LEAP
LEISHMANIASIS
EAST AFRICA PLATFORM
NewsLETTER
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Prof. El Hassan being interviewed

Visceral Leishmaniasis in Sudan: A 25-year Retrospective

By Prof. El Hassan

The Leishmaniasis Research Group of the Institute of Endemic Diseases (IEND) has been working on the problem of visceral leishmaniasis in Gedarif State for the last 25 years. This area of Sudan is inhabited by many poor people; tribes migrated to Gedarif from western Sudan and neighbouring African countries. What we found in our first surveys regarding health services, in general, and visceral leishmaniasis (Kala-azar), in particular, was heartbreaking. Kala-azar was rife and sodium stibogluconate (SSG) used as monotherapy to treat the disease then, was only available in the hospitals and was often in short supply.

Admission to the hospital, diagnosis and treatment was too expensive for the families. Parents lost income, because they had to travel to hospitals and stay with their sick children away from their jobs. It is also during this time that a black market for SSG was flourishing, because of some unscrupulous businessmen who took advantage of the situation, seeing that the drug was very expensive. Therefore, counterfeits were sold, consisting of just water instead of SSG. Parents would buy a few millilitres of the drug - too small to be effective - and inject the drug themselves because they could not afford to pay a nurse to do the job. This practice led to high infection with Hepatitis B and C.

Twice a year for the first few years, Sudan was supported by MSF Holland to diagnose and treat kala-azar and its complications. DND*i* then also came into the arena and the Eastern African R&D collaboration for kala-azar grew to what is today.

Dooka, Sudan - El Hassan Centre and Tropical Disease Hospital

A new found relationship between DND*i* and Sudan began when IEND hosted a first meeting, since that time DND*i* has continued to support research in several endemic diseases including kala-azar. In East Africa, DND*i* worked towards establishing the Leishmaniasis East Africa Platform (LEAP), and Sudan, Kenya, Ethiopia, and Uganda took part.

The goals of LEAP are: to facilitate clinical testing and registration of new treatments for kala-azar in East Africa; to support the development of national kala-azar treatment guidelines for East Africa; and evaluate, validate and support registration of improved treatment options.

LEAP has brought scientists from East African countries to work together on the clinical development of treatment for kala-azar for the first time. This is badly needed considering that the disease does not know political boundaries!

In Sudan, the effect of LEAP was dramatic. Two excellent facilities for research on kala-azar and Post-Kala-azar Dermal Leishmaniasis (PKDL) were established in the Kassab and Dooka villages in Gedarif State. The centres also provide diagnostic and treatment facilities against other common diseases in the area.

Today Sudan, through capacity building activities, has a newly established 0R&D structure that supports clinical trials, treatment, diagnosis and training of staff, by way of the El Hassan Center and Tropical Disease Hospital, in Dooka. This development was achieved with the support of DND*i*. This centre is equipped with a well-functioning research facility, a hospital, lecture hall and accommodation for staff and trainees.

Over the years several drugs, as single or combined regimens, have been tested. The most rewarding was SSG plus paromomycin (SSG&PM), in combination, for the treatment of kala-azar. This is now accepted by the Sudan Federal Ministry of Health and is the recommended treatment. It reduces the treatment time from 30 days (when SSG was used alone) to the current regimen of SSG&PM for 17 days. The use of the two drugs reduces the development of drug resistance.

Some Thoughts for Future Research On Kala-Azar: The Sudanese Perspective.

Today, we are seeing that leishmaniasis in Sudan, due to reactivation of old foci that disappeared in the past several years, has now reappeared, as a result of changes in the biotope that favours transmission. It is still important to continue R&D efforts for today and the future.

LEAP should continue to search for new drugs for the treatment of kala-azar but also PKDL).

There is need for control of PKDL, which is a major reservoir for kala-azar. IEND worked on the development of a vaccine that could help in curing persistent PKDL through immunochemotherapy. This, however, should be further researched, and explored for the prevention of kala-azar.

1. The Gedarif State and the local community should work to improve the health services in the State. There is a need to develop good primary care facilities for the early diagnosis of kala-azar and PKDL and their treatment. Difficult cases can be referred to other centres that should be established and that have better facilities. IEND can contribute to this.

2. There is a need for studies to assess acceptability of the use of impregnated bed-nets, by the community and their use in preventing or decreasing the incidence of kala-azar in selected villages of similar incidence of the disease.

   A previous limited study in Sudan found that the use of nets increased the frequency of subclinical infection. We need to study and evaluate the outcome of moving villages with high frequency of kala-azar to areas with low or absent vectors in the incidence of the disease. It is important that the new villages are provided with drinkable water. Involvement of the community and local government in this is essential.

Professor Ahmed Mohamed El Hassan is the Founder and ex-President of the Sudanese National Acacemy of Sciences. He graduated from the Kitchener School of Medicine in 1955 and had his graduate education at the Universities of London and Edinburgh. He was previously Professor at the Department of Pathology at the Faculty of Medicine University of Khartoum and Dean in the same Faculty. He served as Deputy Vice Chancellor of the University of Khartoum and Minister of Higher Education Government of Sudan. He was also Founder and Chairman of the Department of Pathology and Director of Publications and Translation at King Faisal University, Kingdom of Saudi Arabia. Professor El Hassan is a 'Friend of DND*i*'.

VIEWPOINT

Leishmaniasis Slated as Global Demonstration Project at WHO

67th World Health Assembly (WHA), 2014 – Source WHO photo library. Technical briefing - "Strengthening health security by implementing the International Health Regulations"

By Alexandra Heumber

After ten years of discussions among World Health Organization (WHO) member states on how to effectively incentivize innovation for poverty-related diseases – given the market failure and irrelevance of patents as incentives for these diseases – the World Health Assembly (WHA) endorsed a strategic work plan in 2012. The plan aimed to improve monitoring, coordination, and sustainable funding for health research and development (R&D) to fill health R&D gaps.

Eight 'demonstration projects' were selected by member states, one of which was for visceral leishmaniasis proposed by DND*i* and partners. The aim of these pilot projects is to provide evidence on relevant innovative mechanisms to fund and coordinate public health R&D to address unmet medical needs of developing countries, in order to contribute to further discussions on a sustainable global framework as recommended by the Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG) in 2012. The 'VL Global R&D and Access Initiative' project was specifically selected by WHO AFRO and WHO EMRO. Countries such as France, Switzerland, Spain, and Sudan directly supported the VL project.

VL Global R&D and Access Initiative

The VL project addresses some of the critical R&D gaps by providing the health tools to support the WHO control and elimination targets for VL. It focuses on the Indian sub-continent, by working on asymptomatic cases and PKDL patients, and the urgent need for new treatment options in East Africa and Latin America.

The project is global, involving multidisciplinary stakeholders from five WHO regions (SEARO, AFRO, EMRO, AMRO, EURO) in strong South-South and North-South collaboration, with the following objectives:

- **Objective 1:** To develop new, safe and effective, oral treatments as both monotherapy and, as early as possible, in a combination treatment (medical product) to prevent the risk of resistance development;

and develop a very safe, short-course treatment for asymptomatic VL carriers once their role in disease transmission has been better established;

- **Objective 2:** To develop a diagnostic technology (xenodiagnoses coupled with a quantitative PCR) in order to evaluate the role in transmission of asymptomatic carriers and PKDL patients;

- **Objective 3:** To develop a treatment for PKDL;

- **Objective 4:** To support development of a shared, open-access database to identify determinants of treatment effectiveness.

The VL Global Initiative's aim is to demonstrate that health R&D can be incentivized and optimized through:

- **different innovative incentive mechanisms** to fill R&D gaps and finance R&D, to increase knowledge, decrease the risk of failure, raise the resources needed, capitalize on existing resources, and develop affordable drugs applying the principle of de-linkage (dissociating the cost of development from the price of the product);
- Strengthening **cross-regional coordination with multidisciplinary partners, and reinforcing the key role of endemic countries.**

Demonstration Projects: Process and Pooled Funding

Participation and leadership of member states, particularly endemic countries, are essential, notably through the governance and financial support.

At the 2014 World Health Assembly, still part of this policy process, member states decided to move ahead with the creation of a pooled international R&D fund, to be hosted by WHO-TDR, to 'innovatively' fund pilot projects and to provide enough certainty that the pooled funding mechanism could function globally afterwards.

This process is an opportunity for endemic countries, for the more 'traditional' and new donors to bring their support (operational, political, financial) together to demonstrate that coordination, transparency, capacity-building, and innovative health R&D financing mechanisms can improve the delivery of treatments for patients in need. The process also can pave the way to a global sustainable framework for health R&D. At the World Health Assembly this year, France, Switzerland, Brazil, Kenya, and South Africa expressed their support and are considering financial contribution to the pooled fund.

Essential Role of LEAP and Other Key Actors

Recently, at WHO headquarters, a stakeholders meeting of 'VL Global R&D and Access Initiative' took place, with the participation of LEAP members and a representative of the Kenyan Ministry of Health.

The initiative will coordinate partners across endemic regions, such as that of the LEAP platform, by working in partnership to strengthen research capacities and promote technology transfer in order to facilitate registration, uptake, and sustainable access to new treatments. All of the initiative's partners, particularly LEAP, have an essential role to play in identifying needs, setting up Target Product Profiles, and conducting clinical trials.

LEAP's achievements illustrate the benefit of strengthening capacity and regional coordination, something worthy of serving as a model in other VL endemic regions. It has shown that cross-regional collaboration can optimize R&D, one of the main goals of the VL initiative.

Beyond the scientific objectives, the partners will contribute to the development of innovative mechanisms to finance and coordinate health R&D. These developments will be reported to upcoming World Health Assemblies (2016 and 2019) and will help to build a sustainable framework for global health R&D. Governments specifically must exercise strong public leadership in this important international policy process.

67th World Health Assembly (WHA), 2014 – Source WHO photo library. Each morning countries from each region meet to plan for the day. Here, Dr Luis Gomes Sambo, WHO Regional Director for Africa, discusses the day with delegates.

Alexandra Heumber is the Head of Policy Affairs at the Drugs for Neglected Disease initiative (DNDi) – Geneva. She has 10 years of experience in public affairs at international and European levels, specializing in pharmaceutical issues. She recently served for six years as the EU representative for the Médecins Sans Frontières Access Campaign and two years as consultant for several European generic pharmaceutical companies on access to medicines.

VIEWPOINT

A Journey of Capacity Building in a Decade of Collaborative Research

Yegnasew Takele, at the Leishmaniasis Research and Treatment Centre Laboratory – University of Gondar

By Yegnasew Takele

The Leishmaniasis Research and Treatment Centre laboratory at University of Gondar (UoG) has grown to a fully equipped modern laboratory since the establishment of the centre in 2004. The laboratory started with one working bench assigned for all research activities in a blood bank laboratory unit, with basic laboratory tools such as microscopy, clinical chemistry, and complete cell count and there was only one laboratory technologist working full time and two back-up technicians.

During the early days, the clinical trial sponsor, DND*i*, and the research teams on the ground strongly believed that capacity building would bring a change to the quality of service and the quality of

A one bench research laboratory in 2004, Gordar-Ethiopia

Lab technician working at the research laboratory in 2014

data produced from the research conducted at the Leishmaniasis Research and Treatment Centre. Consequently, in 2008, a new building was built within the collaboration between DND*i* and the UoG that provided space to expand the laboratory, which was at the time one room with basic facilities. The objective for the expansion was to provide good quality service and data for the research.

In 2012, UoG renovated one of its meeting halls, converting it into a laboratory with a wider space to accommodate all the necessary equipment and additional staff. The number of laboratory technologists grew to four, marking a new beginning of progress and renewed opportunities for additional growth.

Therefore, not only did the Leishmaniasis Research and Treatment Centre develop by way of infrastructure, but there was also a concerted investment in building the capacity of technologists working in the laboratory through different training workshops on Good Clinical Practice (GCP) and Good Clinical Laboratory Practice (GCLP). In addition, DND*i* as the sponsor, awarded scholarships for higher level education, Master's and PhD programmes at accredited universities around the world. This capacity building element was established in order to improve the quality of data and service provided as an investment back into the LEAP VL projects. UoG continues to benefit from this kind of investment on an ongoing basis and the benefits to research are significant. They have helped to elevate the level of the R&D work taking place at the Leishmaniasis Research and Treatment Centre.

Currently, the laboratory has a capacity not only for the routine tests, but also has a capacity to grow leishmania parasites, evaluate new diagnostic kits, perform ELISA tests and cell culture. This centre is used as a reference laboratory for other health facilities in the catchment area. Moreover, the staff is actively involved in facilitating training on leishmaniasis for health professionals in the country, especially those working in endemic areas.

There was a lot of investment in the laboratory so that the patients could have access to the diagnostic tests and other laboratory investigations in order to get the help they are seeking. The collaboration between the UoG, DND*i*, and LEAP has brought hope to these poor and marginalized communities, who are affected by leishmaniasis. They now get all the services they require at the recently improved Leishmaniasis Research and Treatment Centre. Now that is the positive impact of capacity building!

The University of Gondar (UoG) marked its Diamond Jubilee in 2014. UoG's sixty years of achievements were celebrated at the Next Steps Conference, held on the 7th of July, 2014. The UoG more recently communicated that this high profile conference was documented by local media, achieving coverage on local television. The conference was attended by H.E. Prime Minister Hailemariam Desalegn, Deputy Prime Minister Demeke Mekonnen, Shiferaw and officials from federal, regional and zonal localities in Ethiopia

PATIENT STORY

Mulat Melkei and His Grand-Father Darso Mengistu

Mulat Melkei talking with his grand-father Darso Mengistu

In the Words of Dorso Mengistu:

'I am the head of our home and I have four grandchildren, who help with farming and household chores. We often have so much to do. So when Mulat was sick, it was very hard for him, so we took him to different health centres to get treatment.

Mulat's sickness started when he came from the desert. Initially, I wanted to take him to UoG Hospital, but the neighbours around suggested that we try the neighbourhood health centres and clinics. At some point, they even gave him traditional medicine because nothing was working, Mulat's condition did not improve… it only got worse.

The period of Mulat's sickness was such a busy time for our family: apart from our day to day activities, we were planning a wedding ceremony, so unfortunately for Mulat, I had to attend to this family affair first. Once it was done, I took him to the UoG Hospital - the Leishmaniasis Research and Treatment Centre.

Upon arrival at the treatment centre, Mulat was examined and the doctor told us that he had kala-azar. I was so worried, I asked if he would survive or not. His response was such a relief. The doctor said that we had come in good time and Mulat would be put on treatment that would cure him of kala-azar.

At the hospital we were further advised that Mulat would stay at the hospital for 17 days and receive medication during this time. I am happy to say that this was so good for Mulat, because his condition improved, his health improved and he was cured.

We celebrated at home when Mulat got cured. Interestingly enough, when his older brother got sick, our family knew just what to do. We took him to the University of Gondar Hospital. He was fortunate, because he did not suffer as much as Mulat.

We are grateful as a family to have a place to go and get help. The treatment was given to us at no cost and the medicine they gave us saved the lives of my grand-children. For that, I will be forever grateful.'

'My name is Mulat Melkei. I am seventeen years old. I come from a family of farmers, and I do not go to school.

I was diagnosed with kala-azar when I went to Gondar University Hospital, but before I went to the clinic, I went to three health centres around my community and also tried traditional medicines. I was told that I had fever, anaemia and typhoid I was given different kinds of medicines. Despite all the treatment I took, I still had fever and I lost a lot of weight.

I thank my grand-father, Dorso Mengistu, for being there to help me when I got ill. It was a very hard time for us.'

VIEWPOINT

Clinical Trials – The Benefits of North-South & South-South Collaboration

Anke carrying out training during Gondar site initiation visit. Prof. Asrat (LEAP principal investigator) and other participants looking on.

By Anke Kip

During the period mid-June 2014 in northern Ethiopia, the initiation of the DND*i* HIV/VL 0511 trial began. This is a trial in which AmBisome® monotherapy is compared to AmBisome®/ miltefosine combination therapy in HIV-patients co-infected with visceral leishmaniasis (VL). Together with a large group of staff from the University of Gondar (UoG) and Abdurafi sites (Ethiopia) and DND*i* Africa trial coordination team, I arrived at the leishmaniasis treatment ward at UoG for the site initiation visit (SIV) of the upcoming trial.

One of the components of the DND*i*-HIV/VL 0511 trial is the pharmacokinetic (PK) sub-study, in which the drug levels of both antiretrovirals and VL drugs are to be assessed for purposes of securely monitoring any drug-drug interactions. The information gained from this study is crucial to our understanding of the clinical implications of the drug combinations.

Headed by Dr Thomas Dorlo, our small group is specialized in the clinical pharmacology of drugs used in the treatment of leishmaniasis. Within this sub-study, I am responsible for the laboratory analysis of the PK samples of this trial. I have developed and validated a dried blood spot sampling technique for miltefosine, which makes storage and transport of the PK samples much easier and, more importantly, less invasive for the patient. During the SIV in Gondar, I provided laboratory training for the collection and storage of plasma and dried blood spot samples. The training consisted of a theoretical part – explaining why we are interested in the pharmacokinetics of the drugs used in this trial – and a hands-on training, during which we elaborated on the practical 'do's and don'ts' during PK sample preparation.

We need more practical laboratory training like the one carried out during the Gondar SIV, as it is very important for the preparation of a clinical trial. This is mainly because it ensures the quality of the samples and subsequent quality of the results and conclusions drawn from the study. Secondly, on a broader scale, meetings like these are essential to exchange experience and knowledge

between the many academic partners, from various African and European countries, involved in clinical trials for neglected tropical diseases. This works in multiple directions: training received by the laboratory and clinical staff at the clinical site ensures that the necessary skills are present and operating procedures are clear. It also functions as a reality check for collaborators, like me, who are normally far away from the actual patients. In Gondar, the discussions during the training identified potential critical issues in the practical procedures on site that I had not thought of before and gave me a much better understanding of the needs of both the local lab team, as well as the vulnerable patients in the trial.

The staff working at the Gondar and Abdurafi clinical trial sites is dedicated, experienced, knowledgeable about their subject area and eager to learn, asking a lot of (challenging!) questions. On top of that, the lab was well equipped for the clinical trial, due to the many scientific collaborations taking place at this site.

Investing in local research talents is of utmost importance to maintain this high level of research ongoing in Gondar. It is a unique site, with a strong medical faculty and a lot of experience in neglected tropical diseases and relatively close to the areas burdened by leishmaniasis. Certainly in the battle against neglected tropical diseases it is pivotal that local governments invest in scientists and R&D close to the remote areas where these diseases are endemic. This is the only way new treatments for neglected diseases can be developed and the local research environment can be strengthened in a sustainable way. All in all, research will greatly benefit from academic partners all over the world, who are working on tackling neglected diseases, thus allowing for improvements in research and science towards meeting the needs of the most neglected patients.

Anke Kip is responsible for PK analysis within the DND*i* HIV/VL 0511 trial. She is also a researcher at the Department of Pharmacy & Pharmacology, Antoni van Leeuwenhoek Hospital, Amsterdam, the Netherlands & Division of Pharmacoepidemiology & Clinical Pharmacology, Utrecht University, Netherlands.

UPCOMING EVENT

In 2003, the Leishmaniasis East Africa Platform (LEAP) was established and every year since then the platform has organized bi-annual meetings to review current research and development (R&D) work in the region, in order to assess progress and address gaps and opportunities in the field of visceral leishmaniasis (VL) research.

For the first time since LEAP's inception, the platform will hold a public scientific conference: 'Bridging The Gap: Progress in Research, Innovation, and Access to Visceral Leishmaniasis Treatment in Africa'. The conference takes place from 29 to 30 September 2014, at Avanti Blue Nile Hotel, Bahir Dar, Ethiopia.

LEAP
LEISHMANIASIS
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1st LEAP Scientific Conference

Bridging the Gap: Progress on the Current Research Innovation & Access to Visceral Leishmaniasis Treatment

29th - 30th September 2014
Bahir Dar, Ethiopia

MEDECINS SANS FRONTIERES

DNDi
Drugs for Neglected Diseases *initiative*

Please visit **www.dndi.org** for more information on the 1st LEAP Scientific Conference.

2014 EVENTS

World Health Day (WHD) – 7 April 2014 – Small Bite Big Threat

Dr Wasunna during a press interview at the Kimalel Health Centre, Kenya – 7 April 2014

Every year, the World Health organization (WHO) hosts World Health Day (WHD). During the 2014 WHD celebrations, the WHO shed light on the seriousness and increasing threat of vector-borne diseases, with the slogan 'Small bite, big threat'. WHO figures state that more than half the world's population is at risk of contracting diseases such as malaria, dengue, leishmaniasis, Lyme's disease, schistosomiasis, and yellow fever, all carried by mosquitoes, flies, sand-flies, ticks, water snails and other such vectors.

Kenya's WHD event took place in Baringo County at both Kimalel Health Centre and Marigat Secondary School. Honourable guests in attendance included: His Excellency, Governor of Baringo County, Hon. Mr Benjamin Cheboi; Principal Secretary of Health, Prof. Fred Segor; WHO Country Representative, Dr Custodia Mandlhate; Director KEMRI, Dr Solomon Mpoke; former KEMRI Board Chairperson, Prof. Ruth Nduati; DND*i* Africa Regional Office Director, Dr Monique Wasunna; and other development partners. DND*i* contributed significantly to the planning and logistics of the WHD event.

WHD in Baringo was well captured by Kenyan media and online newswires, such as: KTN, Standard Media Group, Kenya News Agency, Citizen TV, Reuters, The Star, Daily Nation and The People. During the event, the former Ministry of Health Principal Secretary, Prof. Segor, pledged support to the purchase of treatment and diagnostic tools for patients suffering from visceral leishmaniasis in the country, stating that 'no Kenyan should die of kala-azar [visceral leishmaniasis]'

World Health Day (WHD) – 7 April 2014 – Small Bite Big Threat

Destruction of Anthill: *Former Permanent Secretary for Health, Kenya, Prof. Fred Segor, destroying a dormant anthill located at the Marigat Secondary school*

LEAP Stakeholders Meeting - 11 Feb 2014

LEAP Stakeholder Meeting participants – 11 February 2014

A LEAP stakeholders meeting took place on 11 February 2014 at the Sarova Panafric Hotel in Nairobi, Kenya. The meeting was attended by 55 participants, including the LEAP Principal Investigators (PIs); Director KEMRI; scientists from KEMRI, AMREF, and MSF-Belgium; DND*i* Africa regional office staff and scientists; representatives from the Kenyan Ministry of Health (MoH); and County Directors of Health from Turkana, Wajir, and Isiolo, Kenya. The aim of the meeting was to facilitate a consultative working session for LEAP stakeholders to give input into the next DND*i* Business Plan (2016-2022). DND*i*'s Executive Director, Dr Bernard Pécoul, was a key speaker during the forum.

2014 EVENTS

20th Leishmaniasis East Africa Platform (LEAP) Bi-Annual Meeting - 11 April 2014

Participants who attended 20th LEAP Meeting – 11 April 2014

Held on 11 April 2014, the LEAP bi-annual meeting in Uganda set out to review current research and development (R&D) work in the region addressing the progress to date, gaps and opportunities in the field of VL. The meeting was attended by 43 members from the Leishmaniasis East Africa Platform (LEAP) countries (Kenya, Uganda, Sudan, and Ethiopia).

About LEAP

Created eleven years ago, by the Drugs for Neglected Disease initiative (DND*i*) a non-profit research & development organization, LEAP is active throughout East Africa. LEAP's aim is to strengthen regional research capacities to develop new treatments for visceral leishmaniasis, one of the most deadly diseases in the region. A collaborative effort, LEAP includes the East African Ministries of Health and control programmes, universities, research institutions, NGOs and other like-minded partners in the region and worldwide. Thanks to the platform's work, a new, more affordable treatment, the combination therapy SSG&PM, which has reduced treatment of visceral leishmaniasis from 30 days to 17, has been recommended by the World Health Organization specifically for the disease in East Africa.

The overall aim of the platform is to strengthen clinical research capacity, which is lacking in part due to the remoteness and geographic spread of the patients, most of whom live in the most impoverished regions of Africa. This platform also serves as a base for ongoing educational cooperation between the countries in the East African region and, inasmuch as possible within local regulations, the standardization of procedures and practices. LEAP aims to evaluate, validate, and support registration of new treatments that address regional needs for VL.

LEAP's Mission

- Define patient's needs, taking in consideration the local conditions;
- Bring together key regional health actors, namely representatives of ministries of health, national control programmes, regulatory authorities, academia, civil society groups, and pharmaceutical companies, as well as clinicians and health professionals;
- Utilize, capitalize upon, and reinforce clinical capacities in endemic regions, and address infrastructural requirements where necessary;
- Provide on-site training in clinical research in sometimes very remote settings.

13th LEAP Principal Investigators (PI) Meeting - 11 February 2014

13th LEAP – Principal Investigators' Meeting. Back Row: Mr Bolo, Mr Omolo, Ms Edwards, Dr Alves, Prof. Olobo (Uganda PI), Dr Kimutai. Front Row: Prof. Hailu (Ethiopia PI), Dr Alvar, Dr Wasunna (Kenya PI), Prof. Musa (Sudan PI), Prof. Khalil (Sudan PI), Dr Pécoul (Executive Director DNDi)

The 13th Leishmaniasis East Africa Platform (LEAP) Principal Investigators (PI) meeting took place at the Panafric Hotel in Nairobi, Kenya, on 11 February 2014. All LEAP country PI's were present and discussions were specific to: the platform's envisaged role, with patients' needs as a focus; LEAP partners and members; achievements, including the development of new treatment protocols, contribution to national protocols, data management, South-South and North-South collaborations, good financial practices (GFP), and LEAP publications; LEAP successes and weaknesses; expansion of the visceral leishmaniasis (VL) portfolio (new tools, new treatments); and the role of LEAP beyond VL. The LEAP PI meetings take place on a bi-annual basis before or during the yearly LEAP platform meetings.

Kala-azar in Kenya

To be infected with kala-azar you must have either travelled from or be living in an area where the disease is prevalent. Young boys are observed to be more vulnerable to the disease. This is mainly because of their nomadic lifestyle (herding cattle) and spending nights outdoors in close proximity to sand-fly breeding sites, which are: acacia trees, inactive anthills, bushes and the cracks on mad hut walls. Children are more affected by kala-azar compared to adults; and boys more so than girls.

2014 EVENTS

Site Investigators Meeting/Site Initiation Visit (SIV) – University Of Gondar

Top left: Dr Ermias Diro discussing CRF with participants. Top right: Prof. Asrat Hailu giving a presentation during the training. Bottom: Participants in the Gondar SIV training.

Over the course of four days, the SIV was carried out at the University of Gondar (UoG), in a series of workshops. A total of 21 participants, from Addis Ababa, Gondar, and Abdurafi, took part and contributed to the sessions. The training that was carried out involved tutorials, practical sessions, and working groups. The subject matter included Standard Operating Procedures (SOPs), protocol and study manual of operations review, laboratory sample collection and processing, Case Report Form (CRF) and query completion, safety evaluation, Good Clinical Practice (GCP), and recruitment strategies.

VIEWPOINT

Sudan's Contribution Towards R&D for Leishmaniasis in East Africa

Patient suffering from kala-azar being transported to a health centre

By Eltahiri Awad Khalil

Leishmaniasis in all its clinical phenotypes constitutes a major neglected public health problem in Sudan. Over the years, visceral leishmaniasis (VL) has brought major human catastrophes upon different Sudanese populations. The Jum Jum tribe of Eastern Sudan had been brought to the brink of extinction around the turn of the twentieth century. More than three hundred thousand were killed during the 1988 VL epidemic in Upper Nile State in Southern Sudan.

From the 1950s through to the present day, a national strategic plan for R&D in tropical and endemic diseases was formulated as part of the national health strategy to discover and create new knowledge. Special attention was paid to VL, schistosomiasis, and malaria. Working within national (LRG/Sudan), regional (LEAP/Africa), and international bodies, Sudanese scientists and researchers worked in a number of projects and studies addressing different aspects of leishmaniasis, including epidemiological studies using longitudinal as well rapid assessment approaches elucidating disease prevalence, disease phenotypes/pathogenesis, risk factors and susceptibility to leishmaniasis. Entomological studies mapped the vectors, their feeding, breeding, and resting habits. The vector's distribution has been mapped all over the country and a risk map has been constructed.

Case detection and drug treatment received great attention as the sole available control measure. VL treatment/research sites were built in endemic areas to improve patients' access to treatment and to conduct research. With great success, drug trials have been conducted to: understand the mechanisms of action and find new drugs/drugs combinations; reduce patient suffering; stem the development of resistance; and save money. Limited studies on impregnated bed-nets clearly demonstrated their usefulness and effect on the development of overt and subclinical disease. Vaccine studies (whole parasite adjuvants; recombinant and predicted antigens) have been conducted, generating a wealth of information on vaccine design/development and the conduct of clinical studies. Vaccine study sites are now well developed and functioning.

Training of medical and scientific professionals was part of building capacity for R&D. Considerable numbers of nurses, medical assistants, doctors, and scientists were trained at local, regional, and international institutions.

A number of challenges faced VL R&D in Sudan: financial constraints; embargo against the Sudanese scientific community; political apathy and lack of political will to tackle VL; braindrain of young doctors/scientists; and slowness in implementing the results of applied research. Despite these challenges there is positive momentum: firstly the Federal government has pledged a 1% of national income for research. Secondly, a revised strategy for R&D has been submitted for approval by the Council of Ministers. Thirdly, working closely with State VL control programmes has opened avenues with decision-makers and has led to increased awareness about VL.

In summary, working within the Leishmaniasis East Africa Platform (LEAP) has greatly helped Sudan to overcome financial as well as logistical constraints. However, while LEAP has been going from strength to strength, in order to survive into the future, it may need to expand R&D of leishmaniasis into the field of VL control to examine potential vaccines and impregnated bed nets. Inclusion of more countries in the region into LEAP would widen the area of VL control and bring about the inclusion of more professional hands.

Eltahiri Awad Khalil is the Professor of Pathology at the Institute of Endemic Diseases (IEND) in Sudan. His is also the Leishmaniasis East Africa Platform (LEAP) Principal Investigator (PI) for Sudan.

VIEWPOINT

The Case of Kala-Azar: A Ugandan Story

Child being examined – kala-azar causes a patient to have an enlarged spleen, and a swollen abdomen

By Joseph Olobo

Introduction and Early Cases of Kala-Azar in Uganda

Kala-azar (visceral leishmaniasis, VL) is a vector-borne parasitic disease. It occurs worldwide in tropical and subtropical countries. The infection is transmitted by female sand-flies following a blood meal. Symptoms include fever, loss of appetite, weight loss, distended abdomen due to swelling of the spleen and, at times, the liver. Many of the signs resemble malaria, brucellosis, typhoid fever, tuberculosis, or hydatid disease, all of which are common in Karamoja region of Uganda. Diagnosis of kala-azar can be confusing to the clinician and usually a laboratory test is conducted for confirmation. The disease is fatal if not treated.

The first report of kala-azar in Uganda was in the 1950s in the Moroto district of Karamoja. Early patients were treated in health centres in Kenya and later

Moroto hospital in Uganda. When Amudat health centre was eventually built by missionaries in 1957, it gained prominence as the main treatment centre, being located in a kala-azar endemic area.

Due to prevalent insecurity in Uganda and Karamoja region in particular in the 1970s, 1980s, and early 1990s, coupled with its remoteness, the pastoralist way of life of the communities, high illiteracy rates, lack of interest in kala-azar from academic institutions and the disease posing no immediate military and/or social threat to the authorities, little was done to control it. Thus, for nearly four decades there was total neglect of the disease in Uganda. Consequently, the actual number of people who perished from the disease during that time is anyone's guess.

Current Status

In 1997, MSF-Switzerland re-established management of kala-azar through the Amudat hospital. Patients came not only from Uganda but also Kenya, mainly from the West Pokot area, where the kala-azar belt extends into the Pokot region in Uganda. In 2006, when MSF-Switzerland relocated to Kacheliba, Kenya, for a period of almost one year, Amudat hospital lacked diagnostics and drugs for kala-azar. Hence, suspected patients were referred to Kacheliba, about 60 km from Amudat, until the Leishmaniasis East Africa Platform (LEAP) took over management of kala-azar at Amudat hospital, beginning in 2007 and to date.

Kala-azar patients come mainly from Amudat, Moroto, Kotido, and a few from Katakwi and Napak. Interestingly though, some patients from West Pokot Kenya still seek kala-azar treatment at the hospital and other patients now come from as far away as the Turkana region in Kenya. The area borders Kotido in Uganda, which is about 300 km northeast of Amudat. Patients from northwest Kenya, bordering Kotido, prefer treatment services in Amudat hospital because of improved security, infrastructure, and availability of diagnostics and drugs for kala-azar. The number of VL patients from Kenya tends to increase during the dry season, when Turkana pastoralists migrate with their livestock to Uganda in search of pasture and water. The pastoralist way of life of affected populations, the vast, rough terrain and bad roads in endemic areas, and cross border issues, at times present difficult challenges, especially for active case finding and patient follow up.

Today, Amudat hospital is the only hospital with expertise in the management and treatment of kala-azar in Uganda. Located in Pokot district, an endemic focus for kala-azar, about 100 km South of Moroto town and 340 km northeast of the capital Kampala, this 120 bed hospital serves a community of more than 200,000 inhabitants. Between 150 to 300 kala-azar patients are treated annually, most of whom are children between the ages of 6 and 16 years, who are involved in herding livestock. It is also an established centre for clinical trials, mainly for drug treatments for management of kala-azar.

One of the many notable achievements from the hospital was its involvement as one of the multicentre clinical trial sites for the study that led to the 17-day combination treatment with sodium stibogluconate and paromomycin (SSG&PM). The hospital is also involved in training undergraduate and graduate-level local and international students in basic and clinical sciences.

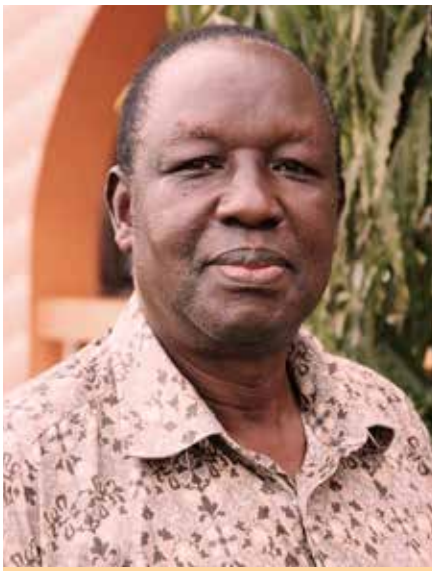
Are We Bold Enough to Consider Elimination of Kala Azar from Uganda and Eastern Africa?

A number of countries, including Uganda, have embarked on elimination or eradication plans for neglected tropical diseases (NTDs). An example of this was the declaration of Uganda as being free of Guinea worm disease (dracunculiasis) by the WHO in 2009. Following that, another bold step was taken to eliminate river blindness, which is targeted for elimination by 2020. Other elimination plans are for trachoma, amongst others, in line with current heightened interest in elimination/eradication of NTDs. It would be fitting to take advantage and 'load leishmaniasis onto the bandwagon', so to speak.

But a bold approach is required for elimination of kala-azar. Already South Asia (India, Bangaladesh, Nepal), which has the world's highest number of cases, has an ongoing programme to eliminate the disease from the region. Eastern Africa, including Uganda, falls second in line after Asia, and can learn from the experience of some Asian countries. Undoubtedly, the programme is formidable, requiring sustainable government commitment; good knowledge of the disease, particularly its epidemiology; financial and human resources; and community awareness, to name but a few. With no efficacious vaccine for kala-azar in sight, the most plausible option for control now is diagnosis and chemotherapy, thus requiring sensitive and specific diagnostic tools and effective treatment.

Though not optimal, current tools for diagnosis combined with 17-day treatment with SSG &PM and active case finding could be aggressively pursued for control in anticipation of better and more superior diagnostics and drugs. Understanding basic epidemiological data about kala-azar and other associated activities/studies would work well to assist in elimination of the disease.

The Leishmaniasis East Africa Platform (LEAP) could be instrumental in such a plan, as it encompasses kala-azar endemic countries in Eastern Africa (Kenya, Sudan, Ethiopia, and Uganda). LEAP, with appropriate strategies in place, could contribute to an elimination plan, by using, for example, Uganda for the pilot project. One advantage is that the kala-azar focus is restricted and is generally defined in the country. Furthermore, Uganda has experience in elimination of certain NTDs, as mentioned above. A bold plan for kala-azar elimination in Eastern Africa should be taken up now using the available tools to achieve the dream in a shorter time and provide a better quality of life for the affected population.



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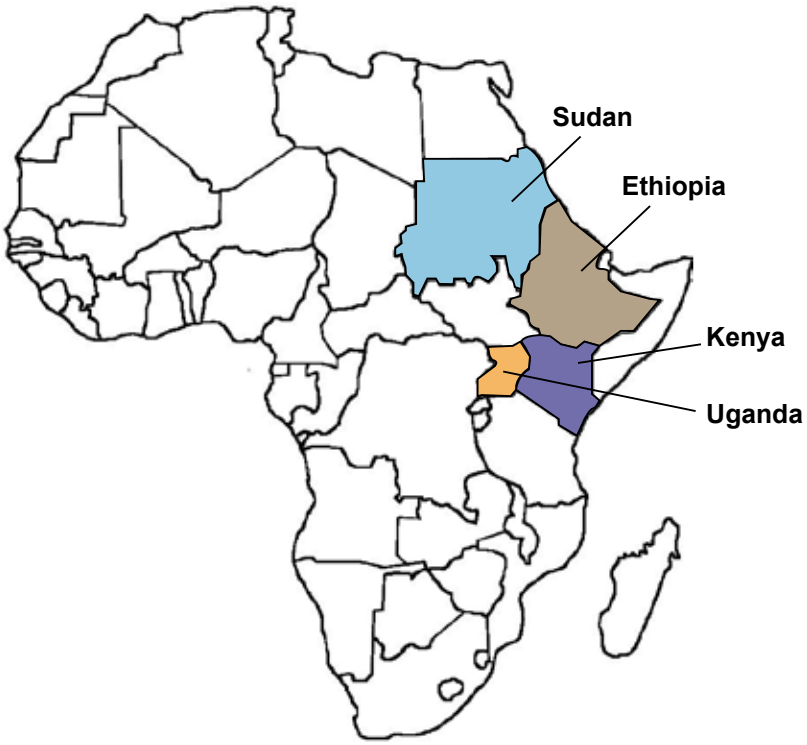

LEAP
LEISHMANIASIS
EAST AFRICA PLATFORM

LEAP consists of a group of scientists and institutions working on developing clinical trial capacity to bring new treatments to patients.

LEAP SITES

- **Sudan: 3 sites**
  (Kassab, Dooka, and Um El Kher)
- **Ethiopia: 2 sites**
  (Gondar and Arba Minch)
- **Kenya: 2 sites**
  (Nairobi and Kimalel)
- **Uganda: 1 site**
  (Amudat)

LEAP collaborates with DND*i*, MSF, iOWH - India, IDA, WHO-TDR and partners in visceral leishmaniansis R&D work in East Africa.

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