Research Foundation in Tropical Diseases and the Environment

BUEA, CAMEROON
Contribution to find solutions to problems paused by Tropical Diseases to African Populations using integrated approach that take into consideration the Human population, the Pathogens, their vectors and the Environment
Agent, Pathogen

Characteristics:
- Toxicity, virulence, infectivity
- Susceptibility to antibiotics
- Ability to survive outside body

Interventions:
- Eradicate
- Genetically modify

Interventions:
- Protect
- Educate
- Alter exposures

Disease

Interventions:
- Remove breeding grounds
- Improve sanitation

Environment

Characteristics:
- Climate
- Physical structures
- Population density
- Social structure

Interventions:
- Housing quality
- Sanitation, water
- Preventive services

Host

Characteristics:
- Age
- Prior exposure
- Susceptibility
- Co-infection
- Immune response

Interventions:
- Treat, isolate
- Immunize
- Nutrition

Interventions:
- Educate
- Change activity patterns
- Quarantine
THE UNIVERSITY OF BUEA

REFOTDE

THE MUTUALISTIC RELATIONSHIP BETWEEN REFOTDE AND THE UNIVERSITY OF BUEA
FILARIASIS RESEARCH HIGHLIGHTS AT REFOTDE
FOCUS ON LOIASIS RESEARCH
DEVELOPMENT OF THE RAPID ASSESSMENT PROCEDURE FOR LOAISIS
GUIDELINES FOR RAPID ASSESSMENT OF LOA LOA
VALIDATION OF RAPLOA IN A DIFFERENT SOCIO_CULTURAL CONTEXT

Wanji et al. Parasites & Vectors 2012, 5:25
http://www.parasitesandvectors.com/content/5/1/25

RESEARCH

Validation of the rapid assessment procedure for loiasis (RAPLOA) in the democratic republic of Congo

Samuel Wanji1,2*, Dowo O Akotshi3, Maurice N Mutro4, Floribert Tepage5, Tony O Ukety6, Peter J Diggle7 and Jan H Remme8
Figure 2 Relationship between the prevalence of high microfilarial loads (> 8000 MF/ml) and the prevalence of microfilaraemia at the community level (original and validation data). The black and red lines show the calibration models fitted to the original and validation data, respectively. The left-hand panel shows the data and models on the log-odds scale, the right-hand panel on the prevalence scale. The original data are from [10].
The Geographic Distribution of *Loa loa* in Africa: Results of Large-Scale Implementation of the Rapid Assessment Procedure for Loiasis (RAPLOA)

Honorat Gustave Marie Zouré¹*, Samuel Wanji²,³, Mounkaïla Noma¹, Uche Veronica Amazigo¹, Peter J. Diggle⁴, Afework Hailemariam Tekle¹, Jan H. F. Remme⁵

¹ African Programme for Onchocerciasis Control, World Health Organization, Ouagadougou, Burkina Faso, ² Research Foundation for Tropical Diseases and Environment, Buea, Cameroon, ³ Department of Biochemistry and Microbiology, University of Buea, Buea, Cameroon, ⁴ Institute of Infection and Global Health, University of Liverpool, Liverpool, United Kingdom, ⁵ Consultant, Ornex, France
Map of the estimated prevalence of eye worm history in Africa
Map of the predictive probability that the prevalence of eye worm $\geq 40\%$
ArcGIS probability kriging: probability that prevalence of eye worm $\geq 40\%$
Assessment of the Impact of CDTI on L. loa Parasitological indicators
Impact of repeated annual community directed treatment with ivermectin on loiasis parasitological indicators in Cameroon: Implications for onchocerciasis and lymphatic filariasis elimination in areas co-endemic with *Loa loa* in Africa

Samuel Wanji1,2*, Winston Patrick Chounna Ndongmo1,2, Fanny Fri Fombad1,2, Jonas Arnaud Kengne-Ouaf01,2, Abdel Jelil Njouendou1,2, Yolande Flore Longang Tchounkeu2, Benjamin Koudou3, Moses Bockarie3, Grace Fobi4, Jean Baptiste Rougou4, Peter A. Enyong1,2
Fig 1. Map showing the locations of the study sites (QGIS software version 2.0.1).

https://doi.org/10.1371/journal.pntd.0006750.g001
Impact of CDTI on L. Loa Prevalence and Intensity

Significant Reduction in L. Loa Prevalence and Intensity in CDTI Areas
Relationship Between *L. loa* Microfilarial Prevalence and Ivermectin Intake

The Reduction in *L. loa* Prevalence is Ivermectin Adherence Dependent
Relation between the proportions of individuals in different L. loa microfilarial load classes and Ivermectin Intake

Heavy microfilarial load of L. loa is rare in people who comply better to CDTi.
It may be very difficult to eliminate L. loa with Ivermectin

This will also have negative implications on the Elimination of Onchocerciasis and Lymphatic Filariasis in areas of co-endemicity with L. loa
Development of the Animal model of Loa Encephalopathy following Ivermectin Treatment in non human primate

LOA/BABOON
RESEARCH ARTICLE

Parasitological, Hematological and Biochemical Characteristics of a Model of Hyper-microfilaraemic Loiasis (Loa loa) in the Baboon (Papio anubis)

Samuel Wanjì1,2*, Ebanga-Echi Eyong2,3,4, Nicholas Tendongfor1,2, Che Ngwa2, Elive Esuka2, Arnaud Kengne-Ouafó1,2, Fabrice Datchoua-Poutcheu1,2, Peter Enyong1,2, Adrian Hopkins5, Charles D. Mackenzie6

1 Parasites and Vectors Research Unit, Department of Microbiology and Parasitology, Faculty of Science, University of Buea, South West Region, Cameroon, 2 Research Foundation for Tropical Diseases and Environment (REFOTDE), South West Region, Cameroon, 3 Department of Biological Sciences, Faculty of Science, University of Bamenda, North West Region, Cameroon, 4 Department of Zoology and Animal Physiology, Faculty of Science, University of Buea, South West Region, Cameroon, 5 Meitzzan Donation Programme, Decatur, Georgia, United States of America, 6 Department of Pathobiology and Diagnostic Investigation, Michigan State University, East Lansing, Michigan, United States of America
Splecnotomised can harbor up to 400,000 Mf L. loa per ml of Blood

Up to 40% of infected Baboon can develop up to 50,000 Mf/ml of blood
RESEARCH ARTICLE

Ivermectin treatment of *Loa loa* hyper-microfilaraemic baboons (*Papio anubis*): Assessment of microfilarial load reduction, haematological and biochemical parameters and histopathological changes following treatment

Samuel Wanji¹,²*, Ebanga-Echi J. Eyong²,³,⁴, Nicholas Tendongfor², Che J. Ngwa², Elive N. Esuka², Arnaud J. Kengne-Ouafο¹,², Fabrice R. Datchoua-Poutcheu¹,², Peter Enyong¹,², Dalen Agnew⁵, Rob R. Eversole⁶, Adrian Hopkins⁷, Charles D. Mackenzie⁸
Baboon showing a Typical Behavioral Response after Ivermectin Treatment: Depression and Reluctance to participate in normal activities
Blocked CNS vessel with eosinophils, Fibrin, Macrophages and *L. loa* Mf debris

Blocked CNS vessel with damage (Vacuolation of the Parenchyma)

Intact *L. loa* Mf caught in a cellular intravascular Mass in the CNS

A degenerated *L. loa* Mf in a Capillary of the CNS surrounded by Fibrin

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**Fig 10.** Microscopic lesions present in the treated animals more than 72 hours after treatment. A. Adult *L. loa* worm in connective tissue beneath the skin. B. Blocked CNS vessel comprised of eosinophils, fibrin, macrophages and parasite debris. C. Blocked CNS vessels with associated damage (vacuolation of the parenchyma). D. Intact microfilariae caught in a cellular intravascular mass in the CNS. E. A degenerating Mf in a capillary of the CNS and surrounded by fibrin. F. Area of vascular and parenchymal damage in the CNS predominately filled with macrophages and eosinophils.
Fig 11. Potential pathogenesis of Loa encephalopathy following the ivermectin treatment of Loa hyper-microfilaraemic individuals.

https://doi.org/10.1371/journal.pntd.0005576.g011
Development and Validation of In vitro Models of Loa loa

With Implications for Drug Screening for Loasisis
Evaluation of *in vitro* culture systems for the maintenance of microfilariae and infective larvae of *Loa loa*

Denis Zofou$^{1,2,1}$, Fanny Fri Fombad$^{1,3,1}$, Narcisse V. T. Gandji$^{3,3,1}$, Abdel Jelil Njouendou$^{3,3,1}$, Arnaud Jonas Kengne-Ouafo$^{1,3}$, Patrick W. Chounna Ndongmo$^{1,3}$, Fabrice R. Datchoua-Poutcheu$^{1}$, Peter A. Enyong$^{3}$, Dizzle Tayong Bita$^{1,3}$, Mark J. Taylor$^{4}$, Joseph D. Turner$^{4}$ and Samuel Wanjii$^{1,3,4}$
Main Effects of different Factors on the Predicted Loa loa microfilariae and L3 Motility

**Fig. 10** Graphical representation of the standardized coefficients of the main effects of different factors on the predicted *Loa loa* microfilariae and L3 motility. Adjusted $R^2$: $L. loa$ mf $= 0.709$; $L. loa$ L3 $= 0.716$
Heterogeneity in the in vitro susceptibility of *Loa loa* microfilariae to drugs commonly used in parasitological infections

Mortality of *L. loa* Microfilariae Exposed to different Concentrations of the active drugs

**Fig. 5** Mortality of *L. loa* microfilariae exposed to different concentrations of the active drugs. Drugs indicated here are those that killed at least one microfilaria at the concentration indicated.
Mouse models of *Loa loa* for anti-filarial translational research

Nicolas P Pionnier¹, †, Hanna Sjoberg¹, †, Haelly M Metuge²,³, Valerine C Chunda²,³, Abdel J Njouendou²,³, Fanny F Fombad²,³, Dizzle B Tayong²,³, Narcisse V Gandjui²,³, Desmond N Akumtoh²,³, Patrick W Chounna²,³, Bertrand L Ndzeshang²,³, Mark J Taylor¹, Samuel Wanji²,³ and Joseph D Turner¹, *
STERILE HOOD + CO₂ INCUBATOR

Rearing of sensitive mice within IVCC system
Recovered *L. loa* adult worms from mice 5 months post-infection were viable and fully mature.
Tissue distributions of adult *L. loa* in NOD.SCID$\gamma c^{-/-}$ or BALB/c RAG2$^{-/-}\gamma c^{-/-}$ mice 1-month post-infection

Embryogram outcome from *L. loa* females recovered from RAG2$^{-/-}$ mice implanted with *L. loa* adults and culled 1 month post-implant
Ivermectin mediates rapid microfilaricidal activity in *L. loa* microfilaraemic mice.
General platform

Baboons (animal reservoir of mf) → In vivo drug pre-clinical development → Achievements Under optimization

Production of mf → Culture system → L4 → L5

K.O. mice i.v. injection → Production of Infective larvae (L3) → K.O. mice s.c./i.p. injection → Recovery: s.c. 20-80%

In vitro drug screening → In vivo drug pre-clinical development

Wanji et al. LOA
Meeting_Seattle,19/04/2014
REFOTDE: VISION FOR THE FUTURE

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