



TRYLEIDIAG PRESS REVIEW

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EVENTS HIGHLIGHTS

Drug Discovery for Protozoan Parasites (D2)

March 22nd – 26th, 2009

Beaver Run Resort • Breckenridge, Colorado

Part of the Keystone Symposia Global Health Series

Supported by the Bill & Melinda Gates Foundation

Organizers: Dennis E. Kyle, Michael A.J. Ferguson and Susan Charman

The discovery and development of new drugs for protozoan parasites has rapidly expanded to include multidisciplinary approaches from academia, government, and industry. Public-private partnerships have focused efforts on translational research and as a result, new drugs have been advanced into clinical evaluation. Unfortunately, development of several promising new drugs has recently been terminated in clinical trials thus leaving a sparse pipeline of new chemical entities that have potential for registration in the next few years. Importantly, the need for effective new drugs for major human parasitic diseases (malaria, leishmaniasis, and trypanosomiasis) is growing and concerns over antimalarial resistance to artemisinin-based drugs are building. This meeting will bring together chemists, biologists, pharmacologists, and clinicians to find solutions to accelerate drug discovery efforts. Key problems to be addressed include identification and validation of new targets, chemical biology and medicinal chemistry approaches to characterize new compounds, novel screening techniques to identify new chemotypes, mechanisms of drug resistance, and cutting edge strategies to progress new drug candidates into clinical trials. The objectives of this meeting are to discuss current methods to identify and validate new drug targets and to screen libraries of compounds to discover novel chemotypes; assess the potential for chemical biology and medicinal chemistry to optimize compounds that are specific and avoid resistance mechanisms; and identify critical paths for compound progression and to discuss the utility of key models for assessing preclinical drug leads.

For more information, please visit:

<http://www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=1016>

7th International Science Conferences on the Human Dimensions of Global Environmental Change

April 26th - 30th, 2009

Bonn Germany

For more information, please visit: <http://www.openmeeting2009.org/index.html>

International Scientific Council for Trypanosomiasis Research and Control

Organisation: African Union / Interafrican Union for Animal Resources
33rd Meeting of the Executive Committee



The council on 16 - 17 October 2008 convened at the Speke Hotel, Kampala/Uganda for the 33rd Executive Committee, a run up to the 30th biennial conference scheduled for September 2009 that will mark 60 years of ISCTRC's existence.

For more information, please visit: <http://www.au-ibar.org/isctrcExecComm33rd.html>

International Conference on Leishmaniasis Vaccines

March 9th – 11th, 2009

Recife, Brazil

The search for leishmaniasis vaccines is more urgent than ever. A meeting gathering 45 of the world's best researchers in the field, debating, exchanging ideas, experiences and data will rush the finding of a vaccine that may free mankind from these scourges. Let's work together, let's think together! Convention center in northeastern Brazil, offering the perfect comfort needed for our meeting.



RESEARCH NEWS

Aggravation of pathogenesis mediated by Ochratoxin A in mice infected with *Trypanosoma brucei rhodesiense*.

Parasitology. 2009 Jan 21:1-9.

Kibugu JK, Ngeranwa JJ, Makumi JN, Gathumbi JK, Kagira JM, Mwangi JN, Muchiri MW, Mdachi RE.

Kenya Agricultural Research Institute, Trypanosomiasis Research Centre, P. O. Box 362, Kikuyu, Kenya.

SUMMARY Mice fed 1.5 mg ochratoxin A (OTA) per kg body weight and infected with *Trypanosoma brucei rhodesiense* were compared with trypanosome-infected placebo-fed and uninfected OTA-fed controls. Uninfected OTA-fed mice showed fever, lethargy, facial and eyelid oedemas, mild hepatitis and nephritis, and high survival. Infected placebo-fed controls had mean pre-patent period (PPP) of 3.26 days, lethargy, dyspnoea, fever, facial and scrotal oedema, survival of 33-65 days, reduced red cell counts (RCC: 10.96-6.87x10⁶ cells/mul of blood), packed cell volume (PCV: 43.19-26.36%), haemoglobin levels (Hb: 13.37-7.92 g/dL) and mean corpuscular volume (MCV) of 37.96-41.31 fL, hepatosplenomegaly, generalized oedemas, heart congestion, hepatitis and nephritis. Compared to infected placebo-fed controls, infected OTA-fed mice had significantly ($P < 0.05$) shorter mean PPP (2.58 days), reduced survival (6-47 days), more pronounced fever and dyspnoea. The latter had significantly ($P < 0.05$) reduced RCC (10.74-4.56x10⁶ cells/mul of blood), PCV (43.90-20.78%), Hb (13.06-5.74 g/dL), increased MCV (39.10-43.97 fL), severe generalized oedemas, haemorrhages, congestion, hepatic haemosiderosis, hepatitis, nephritis, endocarditis, pericarditis and exclusively, splenic macrophage and giant cell hyperplasia, expanded red pulp and splenic erythrophagocytosis. It was concluded that OTA aggravated the pathogenesis of *T. b. rhodesiense* infection in mice, and should therefore be taken into consideration during trypanosomiasis control programmes.

Population genetics of *Trypanosoma brucei gambiense*, the agent of sleeping sickness in Western Africa.

Proc Natl Acad Sci U S A. 2009 Jan 6;106(1):209-14. Epub 2008 Dec 23.

Koffi M, De Meeûs T, Bucheton B, Solano P, Camara M, Kaba D, Cuny G, Ayala FJ, Jamonneau V.

Institut de Recherche pour le Développement, Unité Mixte de Recherche IRD-CIRAD 177, Campus International de Baillarguet, 34398 Montpellier, Cedex 5, France. math_kof@yahoo.fr

Human African trypanosomiasis, or sleeping sickness caused by *Trypanosoma brucei gambiense*, occurs in Western and Central Africa. *T. brucei* s.l. displays a huge diversity of adaptations and host specificities, and questions about its reproductive mode, dispersal abilities, and effective size remain under debate. We have investigated genetic variation at 8 microsatellite loci of *T. b. gambiense* strains isolated from human African trypanosomiasis patients in the Ivory Coast and Guinea, with the aim of knowing how genetic information was partitioned within and between individuals in both temporal and spatial scales. The results indicate that (i) migration of *T. b. gambiense* group 1 strains does not occur at the scale of West Africa, and that even at a finer scale (e.g., within Guinea) migration is restricted; (ii) effective population sizes of trypanosomes, as reflected by infected hosts, are probably higher than



what the epidemiological surveys suggest; and (iii) *T. b. gambiense* group 1 is most likely a strictly clonally reproducing organism

The natural progression of gambiense sleeping sickness: what is the evidence?

PLoS Negl Trop Dis. 2008;2(12):e303. Epub 2008 Dec 23.

Checchi F, Filipe JA, Barrett MP, Chandramohan D.

Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom.

Gambiense human African trypanosomiasis (HAT, sleeping sickness) is widely assumed to be 100% pathogenic and fatal. However, reports to the contrary exist, and human trypano-tolerance has been postulated. Furthermore, there is uncertainty about the actual duration of both stage 1 and stage 2 infection, particularly with respect to how long a patient remains infectious. Understanding such basic parameters of HAT infection is essential for optimising control strategies based on case detection. We considered the potential existence and relevance of human trypano-tolerance, and explored the duration of infectiousness, through a review of published evidence on the natural progression of gambiense HAT in the absence of treatment, and biological considerations. Published reports indicate that most gambiense HAT cases are fatal if untreated. Self-resolving and asymptomatic chronic infections probably constitute a minority if they do indeed exist. Chronic carriage, however, deserves further study, as it could seed renewed epidemics after control programmes cease.

The burden of human african trypanosomiasis.

PLoS Negl Trop Dis. 2008;2(12):e333. Epub 2008 Dec 23.

Fèvre EM, Wissmann BV, Welburn SC, Lutumba P.

Centre for Infectious Diseases, University of Edinburgh, Ashworth Laboratories, Edinburgh, United Kingdom.

Human African trypanosomiasis (HAT, or sleeping sickness) is a protozoan parasitic infection caused by *Trypanosoma brucei rhodesiense* or *Trypanosoma brucei gambiense*. These are neglected tropical diseases, and *T.b. rhodesiense* HAT is a zoonosis. We review current knowledge on the burden of HAT in sub-Saharan Africa, with an emphasis on the disability-adjusted life year (DALY), data sources, and methodological issues relating to the use of this metric for assessing the burden of this disease. We highlight areas where data are lacking to properly quantify the impact of these diseases, mainly relating to quantifying under-reporting and disability associated with infection, and challenge the HAT research community to tackle the neglect in data gathering to enable better evidence-based assessments of burden using DALYs or other appropriate measures.

Co-inhibition of Plasmodium falciparum S-adenosylmethionine decarboxylase/ornithine decarboxylase reveals perturbation-specific compensatory mechanisms by transcriptome, proteome and metabolome analyses.

J Biol Chem. 2008 Dec 10.



van Brummelen AC, Olszewski KL, Wilinski D, Llinás M, Louw AI, Birkholtz LM.

Biochemistry, University of Pretoria, Pretoria, Gauteng 0002.

Polyamines are ubiquitous components of all living cells and their depletion usually causes cytostasis, a strategy employed for treatment of West-African trypanosomiasis. To evaluate polyamine-depletion as an antimalarial strategy, cytostasis caused by the co-inhibition of S-adenosylmethionine decarboxylase/ornithine decarboxylase (PfAdoMetDC/ODC) in *Plasmodium falciparum* was studied with a comprehensive transcriptome, proteome and metabolome investigation. Highly synchronized cultures were sampled just before and during cytostasis and a novel zero time point definition was used to enable interpretation of results in lieu of the developmentally regulated control of gene expression in *P. falciparum*. Transcriptome analysis revealed the occurrence of a generalized transcriptional arrest just prior to the growth arrest due to polyamine-depletion. However, the abundance of 538 transcripts was differentially affected and included three perturbation-specific compensatory transcriptional responses: the increased abundance of the transcripts for lysine decarboxylase (LDC) and ornithine aminotransferase (OAT) as well as the decreased abundance of that for S-adenosylmethionine synthetase (AdoMet synthetase). Moreover, the latter two compensatory mechanisms were confirmed on both protein and metabolite levels confirming their biological relevance. In contrast with previous reports, the results provide evidence that *P. falciparum* respond to alleviate the detrimental effects of polyamine-depletion via regulation of its transcriptome and subsequently the proteome and metabolome.

Neuropeptides kill African trypanosomes by targeting intracellular compartments and inducing autophagic-like cell death.

Cell Death Differ. 2008 Dec 5.

Delgado M, Anderson P, Garcia-Salcedo JA, Caro M, Gonzalez-Rey E.

Instituto de Parasitología y Biomedicina Lopez-Neyra, CSIC, Granada, Spain.

Trypanosoma brucei is the causative agent of African sleeping sickness. Available treatments are ineffective, toxic and susceptible to resistance by the parasite. Here we show that various endogenous neuropeptides act as potent antitrypanosome agents. Neuropeptides exerted their trypanolytic activity through an unusual mechanism that involves peptide uptake by the parasite, disruption of lysosome integrity and cytosolic accumulation of glycolytic enzymes. This promotes an energetic metabolism failure that initiates an autophagic-like cell death. Neuropeptide-based treatment improved clinical signs in a chronic model of trypanosomiasis by reducing the parasite burden in various target organs. Of physiological importance is the fact that hosts respond to trypanosome infection producing neuropeptides as part of their natural innate defense. From a therapeutic point of view, targeting of intracellular compartments by neuropeptides suppose a new promising strategy for the treatment of trypanosomiasis. Cell Death and Differentiation advance online publication, 5 December 2008; doi:10.1038/cdd.2008.161.

Presence of antibodies against *Leishmania chagasi* in haemodialysed patients.

Trans R Soc Trop Med Hyg. 2009 Feb 21.



Souza RM, de Oliveira IB, de Sousa Paiva VC, Lima KC, Dos Santos RP, de Almeida JB, Luz KG.

Department of Infectious Diseases, UFRN, Natal, Rio Grande do Norte - RN, Brazil.

In the last decades there has been an increase in cases of visceral leishmaniasis complicating the post-transplant phase, mainly following kidney transplantation. The aim of this study was to evaluate the reactivity of haemodialysed patients using IFAT. Blood samples of 310 individuals from Natal, RN, Brazil, were collected and analysed. Data regarding blood transfusion, cause of end-stage renal disease and duration of haemodialysis were also analysed. In total, 69 patients (22.3%) were positive by IFAT. This study suggests that antibody detection should be performed in this group of patients since they are possible candidates for kidney transplantation.

IL-17 promotes progression of cutaneous leishmaniasis in susceptible mice.

J Immunol. 2009 Mar 1;182(5):3039-46.

Lopez Kostka S, Dinges S, Griewank K, Iwakura Y, Udey MC, von Stebut E.

Department of Dermatology, Johannes Gutenberg-University, Mainz, Germany.

Resistance to leishmaniasis in C57BL/6 mice depends on Th1/Tc1 cells. BALB/c mice preferentially develop Th2 immunity and succumb to infection. We now assessed the role of IL-17 in cutaneous leishmaniasis. During the course of *Leishmania major* infection, BALB/c CD4 cells and neutrophils produced increased amounts of IL-17 as compared with cells from C57BL/6 mice. This increase was associated with significantly increased IL-23 release from *L. major*-infected BALB/c dendritic cells (DC), whereas IL-6 and TGF-beta1 production by BALB/c and C57BL/6 DC were comparable. Interestingly, lesion sizes in infected IL-17-deficient BALB/c mice were dramatically smaller and failed to progress as compared with those in control mice. Similar amounts of IL-4, IL-10, and IFN-gamma were produced by T cells from IL-17-deficient mice and control mice consistent with development of Th2-predominant immunity in all animals. Improved disease outcome was associated with decreased CXCL2-accumulation in lesion sites and decreased neutrophil immigration into lesions of infected IL-17-deficient mice confirming prior observations that enhanced neutrophil recruitment contributes to disease susceptibility in BALB/c mice. This study excludes an important facilitating role for IL-17 in Th1/Th2 development in *L. major*-infected BALB/c mice, and suggests that IL-23 production by *L. major*-infected DC maintains IL-17(+) cells that influence disease progression via regulation of neutrophil recruitment.

Prevalence of Leishmania infection in adult HIV/AIDS patients treated in a tertiary-level care center in Brasilia, Federal District, Brazil.

Trans R Soc Trop Med Hyg. 2009 Feb 19.

Carranza-Tamayo CO, Assis TS, Neri AT, Cupolillo E, Rabello A, Romero GA.

Laboratório de Leishmanioses do Núcleo de Medicina Tropical, Universidade de Brasília, Campus Universitário, Asa Norte, Caixa Postal 04517, Brasília, DF 70904-970, Brazil; Hospital Universitário de Brasília, Av. L2 Norte S/N, Brasília, DF 70900-970, Brazil.



In order to estimate the magnitude of Leishmania/HIV co-infection, patients with HIV/AIDS at the Brasilia University Hospital, DF, Brazil were used as subjects in a cross-sectional study. One hundred and sixty-three patients were enrolled, seven of whom had visceral leishmaniasis (VL). One hundred and twelve patients (68.7%) were men; 155 (95.1%) had been exposed to HIV infection through unprotected sex. The median age was 37 years (range: 20-74) and the median CD4+ lymphocyte count was 314 cells/mul (range: 2-1600). Symptomatic patients underwent bone marrow evaluations through direct examination of Giemsa-stained films, parasite culture and PCR assay. Blood samples were evaluated by means of an indirect immunofluorescent antibody test (IFAT), an ELISA using a soluble antigen of *L. chagasi* (ELISA), an ELISA with the rK39 antigen (ELISA-rK39) and a PCR targeted to the kDNA region and to the internal transcribed spacer 1 of the rDNA gene. The proportion of positive results was 2.4% for the IFAT, 12.3% for the ELISA and 4.9% for the rK39 tests. The estimated prevalence was 16%. The PCR in the blood was positive in three patients (1.8%). The prevalence of *Leishmania* spp. infection is high among HIV patients attending this Brazilian center suggesting that they should be routinely investigated for VL infection.

The Effect of Topical Liposomes Containing Paromomycin Sulfate (PM) in the Course of *Leishmania major* Infection in Susceptible BALB/c Mice.

Antimicrob Agents Chemother. 2009 Feb 17.

Jaafari MR, Bavarsad N, Fazly Bazzaz BS, Samiei A, Soroush D, Ghorbani S, Lotfi Heravi MM, Khamesipour A.

School of Pharmacy, Biotechnology Research Center and Pharmaceutical Research Center, Mashhad University of Medical Sciences, P.O. Box 91775-1365, Mashhad, Iran; Center for Research and Training in Skin Diseases and Leprosy, Tehran University of Medical Sciences, Tehran, Iran.

The aim of this study was to evaluate the antileishmanial effects of topical liposomal paromomycin sulfate (PM) in *Leishmania major* infected BALB/c mice. Liposomes containing 10 or 15 % PM (Lip-PM 10 and 15) were prepared by fusion method and were characterized for their size and encapsulation efficiency. The penetration of PM from the liposomal PM formulations (LPMFs) through and into skin was evaluated in vitro using Franz diffusion cells fitted with mice skin at 37 degrees C for 8 h. The in vitro permeation data showed that almost 15% of the applied LPMFs penetrated across mice skin and retained amount in the skin was around 60% for both formulations. ED50 of Lip-PM 10 and 15 against *L. major* promastigotes in culture and amastigotes in macrophages were 65.32, 59.73 microg/ml and 24.64, 26.44 microg/ml, respectively. Lip-PM 10 or Lip-PM 15 topically used twice a day for 4 weeks to treat *L. major* lesions on BALB/c mice and the results showed a significantly ($p < 0.001$) smaller lesion size compared to the control group received either empty liposomes or PBS. Eight weeks after the beginning of the treatment every mouse treated with LPMFs was completely cured. Spleen parasite burden was significantly ($p < 0.001$) lower in mice treated with Lip-PM 10 or 15 compared to the mice received PBS or control liposomes, but no significant difference was seen between the two groups treated with either Lip-PM 10 or Lip-PM 15. The results suggest that topical liposomal PM may be a useful tool in the treatment of cutaneous leishmaniasis.

A new focus of zoonotic cutaneous leishmaniasis in Shiraz, Iran.

Trans R Soc Trop Med Hyg. 2009 Feb 13.

Razmjou S, Hejazy H, Motazedian MH, Baghaei M, Emamy M, Kalantary M.



Department of Parasitology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.

Cutaneous leishmaniasis (CL) continues to be an increasing public health problem in Iran. Shiraz, a city in Fars Province in southwestern Iran, is one of the endemic foci of CL. However, there is no formal report of endemicity of CL in rural areas of Shiraz. To our knowledge, this is the first report of an epidemic of zoonotic CL in this area. The purpose of this study was to examine the epidemiological features of leishmaniasis in three villages in rural areas of Shiraz and to identify the causative species of leishmaniasis using nested PCR with clinical direct samples. The prevalence of infection among 1000 inhabitants of the three villages was 23.2%. Prevalences of ulcers and scars were 7 and 16.2%, respectively. The most infected age group was 0-9 years, with a rate of 14.2%. Children are more than twice as susceptible to the infection. In this study, the *Leishmania major* strain was identified in the majority of cases. The results of this epidemiological study indicate a high prevalence of leishmaniasis in rural areas of Shiraz.

PCR diagnosis of visceral leishmaniasis in an endemic region, Mymensingh district, Bangladesh.

Trop Med Int Health. 2009 Feb 14.

Alam MZ, Shamsuzzaman AK, Kuhls K, Schönian G.

Institut für Mikrobiologie und Hygiene, Charité Universitätsmedizin Berlin, Berlin, Germany.

Summary Detection of *Leishmania* parasites in a clinical sample is necessary to confirm a suspected case of leishmaniasis. We compared the sensitivity of internal transcribed spacer 1-PCR (ITS 1-PCR) assay for parasite diagnosis with that of microscopic detection in clinical samples from kala-azar (KA) or post-kala-azar dermal leishmaniasis (PKDL) suspects in Mymensingh. Of 39 specimens collected from 35 KA and four PKDL suspects, 26 were positive by microscopic examination of smears from bone marrow and skin exudates; 38 specimens spotted on filter paper and 27 of the 28 Giemsa-stained slides tested by PCR proved positive by ITS1-PCR.

Vaccines and vaccination strategies against human cutaneous leishmaniasis.

Hum Vaccin. 2009 May 12;5(5).

Okwor I, Uzonna J.

Department of Immunology, Faculty of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada.

One might think that the development of a vaccine against cutaneous leishmaniasis would be relatively straightforward because the type of immune response required for protection is known and natural immunity occurs following recovery from primary infection. However, there is as yet no effective vaccine against the disease in humans. Although vaccination in murine studies has yielded promising results, these vaccines have failed miserably when tested in primates or humans. The reasons behind these failures are unknown and remain a major hurdle for vaccine design and development against cutaneous leishmaniasis. In contrast, recovery from natural, deliberate or experimental infections results in development of long-lasting immunity to re-infection. This so called



infection-induced resistance is the strongest anti-Leishmania immunity known. Here, we briefly review the different approaches to vaccination against cutaneous leishmaniasis and argue that vaccines composed of genetically modified (attenuated) parasites, which induce immunity akin to infection-induced resistance, may provide best protection against cutaneous leishmaniasis in humans.

Sex hormones and modulation of immunity against leishmaniasis.

Neuroimmunomodulation. 2009;16(2):106-13. Epub 2009 Feb 11.

Snider H, Lezama-Davila C, Alexander J, Satoskar AR.

Department of Microbiology, The Ohio State University, 484 West 12th Avenue, Columbus, OH 43210, USA.

Sex-associated hormones such as estradiol, testosterone and progesterone have all been shown to modulate immune responses, which can result in differential disease outcomes between males and females, as well as between pregnant and nonpregnant females. Most parasitic diseases, including leishmaniasis, usually result in more severe disease in males compared with females. This review highlights our current knowledge concerning the role of sex hormones in modulating leishmaniasis in both clinical settings and experimental disease models. Copyright (c) 2009 S. Karger AG, Basel.



Political and regulatory

Leishmaniasis conference hears that patients lack adequate diagnosis and drugs

5 Feb 2009

Bobby Ramakant

Source: TropIKA

At the Fourth Leishmaniasis World Congress had taken place in Lucknow, India, from 3rd to 7th of February. Médecins sans Frontières (MSF) has said that there is a serious need to expand the availability of effective treatments and diagnosis for visceral leishmaniasis in order to reduce the present burden of disease and resistance to treatments.

Leishmaniasis is caused by *Leishmania* parasites and transmitted by the phlebotomine sandfly. One form of the disease (cutaneous leishmaniasis) results in painful, disfiguring and often disabling skin sores. In visceral leishmaniasis (also known as kala azar), internal organs are affected, leading to death in untreated cases. Some 350 million people are at risk of leishmaniasis. WHO estimates that every year there are two million new cases of the cutaneous form and half a million cases of visceral leishmaniasis. Up to half of all cases of kala azar are in India, where the disease is endemic in the eastern States of Bihar, Jharkhand, Uttar Pradesh and West Bengal.

Encouraging results with amphotericin B

MSF is presenting results to the Conference which suggest that liposomal amphotericin B (Ambisome) could play a critical role in the fight against the disease. Operational research in MSF's project in Bihar has shown that treatment with liposomal amphotericin B is very effective, with a 98% cure rate and a low death and default rates. The drug is also linked to a lower rate of relapse, less toxicity and a shorter length of treatment than with other medications.

"While liposomal amphotericin B is not the only possible treatment, it has been shown to be one of the most effective and safe. We believe it should be included in the Indian treatment protocol as a first-line treatment option," says MSF tropical medical advisor Dr Nines Lima.

The most common treatment currently used is sodium stibogluconate (SSG). However, resistance to the drug is a growing problem – especially in India, where as many as 65% of patients acquire drug resistant parasites. Kala azar remains neglected by research and development initiatives.

"Patients with kala azar in developing countries have been neglected for far too long. In our project, most patients come to our facilities when the disease is already at an advanced stage because people are still not familiar with the signs and symptoms or do not know where they can find adequate diagnosis and medication," says Gareth Barrett, MSF Medical Coordinator in India. "Many communities with high prevalence lack access to diagnostics, and poverty often means that the quality of treatment is poor, which in turn poses serious risks of outbreaks and increasing drug resistance."

"A worrying number of our patients, are treatment failures that have come from private sector", says Dr Mrityunjay Kumar Pandey who works with MSF in Biha.

The drug liposomal amphotericin B is expensive at Rupees 21,855 (€350) per patient per treatment. "There is an urgent need for reducing the cost of the drug, developing generic formulations and



validating combination therapy so that the drug can be included as a first line treatment in the protocols of countries such as India”, stresses Gareth Barrett.

In Bihar at the Hajipur referral hospital, MSF is providing diagnosis and treatment for people suffering from kala azar. Since July 2007, MSF has screened over 6,500 patients for the disease and the 2,500 patients found to be positive received treatment with liposomal amphotericin B.

“Until combination therapy is available we need as many people as possible to access diagnosis and effective treatment. We believe dose reduction is a natural next step, and there is enough evidence to support this,” says Dr Gareth Barrett.

MSF has welcomed the fact that India is hosting the World Congress and calls on India to show a strong commitment to fighting kala azar, by strengthening its health structures to improve access to effective treatment and diagnosis for marginalized communities who make up the majority of people who become infected by the disease.

For more information, please visit www.tropika.net/svc/news/20090205/Chinnock-20090205-News-Leishmaniasis



Neglected diseases R&D Global investments report

G-Finder identifies gaps in childhood pneumonia and overall in diagnostics

Tropical Disease Research News item, 4 February 2009

How do policy makers and funders map investments to the critical research needs in global health? That was the question discussed at today's London launch of the G-Finder report on global investment into research and development (R&D) of new products for neglected diseases. Produced by the George Institute for International Health and funded by the Bill & Melinda Gates Foundation, G-Finder surveyed 134 funders in 43 countries for their 2007 R&D investment.

Just over US \$ 2.5 billion was spent on neglected disease R&D in 2007. Of this amount, almost 80% went to three diseases: HIV/AIDS (US \$ 1.08 billion or 42.3%), malaria (US \$ 468.5 million; 18.3%) and TB (US \$410.4 million; 16%). The remaining neglected diseases and disease groupings each received less than 5% of global funding, including diarrhoeal illnesses (US \$ 113.9 million; 4.5%), the helminth infections (US \$ 51.6 million; 2%) and bacterial pneumonia and meningitis (US \$ 32.5 million; 1.3%). Five diseases - leprosy, Buruli ulcer, trachoma, rheumatic fever, and typhoid and paratyphoid fever - received less than US \$ 10 million or 0.4% of total global investment each. Over 80% of total global funding was provided by only 12 organisations.

Around 20% of global funding was invested by public institutions and private companies into internal programmes. The remaining 80% was granted to external organisations either directly or via intermediary organisations such as TDR and Product Development Partnerships (PDPs). TDR is the 8th highest intermediary organization.

Deciding how R&D funding can best be allocated is a complex process, requiring funders to assess the likely health return against the likely cost of any investment, discounted for risk. This depends not only on the burden of disease, but also epidemiological trends, severity of the product shortfall, and the presence or absence of other funders in a given space.

The G-FINDER was set up to provide data to support funders in making investment decisions by identifying where funding is lacking and where additional funding can potentially have a high impact. Although there is no direct link between Disability Adjusted Life Years (DALYs) and funding needs, DALYs are an important multiplier of the likely health impact of any given investment, and give a sense of the differences in scale of funding between diseases. For instance, pneumonia and the diarrhoeal illnesses combined have a disease burden one-third higher than HIV, malaria and TB combined in low and middle income countries (165 million DALYs compared to 125 million DALYs in 2004), but collectively received only 5.7% of global R&D funding compared to nearly 80% for HIV, malaria and TB.

The report recommends broadening funding efforts so that all who are able to contribute do so, and so that all diseases receive the attention they deserve.

For more information please visit <http://www.who.int/tdr/svc/news-events/news/g-finder-report>

For the full report, please visit [http://www.thegeorgeinstitute.org/events/latest-news/funding-for-neglected-diseases-increases-to-us\\$-2.5-billion-but-big-killer-diseases-miss-out.cfm](http://www.thegeorgeinstitute.org/events/latest-news/funding-for-neglected-diseases-increases-to-us$-2.5-billion-but-big-killer-diseases-miss-out.cfm)