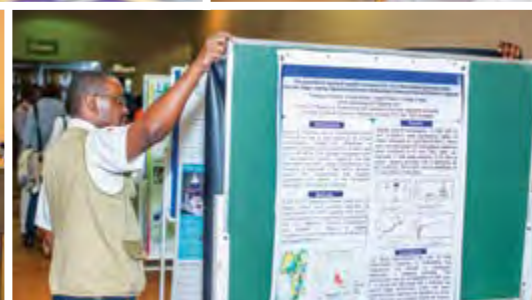
Between August 2015 and December 2016, 45,299 patients were screened, and 81 cases were diagnosed, of whom 65.4% were at stage 1 and 48.1% had been found RDT-positive at facilities that only performed RDTs. A further 55 cases (90.9% at stage 1) were identified by reactive screening. Considering the dynamics of the disease in the province, the programme was strategically scaled back to 142 facilities (14 of them performing microscopy, and 4 both microscopy and LAMP). In this second phase of the programme, between May 2017 and May 2018, a further 13,203 RDTs were performed with 20 cases diagnosed, but unlike the first phase, only 30% were at stage 1. A further two cases (one at stage 1) were identified by reactive screening. A third phase of the



HAT detection was based on a hierarchical diagnostic algorithm, whereby RDT-positive patients were referred for confirmatory microscopy testing at 23 of the 600 facilities. A further five facilities of the 23 provided molecular testing using LAMP on samples from RDT-positive patients which had not been confirmed by microscopy. In addition, reactive active

programme was initiated in August 2018, to scale back to 61 strategically located facilities, selected to provide an efficient coverage of the population.

This approach demonstrates that passive screening can be extended and used to drive local elimination of HAT, and that enhanced passive screening can be effective in identifying cases in early stage of infection.





Evaluation of the sensitivity of primers used for PCR diagnosis of *gambiense* human African trypanosomiasis in Guinea costal foci

Hamidou Ilboudo *et al.*



HEALH SCIENCE-
RESEARCH INSTITUTE,
NANORO, BURKINAFASO

The control of human African trypanosomiasis (HAT) relies mainly on patient screening and treatment. Screening is based on serology tests followed by parasitological confirmation, but these methods lack sensitivity and specificity. Several

Polymerase Chain Reaction (PCR) techniques using different types of primers were developed to improve

the diagnostic algorithm. The objective of our study was to evaluate the sensitivity of several primers used for the molecular diagnosis of gambiense HAT.

The study was carried out in three active HAT foci (Dubreka, Boffa, and Forecariah) located in mangrove areas of coastal Guinea. A total of 204 patients were included in the study, and a blood sample was taken from each included patient for molecular analyses with TBR, 18S, LiTaT 1.3, AnTaT 11.17, TgsGP, and TgsGP nested primers. The study results are reported below.

Sensitivity of primers

Primers	N	Pos (%)	Pos (%)
TBR	204	190 (93.1)	14 (6.9)
18S	204	193 (94.6)	11 (5.4)
LiTaT 1.3	204	182 (89.2)	22 (10.8)
AnTaT 11.17	204	176 (86.3)	28 (13.7)
TgsGP	204	160 (78.4)	44 (21.6)
TgsGP Nested	204	175 (85.8)	29 (14.2)

This study confirms the sensitivity of the TBR and 18S primers compared to the other primers tested. Although specific for *T. b. gambiense*, the TgsGP primers have a lower sensitivity, which increases with nested PCR. The authors show that LiTaT 1.3 and

AnTaT 11.17 primers can be also used for molecular diagnosis of *T. b. gambiense*, but further studies are necessary to determine whether these primers are specific to *T. b. gambiense* only.

Use of immune trypanolysis to detect *T.b. gambiense* specific antibodies in the sera of domestic animals in silent and hypo-endemic sleeping sickness foci in the DRC (foci of Boko-Kivulu and Boma in Kongo Central province)

Pyana Pati et al.

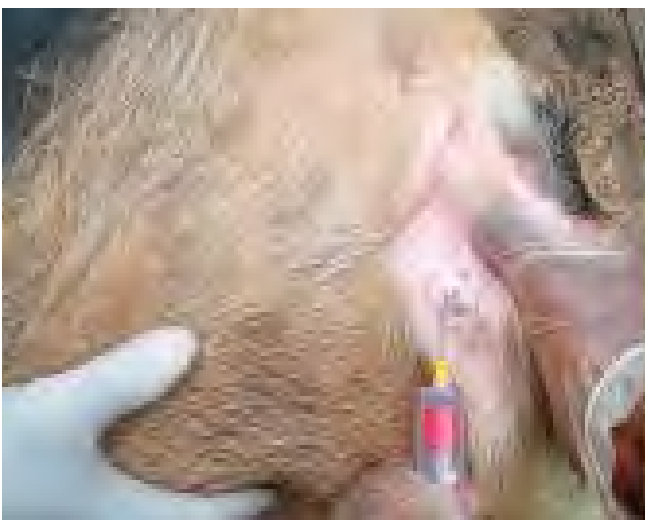


NATIONAL INSTITUTE
OF BIOMEDICAL
RESEARCH, DRC

Trypanosomiasis caused by the subspecies *Trypanosoma brucei (T.b.) gambiense* is considered to be an anthroponozoonosis. In accordance with WHO guidelines, diagnosis and treatment, sometimes combined with vector control, are performed by the National Sleeping

Sickness Control Programs (NSSCP) to control and eventually eliminate gambiense human African trypanosomiasis (gHAT) by 2020. However, the elimination of gHAT may be challenged by the presence of a possible wild and/or domestic animal reservoir, which may explain the hypoendemicity in the Kongo Central province of the Democratic Republic of the Congo, where 21 of 31 health centres continued to record new HAT cases over the past 15 years.

In order to investigate the existence of a possible domestic animal reservoir in the Kongo Central province, authors collected sera from 121 goats, 57 sheep, 30 pigs and 30 cattle in the Boma district and Muanda territory, located in a hypo-endemic focus where at least 100 HAT cases have been reported each year over the past 15 years. During the same period, they also tested sera of 66 sheep, 2 pigs and 9 cattle from Boko-Kivulu, located in a historic focus where no new HAT case was recorded. Immune trypanolysis (TL) was performed on all sera with both *T.b. gambiense* LiTat 1.3 and 1.5 variable antigen type. Only one pig serum from Boko-Kivulu was TL positive with LiTat 1.3. This contradicts the theory of an animal reservoir, since in that silent focus, no human case has been reported over the past 15 years. They recommended further studies on a putative animal reservoir of *T.b. gambiense* using the immune trypanolysis test.



Blood collection in domestic animals

Surveillance model combining rapid diagnostic tests and collection of filter papers in a network of sentinel sites in the northern Equateur province of the DRC

Charles Kambo *et al.*



PNLTHA, DRC

The number of HAT cases has been decreasing sharply over the last decade thanks to intense mass screening campaigns in the endemic areas. The elimination of HAT as a public health problem is becoming an achievable goal. In the provinces of Mongala,

North and South Ubangi, DRC, the number of cases dropped from 14,764 in 1997 to 47 in 2014. There is no passive surveillance model currently available for post-elimination settings. This project aims to test a sensitive surveillance system adapted to low prevalence areas.

In 15 health zones of the Provincial Divisions of North Ubangi, South Ubangi and Mongala, a network of sentinel sites was set up with 28 facilities

performing TDR screening and paper filter collection for trypanolysis when parasitological confirmation tests were negative. If the trypanolysis results are positive, the suspect is located in order to conduct another parasitological test.

The preliminary results show that TDR screening was performed in 8,112 people, of whom 1.89% ($n = 153$) were positive with 16 new cases confirmed parasitologically. Trypanolysis was performed in 80% of parasitologically unconfirmed positive RDTs, i.e. in 109 cases out of 137 in total. One trypanolysis was positive, and the patient was located and confirmed parasitologically.

In conclusion, the study showed that monitoring that combines RDTs and filter paper collection for trypanolysis is possible in a low prevalence area as part of a passive surveillance scheme. However, it is still too early to determine the sensitivity of this model.

Performance of diagnostic algorithms based on rapid diagnostic tests to detect sleeping sickness in the DRC

Jacques Makabuza *et al.*



PNLTHA, DRC

It is essential to integrate HAT screening into peripheral healthcare facilities to eliminate the disease. This requires effective diagnostic tools that are easy to use in the remote areas with limited resources where HAT cases are found. We conducted a prospective

study to evaluate the performance of recently developed rapid diagnostic tests (RDTs), followed or not by serology tests and/or the molecular reference test (RT) performed in the regional referral centres.

Suspected HAT cases were tested with the various available RDTs. Positive RDT cases were referred to

the diagnostic centre for parasitology tests and blood sampling on filter paper for the RT (ELISA, Immuno-Trypanolysis, LAMP or real time PCR) in the regional referral centres. If the RT was positive, the patient with suspected HAT was asked to return to the diagnostic centre for a second series of parasitology tests. The confirmation of HAT cases was based on one positive parasitology test. All suspect cases with a positive RDT and/or a positive RT, and a negative parasitology test were monitored with a parasitology follow-up for 6 months.

Over the first five months, 1,104 people were registered and 138 (12.5%) were RDT positive and considered as suspected HAT positives. Among the suspect cases, parasitology tests were performed on 106 (76.8%) and 13 were confirmed as HAT (1.2% of the people screened, 12.3% of the suspected HAT cases).

Timely compliance for referred suspects and samples was 34% and 47%, respectively.

The combination of TDRs with RT and parasitology tests is achievable in remote and relatively small areas. The referral of suspected cases and samples worked well, but it still needs substantial improvement.

The distance between peripheral health facilities and the diagnostic centre was a major stumbling block.

This study is part of the EDCTP2 programme, supported by the European Union, grant number DRIA-2014-DiTECT-HAT.



Photos showing quality control activities

Diagnostic potential of neuron-specific enolase and interleukin-10 to discriminate between early- and late-stage *rhodesiense* HAT

Twesigye Dorothy et al.



MAKERERE UNIVERSITY,
UGANDA

The authors hypothesize that cytokines modulates disease progression and the severity of the neurological response.

A total of 107 HAT patients and 14 healthy controls were recruited passively at Lwala Hospital in northern

Uganda. NSE and IL-10 levels were measured from paired plasma and cerebrospinal fluid (CSF) samples. Cytokine concentrations were analysed based on disease progression, clinical presentation, and severity of neurological symptoms.

Median plasma levels of NSE (571.2 pg/ml) and IL-10 (85.44 pg/ml) were significantly higher in HAT cases than in controls ($p < 0.0001$). When early stage and late stage CSF and plasma cytokines were compared,

IL-10 and NSE were up-regulated in late-stage patients and were associated with reduced tremor and cranial nerve neuropathy. IL-10 had superior staging accuracy with a sensitivity of 92.31% (95% CI, 63.97% to 99.81%) and a specificity of 71.43% (95% CI, 51.33% to 86.78%), while NSE had a specificity of 80% (95% CI, 51.91% to 95.67%) and a sensitivity of 41.18% (95% CI, 27.58% to 55.83%).

In conclusion, the study demonstrates the role of host inflammatory cytokines in modulating the progression and severity of neurological responses in sleeping sickness.

They demonstrated here an up-regulation of NSE and IL-10 during the late stage with potential as adjunct stage biomarkers. Given that both cytokines could potentially be elevated by other CNS infections, our findings should be further validated in a large cohort of patients including those with other inflammatory diseases such as cerebral malaria.

Therapeutic approach in experimental trypanosomiasis by assessment of posaconazole

Nzoumbou Romaric et al.



UNIVERSITY OF BANGUI,
CAR

Trypanosomes cause important but neglected infectious diseases in both humans and animals. In intertropical Africa, human and animal sleeping sickness are endemic parasitic diseases. Diagnosis and treatment of trypanosomiasis remains a challenge to controlling the disease. Because of

limited alternatives and the toxicity of treatments, new treatment options are urgently needed for HAT patients. In this study, we evaluated the trypanocidal activity of posaconazole and identified the potential target involved.

The parasite cell lines *T.b. brucei* EATRO 1125 and *T.b. brucei* 427 90.13 were used for this study. The oral drug candidate posaconazole was evaluated *in vitro* and *in vivo* against *T.b. brucei* EATRO 1125. *In vitro* assessment of posaconazole was performed on a 96-well plate, and cultures were maintained at 37°C with 5% CO₂ in an incubator for 24h.

The activity was expressed in terms of IC₅₀ (concentration required to inhibit 50% of the parasite's cell growth). For *in vivo* assessment, swiss (OF-1) mice were infected on day 1 by subcutaneous injection with 104 bloodstream forms of *T.b. brucei* EATRO 1125. Treatments started at day 5 post-inoculation. The target for posaconazole was demonstrated with a tetracycline-inducible RNAi system using the p2T7tiB/GFP plasmid transfected in *T.b. brucei* 427 90.13.

We noted trypanocidal activity of posaconazole *in vitro* compared to controls. *In vivo*, posaconazole significantly prolonged the survival of *T.b. brucei* infected-mice by 15 days compared to the controls. A reduced growth rate was observed for induced cells compared to the non-transformed parent cell line (WT) and the non-induced CYP51RNAi cells, and cell growth stopped after 14 days of induction, demonstrating that TbCYP51 is essential to *T.b. brucei* BSFs. These results support a HAT treatment targeting CYP51. Therefore, a combination therapy based on posaconazole may represent a treatment alternative for trypanosomiasis.

Evolution of nutritional status of children included in the DNDiFEX006 study in the DRC, between diagnosis and end of 12-month follow-up

Digas Ngolo et al.



PNLTHA, DRC

In the Gambia, human African trypanosomiasis is a chronic parasitic disease regularly associated with nutritional deficiencies. DNDiFEX006 was an open prospective clinical study, evaluating the efficacy and safety of fexinidazole in children at least 6 years old and over 20 kg and suffering from HAT,

to describe the nutritional status of children with all stages of the disease, prior to treatment, at the end of hospitalization, and at the end of the 12-month follow-up.

The data were extracted from the DNDiFEX006 clinical study which took place in the DRC from 2014 to 2017 in 8 referral hospitals. The nutritional parameters collected during the study included age, sex (pre-inclusion visit), weight, height, and BMI (all visits), as well as haemoglobin, blood urea nitrogen (BUN), alkaline phosphatase, and blood albumin (during hospitalisation and at 9-week follow-up visit for some of them).

A total of 125 children with human African trypanosomiasis were included in this study. The authors concluded that human African trypanosomiasis is a parasitic disease often associated with protein-energy malnutrition in children. Management should include nutrition as is the case with some chronic infectious diseases, such as tuberculosis and AIDS.

Anthropometric and biochemical parameters before treatment and at 9 weeks or 12 months of follow-up

Parameters	n	Means +/- SD		
		Before treatment	9 weeks	12 months
Weight (kg)	125	28.3 ± 7.5	—	31.4 ± 8.7
Height (cm)	125	131.5 ± 12.9	—	135.7 ± 13.5
BMI(kg/m ²)	125	15.9 ± 1.3	—	17.0 ± 1.8
Albumin (g/dL)	89	3.4 ± 0.3	3.7 ± 0.3	—
Hémoglobin (g/dL)	89	11.6 ± 1.6	12.0 ± 1.5	—
Blood urea nitrogen(mg/dL)	89	6.5 ± 2.4	5.7 ± 2.4	—
Alkaline phosphatase(IU/L)	89	45.4 ± 74.7	195.4 ± 68.1	—

DNDi

Potential of CSF interleukine-6 and neopterin levels to discriminate between early- and late-stage *rhodesiense* HAT patients in Uganda

Asiimwe Immaculate et al.



MAKERERE UNIVERSITY,
UGANDA

Some patients with stage 1 HAT receive the highly toxic treatment for stage 2 HAT, and in other instances stage 2 patients are under-treated with stage 1 drugs, which impairs their chances of survival. It is important to improve HAT staging, and to eliminate the need for

lumbar punctures.

In this study, cerebrospinal fluid (CSF) samples were collected from HAT patients recruited passively at Lwala Hospital. Routine diagnosis of suspected HAT patients was done by microscopic examination of wet and thick blood films prepared from finger prick blood. For patients with positive blood smears, a lumbar puncture was performed to stage the disease. IL-6 and neopterin were assayed using sandwich ELISA and competitive ELISA, respectively. Based on

disease progression, these biomarkers were compared in early- and late-stage patients with ROC curves to determine the stage discriminatory potential.

Results showed that median CSF neopterin levels were significantly higher in late-stage patients (21.02 ng/mL) than in early-stage patients (9.92 ng/mL). Similarly, median CSF IL-6 levels in late-stage patients (28.7 pg/mL) were significantly higher than in early-stage patients (14.25 pg/mL). Neopterin demonstrated a high staging potential with a sensitivity of 71.43% (95% CI, 41.9%-91.61%) and a specificity of 71.43% (95% CI, 29.04%-96.33%). IL-6 also demonstrated a high staging potential with a sensitivity of 66.67% (95% CI, 46.04%-83.48%) and a specificity of 76.92% (95% CI, 46.19%-94.96%).

In conclusion, further studies analysing IL-6 and neopterin as panels with other previously identified markers are required.

Assessment of the project's socio-economic and environmental impacts to create areas permanently freed from tsetse flies and trypanosomiasis four years after the end of the campaign

Percoma Lassane et al.



PATTEC, BURKINA FASO

Launched in October 2006, the pilot phase of the pan-African tsetse and trypanosomiasis eradication campaign ended in December 2013 in Burkina Faso. Its implementation was based on the following procedures:

The objective of this study is to evaluate the impact of the project's actions, 4 years after its closure. The methodology used was based on analytical approaches integrating the environment and the participation of the population and local authorities. The LEOPOLD matrix was used to identify the impacts, and the FECTEAU grid was used to describe and evaluate their absolute importance.

The authors noted among other things an increase in crops grown using draught animals (97.47% vs. 90.40% in 2013), a significant decrease in animal mortality (62.09%), an increase in average herd numbers with a 48.73% relative variation between 2008 and 2017, and an increase in average income per agropastoralist. Overall, 97.98% of respondents reported being satisfied with the results of the project and 95.29% with the control methods used. Negative changes attributable to the project were poaching, opening and extension of fields (51.76% of farmers), immigration (47.06%), overgrazing (40%) and the destruction of sacred sites (17.76%). These results were confirmed by direct observation of the biophysical environment.

In view of all these results, measures to protect the environment, enhance positive impacts and mitigate negative impacts were proposed.

❑ Integrated pest management strategy

- Deployment of 42,138 screens and 1,320 impregnated traps



- Ground spraying in the barrier zone and in the persistence zone of tsetse flies



- Aerial spray on 100 km of river and 100 km of tributaries



- Epicutaneous and trypanocidal treatment of more than 1 million cattle



- ❑ Four years after the end of the project, the socio-economic and environmental impacts must be assessed

Increasing the toolbox for trypanosomiasis control: exploring efficacy of metacyclic antigens for mammalian vaccines

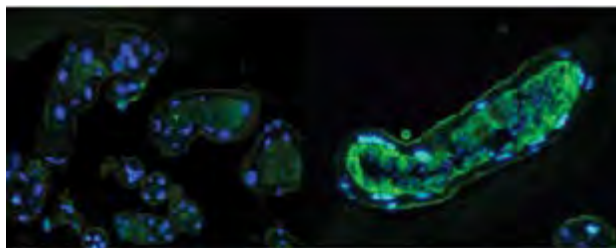
Serap Aksoy et al.



YALE SCHOOL OF PUBLIC
HEALTH, USA

To date, most vaccine efforts targeting mammalian bloodstream forms (BSFs) have been unsuccessful. Knowledge on the metacyclic parasites present in tsetse saliva, which the host is initially exposed to during the infection process, is also sparse.

In vector-borne diseases such as HAT and AAT, prior efforts targeting attenuated salivary gland stages of the parasite provided promising results. Transcriptomics studies identified a family of surface proteins specific to *T. brucei* spp. (*Trypanosoma brucei* salivary gland metacyclic forms, or tbsgm2), which are preferentially expressed by the mature metacyclic parasites present in tsetse saliva, and in mammalian blood for at least 24h after inoculation through the bite of an infected tsetse. Immunohistochemistry and immunogold labelling with antibodies against recombinant rtbsgm2 localized the protein on the surface of the metacyclic cells.



Anticorps recSGM2 antibodies
reconnaissent parasites infectant
les glandes salivaires et
agglutinant les metacyclic
in vitro



Control AC

#recSGM2 AC

ELISA analysis detected high levels of antibodies for Tbsgm2 in sera from experimental mice challenged by infected tsetse bites, as well as in sera from gambiense patients, but not in sera of endemic controls. Passive transfer of rtbsgm2 specific IgG to naïve mice demonstrated protective efficacy against trypanosome infections acquired through a fly bite. In the first experiment, parasitemia was significantly delayed while in the second experiment, one of the three animals had no parasitemia, while the other two had significantly reduced parasite levels 3 days post fly challenge. Future studies are warranted to investigate the efficacy of tbsgm2 as a potential transmission-blocking vaccine candidate antigen to help ongoing efforts to control African trypanosomiasis.

Temporal genetic differentiation in *Glossina pallidipes* populations in Kenya

Winnie Okeyo *et al.*



In Kenya, the tsetse fly *Glossina pallidipes* is a major vector of both human and animal African trypanosomiasis (HAT and AAT). The disease imposes an economic burden on the country's endemic regions, including south-west Kenya, where intense but unsuccessful tsetse fly control measures were

implemented.

For this study, 387 *G. pallidipes* flies were genotyped on 13 microsatellite markers to evaluate levels of temporal genetic variation in two regions: the Nguruman escarpment which had been subject to habitat alteration due to human activities, and Ruma National Park which had not. Between 2003 and 2015, we collected samples from three sampling sites for each of the two regions, i.e. ~96 tsetse fly generations.

The authors showed that allelic richness averaged from 3.49 to 3.63, and temporal estimates of the effective population size (N_e) averaged 594 in the Nguruman Escarpment and 1120 in Ruma National Park. The similarity of genetic diversity compared to previous studies from Uganda and Kenya implies that we could not detect a reduction in genetic diversity after the control efforts between the 1960s and the 1980s. However, we did find differences in temporal patterns of genetic variation between the two regions.

In the Nguruman Escarpment, findings indicated differentiation among samples collected in different years, and evidence of local genetic bottlenecks. In contrast, there was no consistent evidence of differentiation among samples collected in different years.

Their findings suggest that tsetse flies in these regions display a genetic diversity similar to that of populations that were not subject to extensive control measures. The difference in temporal differentiation between the two regions indicates that genetic drift is stronger in the Nguruman Escarpment, for as-yet unknown reasons, which may include differences in land management. This suggests that land management may have an impact on *G. pallidipes* population genetics, and it reinforces the importance of long-term monitoring of vector populations to improve modelling and plan effective species-specific control measures.

Poster session

13 abstracts were selected for the poster presentations, and the best one is shown below.

Title of poster

Diagnostic potential of neuron-specific enolase and interleukin-10 to discriminate between early- and late-stage *rhodesiense* HAT

Author: Twesigye Dorothy, Makerere University



Closing address of the 5th Joint Scientific Meeting HAT Platform-EANETT

Preamble

The 5th Joint EANETT/HAT Platform Scientific Conference was held from 3-4 October 2018 at Speke Resort, Munyonyo Kampala, Uganda. The theme of the conference, supported by the Drugs for Neglected Diseases *initiative* (DNDi), was “Research and control activities challenges to keep HAT below the elimination threshold by 2020”. The event was attended by over 100 scientists, collaborators, partners, donors and HAT control managers from various endemic and non-endemic countries, with a renewed interest in finding solutions to eliminate the disease and maintain it below the projected elimination threshold. The conference was officially closed by Prof. Charles Waiswa, Executive Director of the Coordinating Office for Control of Trypanosomiasis in Uganda (COCTU).

Reflecting on the previous conference themes, the meeting acknowledged that research forms an integral part of disease elimination, and its role becomes more prominent as we approach the elimination threshold as set in WHO's strategy. During the conference, scientific papers were presented on the following themes: diagnosis, drug discovery, clinical trials & treatment, public health & socioeconomics, vector biology & control, and epidemiology.

It was noted with appreciation that the quality of the presentations has improved significantly, and that more papers originated from Central Africa compared to previous years.

Key achievements to date

The decline in new cases was made possible through the partners' commitment to provide funds for research and capacity strengthening in the following areas:

- New diagnostic tests
- Development and access to new drugs /drug combinations
- Improvement of diagnostic facilities to improve the coverage of populations at risk
- Creation of ethical committees in various HAT endemic countries to improve the quality of clinical research, and enhance data sharing
- Preparation of the HAT elimination dossier for the countries
- Training health workers to improve case detection and management
- Post-graduate training for scientists
- Mentorship of young scientists

Challenges and current needs

- Funding is dropping, even though more investment is required to design new approaches to understand and sustain the control of an increasingly rare disease. Any complacency could lead to resurgence
- Consolidation of efforts and effective coordination of all stakeholders in each country/region
- Endemic countries should be more involved, claim ownership of these efforts, demonstrate commitment and ensure sustainability
- Improve access to diagnostic tests
- Provide more sensitive diagnostic tools
- Raise awareness in communities
- Harmonise tools for M&E
- Improve knowledge on population genetics/genomics and their potential exploitation to drive an integrated approach to elimination
- Find new approaches to vector control (such as repellents, attractants) to strengthen existing ones and completely break the transmission cycle
- Conduct social anthropological research to use available indigenous knowledge to support passive surveillance and access to treatment

Discussion and recommendations

The participants acknowledged that HAT is on the decline and that countries need to initiate steps to declare elimination in line with the guidelines provided by WHO. Reports from the DRC on *T.b. gambiense* in pigs require further investigation into the role of animal reservoirs in disease epidemiology. As more HAT endemic countries move closer towards elimination, the question raised in previous scientific conferences, and still unanswered, is which factors sustain epidemics? This re-emphasizes the need to increase our efforts to understand HAT epidemiology.

To avoid a resurgence of HAT, the participants were encouraged to continue seeking support from their governments, starting with consolidation of key stakeholder activities in vector and disease research and control.

EANETT and HAT Platform member countries encouraged the participants to ensure that quality

baseline data are collected, and that M&E is performed in accordance with internationally recognized standards. This will help assess the impact on elimination.

The HAT endemic countries commend the efforts of WHO, DNDi, FIND and other supporting partners for their roles in supporting drugs/diagnostics R&D, by making these products available to the affected countries. Countries whose disease situation is not well known should take advantage of this and plan measures to establish the presence/absence of disease.

The EANNET Board and the HAT Platform Steering Committee wish to thank all those who have supported the activities and ideals of the two organisations by contributing significantly to the HAT elimination programme.

Grace Murilla PhD
Chair EANETT

Dr. Florent Mbo
HAT platform coordinator



Welcome to

Dr Constantina Pereira Furtado Machado

Executive Director of ICCT Angola

Doctor of Internal Medicine

Former Secretary of State for Health

Report on the regional HAT Platform steering committee meeting, 5 October 2018, Kampala, Uganda



The meeting was chaired by the Director of the Coordinating Office for Control of Trypanosomiasis in Uganda (COCTU) assisted by the HAT Platform Coordinator. The speeches of the HAT Platform coordinator and the Executive Director of the Uganda Trypanosomiasis Coordination Office, representing the Ministry of Health, were followed by a presentation of the countries and the partners.

The HAT Platform coordinator reviewed the activities of the platform in 2017 and 2018 and gave an outlook for 2019. DNDi presented the results of clinical trials on fexinidazole, the first all-oral drug for HAT, to the member countries' Focal Points and other partners.

Activities performed in 2017 and 2018

- Dissemination of the Newsletter N° 19
- HAT Platform Steering Committee Meeting and 5th Joint HAT-EANETT-Platform Scientific Meeting
- Support to the ethical committees of Guinea (revision of the guidelines) and Uganda (training on research ethics)
- Revitalisation of country HAT platforms through meetings (Angola, Chad, Guinea, DRC, Congo, Uganda)

- Exchange visit between member countries (visit of clinical trial sites and field control activities in the DRC by the national coordinator of Guinea)
- Participation of the coordinator in international conferences (9th EDCTP Forum, 9th CIPIP congress and ISCTRC)

Activities planned for 2019

- Advocacy with member countries on the use of fexinidazole after approval by the European Medicines Agency and production of treatment algorithms by WHO
- Organisation of the HAT Platform Steering Committee meeting on the sidelines of the next ISCTRC
- Organisation of the HAT Platform's participation at the next ISCTRC congress

After the HAT Platform report, several presentations were given by countries and partners.

Recommendations

At the end of the day, the members of the HAT Platform Steering Committee made the following recommendations:

- The legal status of the HAT Platform should be finalised at the beginning of 2019, following the final feedback given at the end of 2018;
- The HAT platform will undertake country-level advocacy on the use of fexinidazole;
- Continue the revitalisation of national HAT platforms;
- Training of the new national coordinator of the Republic of the Congo;
- Support to the HAT Platform coordinator for the monitoring of the different countries;
- Ensure equality of activities carried out in different countries and advocate with partners to support the training of technicians in the countries.

Rapporteur Florent Mbo

Visits and meetings



Participation in the transboundary HAT elimination project meeting for DRC, Angola and Congo, 8 May 2018, Luanda, Angola



Visit to a HAT clinical trial site in the DRC by the National Coordinator of the NSSCP of Guinea, 1-9 June 2018



Launch of DRC's National Day of Human African Trypanosomiasis, Kinshasa, DRC, 30 January 2018



Visit of the HAT Platform coordinator in Congo, 23 August 2018



Training of two laboratory technicians from Guinea and Burkina Faso at the National Institute of Biomedical Research in Kinshasa, DRC, 18 January 2018



Meeting to review the guidelines of the National Ethics Committee for Health Research Guinea, Conakry, 29 April 2018



Participation in the DNDi Gala where Dr. Kande received a prize as the principal investigator of the fexinidazole clinical trials, New York, USA, 24 October 2018



Participation in the 67th meeting of the American Society of Tropical Medicine and Hygiene, New Orleans, USA, 28-30 October 2018



Participation in the 9th EDCTP Forum, Lisbon, Portugal, 18-20 September 2018



Participation in the 9th International Conference on Infectious and Parasitic Pathology, Lubumbashi, DRC, 20-23 June 2018



Participation in the DRC PNLTHA Partner Meeting Kinshasa, DRC, 30 January 2018



Training in Research Ethics, Kampala, Uganda, 7-9 May 2018



Visit of the HAT Platform coordinator in Chad,
19-21 May 2018



Field visit of DRC PNLTHA director, Maindombe
Province, 21 January 2018



Initiation of Dubreka HAT clinical trial site in Guinea,
7 February 2018



Participation at the HAT clinical trial site's visit by
joint team PNLMTN_CTP and Filariasis Geneva
DNDi team, Kimpese, DRC, 15 November 2018

Participation in the 11th DNDi Partner's Meeting:
innovation and access through a successful
partnership, Kampala, Uganda, 4 October 2018

Recent scientific publications in 2018

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Aita Signorell

International meetings planned for 2019

- 16-20 September: 11th European Congress on Tropical Medicine and International Health (ECTMIH) – Liverpool, United Kingdom
- 23-27 September : 35th International Scientific Council for Trypanosomiasis Research and Control (ISCTRC), Abuja, Nigeria
- 20-24 November: 68th American Society of Tropical Medicine and Hygiene (ASTMH) – Annual meeting, Gaylord National Resort and Convention Center, National Harbor, Maryland, USA

Doctors Without Borders (MSF) Activities in Maniema Province, DRC

January 30th: National Day of African Human Trypanosomiasis

Maniema Province: The MSF-Holland team celebrated the National Day for human African trypanosomiasis (HAT) with partners from the Central Office of the Kibombo Health Zone with community participation in Kibombo.

For the occasion, MSF-Holland's mobile HAT team organised a workshop during which it presented the history of the project since 2013 in the DRC and its achievements in the Maniema province since 2016. With the participation of the Ministry of Health represented by the members of the Central Office of the Health District (BCZS) of Kibombo, the politico-

administrative authorities and members of the local civil society, a march was organised through the territory of Kibombo to raise population awareness of the importance of screening and treatment of sleeping sickness.

Although progress has been achieved in the DRC through the action of humanitarian organisations such as DNDi, sleeping sickness remains one of the world's neglected tropical diseases, especially prevalent in remote areas. Access to quality diagnosis and treatment remains a serious problem for endemic and far-flung areas.

MSF continues to screen and provide free treatment to patients.

With the help of the provincial coordinator and the central offices of the health districts, MSF helps the Ministry of Health to identify areas that are difficult to reach through the National Sleeping Sickness Control Program (NSSCP). Teams continue to work in the field to screen and provide free quality care to people with this disease.

Since 2016, MSF has already visited three health districts (Kasongo, Kibombo and Tunda), including 25 health areas. A total of 59,680 people were screened

out of an expected 67,255, i.e. 88.7% coverage. Of those screened, 117 HAT cases were confirmed and received free quality treatment.

MSF plans to focus its activities in the Lusangi health district of the Kabambare territory in the south-east of the Maniema province, including advocacy work with other actors to increase access to health care for the entire population.

Kabundi Elysé and Kana Alimasi



Activities of the DNDi filarial disease programme in 2018 and 2019

Feasibility visits for clinical trials on onchocerciasis by the DNDi Geneva filarial team, DRC

DNDi Geneva filarial team members carried out a first visit to the DRC in 2018 with staff of the preventive chemotherapy NTD program and of the DNDi Kinshasa office, to determine the feasibility of clinical trials on onchocerciasis. They also met the director of the preventive chemotherapy's neglected tropical diseases programme (PCT NTD program)- and made a field visit to Kikwit within the Bandundu coordination province.

In order to appropriately select the villages from which the patients will be recruited, NTD-PCT conducted a REMO survey in December 2018 in the Pay Kongila health district in Kwilu province, with the help of the French Research Institute for Development (IRD).

In 2019, we will plan and prepare sites for the clinical trials to be conducted in 2020.

Belen Pedrique, Karen Dequatre et Florent Mbo



Obituary



Professor **Henri Joseph Parra** passed away on May 26, 2019 in Brazzaville

Professor of Medicine.

Former Director of National Public Health Laboratory of Congo from 1998 to 2018.

Former adviser to the presidency of the Republic of Congo.

One of the focal points of the HAT Platform in Congo and among its founders.

Tribute from Dr Augustin Ebeja, former coordinator of the HAT Platform, to the late Prof. Henri Joseph Parra

The last of the trio behind the HAT Platform in Congo Brazzaville has fallen !!

Yes, the professor Henri Joseph Parra was, the key to open the doors to the Congolese authorities, university professor and director of the national public health laboratory, as well as advisor to the head of state (president) in health matters.

Thanks to him, the big HAT meeting at the Marina Hotel was a success and we have a good memory of it. As I said before at the death of Dr. Stephane, Prof. Parra made the work climate enjoyable through his sense of humor and consideration of others. He also successfully chaired the Brazzaville focus on the development of the national policy of PNLTHA Congo.

In Congo Brazzaville in particular and in the HAT Platform in general, this disappearance proves to us that the old generation is passing and that the new generation must ensure that the HAT Platform continues to live.

Dr Augustin Ebeja



Onesime Mbilimpili,

Former Head of Mobile team in Kwilu province (formerly Bandundu Province),
50 years in fighting against HAT
Deceased on December 03, 2018



Junior Kande,

Employee at PNLTHA DRC
Contributed a great deal to field visits
for the PNLTHA staff
Born on May 14, 1986
Deceased on May 29, 2019

Birth Notices

Ellya Ntumba Barata Mulamba

Born on January 4th, 2018, Kinshasa
Daughter of Edmond Mulamba, clinical monitor,
DNDi DRC



Maeva Kuikumbi

Born on March 14th, 2019, daughter
of Florent Mbo, HAT Platform
Coordinator, DRC



Cris Dylan Moke

Born on June 29th, 2018,
son of Christian Mpia
Clinical Monitor DNDi, DRC



Sergina Luwawu Bondi

Born on December 28th, 2018,
daughter of Serge Luwawu,
Coinvestigator King Baudouin
Referral General Hospital



Diego and Digas Mvumbi

Twins born on August 17th, 2018,
son of Richard Mvumbi, HR &
Travel Manager DNDi DRC



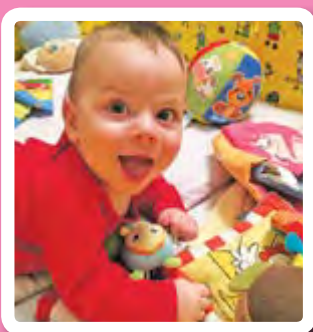
Thomas Olivier Wass

Born on March 08, 2019, son of
Jennifer Palmer, School of Medicine,
London school of tropical medicine
and hygiene, United Kingdom



Gad KABEYA MUTOMBO

born on 28 September 28th, 2018,
son of Dr Wilfried Mutombo,
DNDi DRC Project Coordinator



Lucas Kornmann

Born on Jul 22nd 2018, son of
Cleila Bardonneau, Clinical
Manager DNDi Switzerland



Joyce Victoria yango, born on

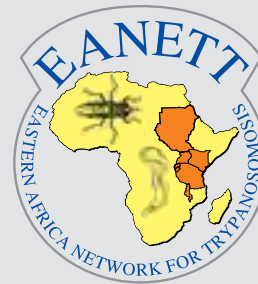
April 5th, 2019,
Little daughter of Dr Augustin
Ebeja, NPO WHO DRC



Lina Sander Biswas

Born on July 30th, 2018, daughter
of Christina Sander, external
relations manager, DNDi Geneva

Announcement



6TH JOINT SCIENTIFIC MEETING HAT PLATFORM-EANETT

Kinshasa, DRC 2020

The HAT Platform and DNDi wish to express their gratitude to the following donors for their support since 2003:

- Brian Mercer Charitable Trust, UK
- Dutch Ministry of Foreign Affairs (DGIS), THE NETHERLANDS
- European Union (Framework Programme 6)
- Federal Ministry of Education and Research (BMBF) through KfW
- French Development Agency (AFD), FRANCE
- French Ministry for Europe and Foreign Affairs (MEAE), FRANCE
- Médecins Sans Frontières International
- Medicor Foundation, LIECHTENSTEIN
- Norwegian Agency for Development Cooperation (Norad), NORWAY
- Republic and Canton of Geneva, International Solidarity Service, SWITZERLAND
- Spanish Agency for International Development Cooperation (AECID), SPAIN
- Swiss Agency for Development and Cooperation (SDC), SWITZERLAND
- UK aid, UK
- Other private foundations and individual donors

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