European and Developing Countries Clinical Trial Partnership
Third Annual Forum 8-11 October 2006
Stockholm, Sweden

Partnership and African Leadership:
Challenges and Opportunities
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ES      EDCTP Secretariat
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The conference organisers acknowledge the generous support of:

• European Commission
• City Council of Stockholm, Sweden
• Swedish Society of Medicine
• Karolinska Institute, Sweden
• Netherlands and African Partnership for Capacity Development (NACCAP), Netherlands
• Instituto de Salud Carlos III, Spain
• Medical Research Council, United Kingdom
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Dear Colleagues

It gives us great pleasure that you are participating in the Third EDCTP Annual Forum that is being held in Stockholm from October 9 to 11 2006. On behalf of the Organising and the Programme Committees we would like to warmly welcome you to this beautiful city and the forum.

As you know the theme of the forum is Partnership and African Leadership: Challenges and Opportunities. We believe EDCTP is a unique and exciting partnership that has relevant experience to contribute to the exploration of this theme. As a partnership between 15 European and the sub-Saharan African countries, EDCTP aims to join relevant European national research programmes and their African partnerships to develop new clinical tools against malaria, HIV/AIDS and tuberculosis. At this forum we aim to share our experiences with each other and hope to benefit from other’s experiences in return.

The programme of the coming days will focus on various themes including building of capacity in scientific skills and leadership in Africa, networking within the partnership and making clinical trials run cost-effectively and without unnecessary constraints.

On the first and second day, the morning sessions will consist of plenary lectures while the afternoons reserved for parallel round-table discussions which will be introduced by one or two speakers. On the third day there will be keynote lectures from current African leaders in the three main poverty-related diseases followed by reports from researchers that are currently supported by EDCTP. We will end the forum with a plenary session during which reports form the parallel round-table discussions of the previous two days will be discussed. We hope that this discussion will end with recommendations on the way forward.
Please note that the scientific information that from this forum is not limited to the lectures and round-table discussions. In your forum bags you will find memory sticks that contain ‘pragsters’ that were submitted by many participants to this meeting. Pragsters are in fact short slide presentations with a similar aim as posters and as such are electronic poster presentations. The pragsters will be accessible on computers screens at various locations throughout the event. Authors of these pragsters will be introduced to you and are prepared to discuss their work. Please do not hesitate to approach them if you would like to know more about their presentations.

Since networking is high on the agenda of EDCTP we hope that our encounters will not limit themselves to the activities of the forum. In fact the first opportunity for you to informally engage with the other participants of this event will start on Sunday October 8 with a welcome party. The City of Stockholm administrators also understand the importance of networking and graciously invite you to attend the Forum dinner in the City Hall on Monday October 9.

We look forward to meet you in Stockholm!

Cynthia Naus
Chair, Organising Committee

Charles Mgone
Chair, Programme Committee
Guide to Surviving the Stockholm Forum 2006

Partnership and African Leadership: Challenges and Opportunities
Introduction

To enable you to enjoy the Stockholm Forum as much as possible, we have put together for you some important information that includes foreign exchange, travel and an accommodation guide in Sweden among other things.

If you have any questions that are not detailed in this booklet please find an EDCTP member of staff who will be pleased to help you.
To the Airport

The Airport Coach leaves City Terminalen next to Central Station every 5-10 minutes. The coach journey takes about 40 minutes. A one-way trip costs SEK 95 (about 10 euros). Tickets are cheapest when bought in advance.

There is also the Arlanda Express, which is the train that leaves every 20 minutes from Central Station in Stockholm. This costs around SEK 200 (around 21 euros). You can buy your ticket on board for a small surcharge.

Taxi’s have a fixed price, from the city centre to the airport costs about SEK 350-400 (around 40 euros).
Transport

Taxi Stockholm
Telephone: +46 (0)8 15 00 00

You can find these taxis at taxi ranks or you can hail one on the street. All cars are black with the Taxi Stockholm logo clearly displayed. You can pay in SEK, Euro, US Dollars or GPB.

Trains

Arlanda Express is the fastest way to travel between Stockholm Arlanda Airport and central Stockholm. The journey takes just 20 minutes. You will also be kind to the environment if you choose Arlanda Express instead of a car or a bus.

Arlanda Express is a fast frequent service. During peak traffic, there are six trains an hour. Lifts connect the flight terminals directly to the train platforms.

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103 27 Stockholm
Sweden

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Fax: +46 (0)8 517 26311
www.scandic-hotels.com/sergelplaza
The Venue

Swedish Society of Medicine (Svenska Läkaresäskapet)

Klara Östra Kyrkogata 10
101 35 Stockholm
Sweden

Telephone: +46 (0)8 440 8860
Fax: +46 (0)8 440 8899

www.sls.se
Directions

From Arlanda Express Station to the Hotel

10 minutes walk

- Depart on Sergels Torg
- Continue straight ahead onto Klara-bergsgatan
- Turn right onto Klara Norra Kyrkogata
- Turn right onto Mäster Samuelsgatan
- Turn right onto Malmskillnadsgatan
- Turn right onto Brunkebergstorg
- Arrive at your destination

From the Hotel to the Venue

2 minutes walk

- Depart on to Klara Östra Kyrkogata
- Turn left onto Klarabergsgatan
- Turn right on Klara Norra Kyrkogata
- Turn right onto Mäster Samuelsgatan
- Turn right onto Malmskillnadsgatan
- Turn right onto Brunkebergstorg
- Arrive
Currency

The Swedish monetary unit is the Swedish Crown, abbreviated to SEK. One Swedish Crown is 100 öre.

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Forex Exchange Shops

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Emergency numbers

Call 112 for all emergencies. For non emergencies the telephone numbers can be found in the local telephone catalogue. The Fire department can be found in the green pages in the local telephone catalogue (Fire department = Brandstasjon). Hospitals and emergency rooms can be found in the blue pages (Hospital = Sjukhus, Emergency room = Akutintag) and the police can be found in the red pages in the local telephone catalogue (Police = Polis).

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- American Express: +46 (0)8 729 00 95
- Diners Club: +46 (0)8 655 8585
- Euro Card: +46 (0)8 80 23 90
- Master Card: +46 (0)8 790 23 90
- VISA: +46 020 739 146
Sunday
08 October 2006

17:00 - 19:00
- Early registration
- Welcoming Party

Monday
09 October 2006

08:00 - 08:30
- Registration

08:30 - 12:15
Plenary Session I

Chair: Britta Wahren

Themes:
- Building capacity in scientific skills and leadership in Africa: strategies and experiences
- Networking within the partnership

Opening:
08:30 - Diana Dunstan, EEIG-EDCTP Chair
  - Welcoming address and an update since the Second Forum
09:00 - Pascoal Mocumbi, EDCTP High Representative
  - European and African Partnership: Challenges and Opportunities
09:30 - Lennarth Hjelmåker, HIV/AIDS Ambassador, Sweden
  - Official opening address

10:00 - Break
Monday
09 October 2006

Plenary Session I

Key-note addresses

Chair: Britta Wahren (Sweden) and Charles Mgone (ES)

10:30 - Hannah Akuffo/Berit Olsson (Sweden)
  • Research capacity building in Africa: Learning from the SIDA/SAREC experience

11:00 - Eric Buch (NEPAD)
  • NEPAD strategies for developing regional capability in combating diseases of poverty in Africa

11:30 - Diana Dunstan (EEIG-EDCTP)
  • North-North networking: EDCTP as a vehicle for European member state collaboration and implications for partnership in Africa

12:00 - General discussion

12:15 - Lunch and electronic poster viewing
14:00 - 17:00 Round Table I - Partnership and Networking

14:00 - Introductory presentations and facilitated discussion

16:00 - Break

16:30 - 17:00 Rapporteur’s provisional report (Plenary)
- Developing multicentre clinical trial partnership at country level - involving diseases control programmes, communities and other stakeholders in clinical trials in Africa.
- North-North networking - is integration of national programmes achievable and why is it important?
- North-South partnerships and co-funding/supplementary grants on EDCTP projects - why, how and whose responsibility?

Room A: North-North networking, co-funding and supplementary grants in North-South partnerships
Facilitator/Rapporteur: Stefan Wagener (Germany), Olle Stendahl (Sweden) / Judith de Kroon (Netherlands), Getachew Aderaye (Ethiopia)

- Bruno Gryseels (Belgium)/ Alioune Dieye (Senegal)

Room B: Multicentre partnerships for clinical trials in Africa
Facilitator/Rapporteur: Abdoulaye Djimde (Mali), Christiane Manyando (Zambia)

- Abdoulaye Djimde (Mali)

Conference dinner - Stockholm City Hall
Tuesday
10 October 2006

08:30 - 12:15
Plenary Session II

Theme

• Making clinical trials run cost-effectively and without unnecessary constraints: Harmonising regulatory and ethics requirements, ensuring efficient trial/project management, networking, sharing of infrastructure and knowledge, sustaining clinical research capacity, centralising/standardising quality assurance and laboratory support.

Chairs: Simon Agwale (Nigeria) and Laura Brum (Portugal)

08:00 - Andrew Kitua (Tanzania)
  • South-South networking: need for nodes of excellence
08:30 - Precious Matsoso (WHO)
  • Harmonising drug regulation in Africa
09:00 - Armand van Deun (Belgium)
  • Supranational laboratories for quality-assurance and training
09:30 - Jelle Thole (Netherlands)
  • Managing networks: lessons for multicentre clinical projects
10:00 - Break
10:30 - Lahouari Bergharbi (WHO Geneva)
  • Regulatory challenges to clinical trials of vaccines in Africa
11:00 - Kalifa Bojang (Gambia)
  • Experiences in the conduct of clinical trials
11:30 - Tumani Corrah (Gambia)
  • Sustaining trial capability: strategies for building and retaining skills
12:00 - General discussion
12:15 - Lunch and electronic poster viewing
Thursday
10 October 2006

14:00 - 17:00 Round Table II - Capacity Building and Development of Scientific Leadership

14:00 - Introductory presentations and facilitated discussion

16:00 - Break

16:30 - 17:00 Rapporteur’s provisional report (Plenary)

- Sustainable institutional capability and human resource capacity building for clinical research and laboratory support in Africa - what will it take to successfully achieve this goal?
- Defining the necessary framework for career development and effective utilisation of existing skills in clinical and laboratory research in Africa
- Development of Scientific Leadership in Africa - is an integrated effort from international cooperative programmes called for?

Room A: Capacity building for clinical trials in Africa
Facilitator/Rapporteur: Lynn Zijenah (Zimbabwe), Michael Makanga (ES)

- Peter Ndumbe (Cameroon)
- Kalifa Bojang (Gambia)

Room B: Scientific leadership and development in Africa
Facilitator/Rapporteur: Walter Jaoko (Kenya), Francine Ntoumi (ES)

- Ogobara Doumbo (Mali)

Room C: Framework for career development in clinical trials
Facilitator/Rapporteur: Aissatou Toure (Senegal), Thomas Nyirenda (ES)

- Steve Wayling (WHO/Geneva)
Wednesday
11 October 2006

08:00 - 12:30  Plenary Session III

Theme
- Partnership and African Leadership for conducting clinical trials
- Experiences from the field and reports from EDCTP projects

Chairs: Richard Adegbola (Gambia) and Peter Kremsner (Austria)

Key-note addresses

08:30 - Joseph Odhiambo (Kenya)
- Partnership and African leadership in tuberculosis drug and vaccine research

09:00 - Sodiomon Sirina (Burkina Faso)
- Partnership and African leadership in malaria drug and vaccine research

09:30 - Souleymane Mboup (Senegal)
- Partnership and African leadership in HIV/AIDS drug and vaccine research

10:00 - Diarmuid McClean (Ireland)
- Partnership and African leadership from funders’ perspective

10:00 - Break

Report from the First EDCTP Investigators’ Meeting

11:00 - Abraham Alabi
- Viral load dynamics as an insight to the therapeutic vaccine efficacy in HIV dual infections

11:20 - Muhammed Bakari
- The HIVIS project - a North-South collaborative study of safety and immunogenicity of multigene, multiclade HIV-1 plasmid DNA prime and MVA boost

11:40 - Paul van Helden
- Surrogate markers to predict the outcome of antituberculosis therapy

12:00 - Maowia Mukhtar
- Surrogate markers to predict the outcome of antituberculosis therapy

12:20 - General discussion
Edctp (edctp) 3rd annual forum 2006 - partnership and african leadership: challenges and opportunities

Wednesday
11 October 2006

08:00 - 12:30 Plenary Session IV

Summary and recommendations from roundtable discussions

Chairs: Bernard Fourie (South Africa) and Patrice Debre (France)

14:15 - Charles Mgone (ES)
  • The approach of EDCTP towards capacity development in developing countries

14:30 - Rapporteurs’ report from Round Table I - Partnership and networking
  • North-North networking, co-funding and supplementary grants in North-South partnerships
  • Multicentre partnership for clinical trials in Africa

15:00 - Rapporteurs’ reports from Round Table II - Capacity building and scientific leadership development
  • Capacity building for clinical trials in Africa
  • Development of scientific leadership in Africa
  • Framework for career development in clinical trials

15:30 - General discussion

16:00 - Pascoal Mocumbi (EDCTP High Representative)
  • Concluding remarks

16:15 - Closing
Presentations:
Abstracts and Pragsters

Partnership and African Leadership:
Challenges and Opportunities
Abdoulaye Djimde

Title:
Head, Molecular Epidemiology and Drug Resistance Unit

Affiliations / Organisations:
Malaria Research and Training Center
DEAP- FMPOS- University of Bamako, Mali

Research interest:
Molecular epidemiology, Drug Resistance

Multicentre partnerships for clinical trials in Africa

Several recent progresses have been made in the understanding of the immunology, pathogenesis and mode of transmission of the main poverty-related diseases. These and a sharp increase in interest and funding from the scientific community and various international funding agencies carry much hope for a brighter future in the fight against these diseases. As a result, several promising vaccines, drugs and diagnostics have been discovered and carried to the phase of clinical testing. It is essential to conduct these trials in those very countries where the diseases are most prevalent. Yet the infrastructure, legal and regulatory environment and human expertise are very scarce in Africa. This makes it all the more indispensable for African institutions to team up and work together in close collaboration with their Northern partners. Multicentre partnerships are necessary in all stages of a clinical trial in Africa including planning, recruitment, conduct, data management ethics and dissemination of information. Several recent initiatives either driven from within Africa or inspired from the North are attempting to promote closer ties between African scientists and trial centers. These initiatives will be reviewed and major roadblocks for efficient collaboration, strategies for better output and advocacy issue will be discussed.
Abstracts

Alioune Dieye

Title:
Professor

Affiliations / Organisations:
Institut Pasteur de Dakar, Sénégal

Research interest:
Malaria vaccine development

African perspective of co-funding in N-S partnerships within EDCTP activities

EDCTP programme is taking place in a general context where several European countries are seeking a long-term partnership model between Europe and developing countries. Through a decision of European Parliament and the Council, a specific programme aimed at developing new clinical interventions to combat HIV/AIDS, malaria and tuberculosis in cooperation with Developing Countries, particularly in sub-Sahara Africa. A financial contribution of euro 200 million was made by the Commission for a five-year period. European states, pharmaceutical companies and funding agencies were approached to participate in kind in the programme. African Heads of States have also been approached by the European Commission through African Union and NEPAD.

EDCTP activities are taking place in Africa and it becomes necessary to involve the participating countries in the co-funding of the programme. Number of activities including strengthening of capacities, clinical site development, upgrading or creating ethical committees, etc could be undertaken by the local health authorities as part of the financial contribution.

It is time to think beyond the period covered by the Commission’s framework programme 7 in order to ensure the development and the sustainability of EDCTP.
Andrew Yona Kitua

Title:
Dr.

Affiliations/Organisations:
National Institute for Medical Research, Tanzania

Research interest:
Clinical and Epidemiological research, ethics in health research

South- South Networking: Need for Nodes of Excellence

While developing countries, bear 90% of the global disease burden, they are only able to access about 10% of the globally available health research funding. Weak south–south networking limits effective use of limited resources and the production in numbers and quality of scientists. It further limits career opportunities, incentives and rewards needed to retain the few produced scientists. In order to effectively reduce the high disease burden, the south must re-organize to accelerate generating talented scientists, create enabling environment, which rewards, motivates, retains available scientists and attracts back scientists in the diasporas. We suggest the creation of strong networks around nodes of excellence among Southern academic and research institutions as a novel approach to accelerate the generation of quality scientists in sufficient numbers to mitigate the high disease burden. It will provide the required enabling environment offering better career opportunities and incentives preventing brain drain. Consequently the South and Africa in particular will better have active participation and ownership of the means of solving its own health problems. This approach will furthermore raise the professional quality and capacity of southern institutions to forge better and equal partnership northern institutions.
Abstracts

Armand Van Deun

Title: Medical Doctor

Affiliations / Organisations: 1. Mycobacteriology Unit, Institute of Tropical Medicine, Antwerp, Belgium 2. International Union Against Tuberculosis and Lung Disease (IUATLD), Paris, France

Research interest: 1. Operational research around microscopy for acid-fast bacilli (TB) and its quality assurance 2. Investigations into development of acquired resistance of M. tuberculosis to rifampicin in the course of various standard mass treatment regimens 3. Quality assurance and improvement of drug susceptibility of M. tuberculosis 4. Standardised regimens for treatment of multidrug-resistant tuberculosis in low-income settings

Supra-national TB reference laboratories (SRL) for quality-assurance and training

In 1994 a network of TB laboratories of excellence was established to guide WHO/IUATLD TB global drug resistance surveillance. At present, 26 TB laboratories make up this network on a voluntary basis, about half of them in Western Europe. They participate in annual rounds of quality assurance of TB drug susceptibility testing (DST) for first-line drugs as part of their accreditation process, organised by the Antwerp coordinating SRL. The SRL are supposed to do the same for their own regional networks of National TB Reference Laboratories (NRL), but due to lack of funding and other obstacles such as severe limitations on international transport of TB strains, this has been realised only partly. Particularly in Africa the situation is confused, most NRL having rather vague and not always efficient links with scattered SRL, mainly in Europe. Apart from the Pretoria laboratory, no SRL exists in sub-Saharan Africa. Activities have consisted mainly in exchange of strains for DST quality assurance, and occasional hands-on training. Although research does not make part of the original objectives of the network, some SRL have been involved, i.e. in the IUATLD clinical trials programme, and this could certainly be extended on an individual basis. An organized SRL research agenda would also respond to currently felt needs, but so far it has not been realised due to lack of funds.
Abstracts

Berit Olsson

Title: Dr

Affiliations / Organisations:
Sida/SAREC

Research capacity development – 30 years of Swedish experience

Sweden has supported research cooperation over the past 30 years with increasing importance placed on capacity development. The modalities of research cooperation have evolved following experiences gained. From an approach focused on support to research councils, to support to individual researcher and subsequently groups, Sida currently supports research in the context of universities and research systems following the research strategies of cooperating universities or countries.

The presentation will describe these phases and the lessons learnt. Examples will be given to illustrate the extent of the research cooperation and the emphasis on country specificity.

Approaches for finding collaboration between research supporting organisations and development agencies will be discussed.
Abstracts

Charles S Mgone

Title:
Prof.

Affiliations / Organisation:
EDCTP

Research interest:
Poverty related diseases

The EDCTP approach to clinical research capacity development

The goal of EDCTP is to contribute towards poverty reduction in developing countries, especially in the sub-Saharan Africa through accelerated development and deployment of new or improved intervention tools against poverty-related diseases namely HIV/AIDS, malaria and tuberculosis. From the outset EDCTP has recognised that for this to succeed and be sustained this partnership should be mutual with a two-way contribution from all partners and stakeholders with equal commitment and ownership. Furthermore, the partnership recognises the needs and priorities of the African countries, especially in research capacity to conduct clinical trials. This requires a strong African input and leadership channeled through the Developing Countries Coordinating Committee. Sometime research capacity development is not viewed as a worthwhile and effective way of spending available meager resources by some. This is partly because the outcomes of such undertakings may be long-term and not easily related or even connected to the primary activity. Moreover, when not well coordinated such capacity development may be fragmented, incomplete, duplicated and redundant and therefore not fully utilised and sustained. To avoid this, EDCTP has developed a programmatic approach whereby capacity development forms an integral part of the programme.
Thus since conduct of clinical trials is the core function of the partnership, EDCTP grants encourage capacity development and networking to enable successful undertaking of the trials including possible future ones. Such capacity development must, however, be customised for carrying out the task in question. This way one ensures that the enhanced capacity is utilised to successfully deliver the outcomes as well as a practical learning activity to provide experience and encourage sustainability. As an added value EDCTP encourages networking among projects. This is in the form of both south-south and south-north partnerships. Where resources and expertise are very much limited as is often the case in developing countries, networking may be vital for creating the critical mass that may be required to undertake an activity. This also allows efficient use and sharing of resources including expertise, transfer of technology and mentorship where young institutions and the well-established ones benefit from each other. It also removes isolation and lends a stronger voice to advocacy when needed. For this to be more effective EDCTP encourages utilisation and strengthening of the already existing networks rather than creating new ones.
Diarmaid McClean

**Title:**
Dr

**Affiliations / Organisations:**
Irish Aid

**Research interest:**
The speaker is a development practitioner with interest in a broad range of research.
Partnership and African Leadership from a bilateral donor’s perspective.

Irish Aid’s perspective will be presented. This is likely to coincide with the views and experiences of a number of bilateral donors, especially the so-called like-minded donors. Whilst Irish Aid does not directly fund clinical trials, considerable support is provided to a number of Global Health Partnerships for health, HIV and AIDS. Irish Aid is also initiating support clinical trials through EDCTP.
The presentation will draw upon Irish Aid’s experiences in its engagements with these bodies and in its effort more generally to support and strengthen leadership in health development as well as in HIV & AIDS. This will primarily focus on Irish Aid’s Programme Countries but reference will be made to relevant activities in Ireland and with other leadership.
Particular attention will be given to the place of research in this area and the special value of leadership in research.
Abstracts

Jelle Thole

Title: Dr

Affiliations / Organisations:
Division of Infectious Diseases, Animal Sciences Group,

Research interest:
Human and veterinary mycobacterial infections; development of diagnostics and vaccines

The TB-VAC project

In recent years several promising tuberculosis vaccine candidates have been developed at the preclinical level in the context of the FP5 TB vaccine cluster project. The overall aim of the FP6 TB VAC project is to further integrate preclinical European efforts towards development of novel tuberculosis vaccine candidates and to forward lead vaccines to initial Phase I clinical trials in Europe and Africa. TB VAC joins 33 leading institutions from 9 European countries and 3 African countries and has a budget of approximately 18.5 mE for a period of five years.

The main goals are:
• Discovery and optimization of vaccine candidates
• Definition of correlates of protection and disease
• Evaluation of lead candidates in small initial human phase I trials
• Capacity building in developing countries for clinical evaluation of vaccines
• Liaise with other consortia (e.g. MUVAPRED) to co-ordinate specific activities
• Liaise with EDCTP to enable further large clinical trials in African Countries

In my presentation, I will focus on the coordination activities of this so-called integrated project including organization, 18 month cycle of planning, conduct and reporting of activities, finance management and accountability. More information can be obtained at www.tb-vac.org.
Joseph A. Odhiambo

Title: Dr

Affiliations / Organisations: Kenya Medical Research Institute (KEMRI) / Centers for Disease Control and Prevention (CDC), Kenya

Research interest: TB/HIV

Partnership and African leadership in Tuberculosis drug and vaccine research

Africa’s TB epidemic is driven primarily by HIV and poverty. Over and above present TB/HIV interventions, new TB drugs and vaccines are urgently needed. The reason TB persists as a killer is that treatment takes up to 8 months and missed doses, in turn, fuel MDR-TB. Yet the only new TB drugs in the last 4 decades are variations of existing ones. Innovative new drugs must improve patient compliance through shorter and simpler TB treatment regimens, address the needs of HIV+ persons, treat MDR-TB and eradicate latent infection. New and more efficacious TB vaccines could be pivotal adjuncts to new drugs especially if proven effective in high HIV populations. New interventions need commensurate investment in research, a position that puts Africa at crossroads given her greatest need against the weakest economic base. At political, scientific, regional and global levels, this paper will review where we are in TB drug and vaccine research, the strengths of existing initiatives and opportunities for partnerships and Africa’s leadership in this process. Under the ambits of African Union (AU) and New Economic Partnerships for Africa’s Development (NEPAD), African leaders have identified TB and HIV control among key priorities for poverty reduction. Beyond increased investment in health delivery systems supported by African-led strategies, Africa must also increase investment in adequate research capacity. Such capacity is required to undertake basic research to identify and develop new TB lead compounds, prepare clinical trial sites and undertake trials to validate efficacy and safety of simplified TB and TB/HIV regimes or new products. Due to economic disparity between north (N) and south (S), these efforts call for partnerships that prioritize the need to assist Africa solve her own problems. It is essential that existing human and infrastructural TB research capacity is harnessed and strengthened through comprehensively updated inventories, stronger leadership and coordination of S-S networking, louder advocacy and more strategic N-S partnerships.
Kalifa Bojang

Title:
Dr

Affiliations / Organisations:
Medical Research Council,
Laboratories, The Gambia

Research interest:
Clinical trials of malaria interventions.

Capacity Building for clinical trials in Africa

Development of new interventions against infectious diseases involve phased series of studies designed and executed according to scientifically rigorous and appropriate ethical standards so as to demonstrate safety, optimize dose and schedule, and demonstrate efficacy. Clinical trials are important steps in this process and must be conducted in such a way as to assure the integrity of the process and validity of the outcomes. In order to undertake such trials, countries must have in place capabilities and infrastructure needed to ensure proper conduct of studies, including ethical review of the protocol, volunteer recruitment, protocol adherence, documentation, quality assurance and control, and data management.

There is currently a mismatch between disease burden caused by infectious diseases and the technical and human capacity of many African countries to conduct clinical trials of new interventions to combat these diseases. It is therefore important to build research capability of African researchers so they can undertake clinical trials in their own local settings. Building indigenous research capacity will enable African scientists to contribute to the development of appropriate control strategies in their countries and translate results of studies carried out elsewhere into their individual national settings. Eventually results of such clinical trials will contribute to finding appropriate solutions to health problems in Africa.

Requirement for building successful research capacity in clinical trials will be discussed.
Abstracts

Malebona Precious Matsoso

Title: Director Department of Technical Cooperation for Essential Drugs and Traditional Medicine

Affiliations/Organisations: World Health Organisation

Harmonising Drug Regulation in Africa

In the past there were many 'roadblocks' to the rapid development of quality medicines, because of the need to comply individually with each nation's regulatory requirements. Duplication of effort and attempted leveraging of various databases for multinational product registrations were often fraught with delay, excessive expenditures and frustration (Hoff, 2000). Thus, there has always been interest to promote as much similarity as possible in the form and content of registration dossiers in multiple countries. Different regulatory models exist across the world and these are informed by the size of the pharmaceutical market, the availability of resources as well as public health needs. Histories, cultures and political experiences as well as economic profiles of countries have informed the construction of different institutional arrangements for the regulation of medicines. In addition, to ensure effective medicine regulation, appropriate systems and structures must be in place.

In many countries, drug regulatory procedures are still largely ineffective due to chronic shortages of human and technical resources. Staffing is probably the key challenge, but sound, consistent standards, existence of laws, regulations, guidelines and their effective implementation, are also necessary, for ensuring only medicines that meet set standards are available in the country. There are a number of factors that explain observed weaknesses of drug regulation, and these differ from country to country and depend also on the health system.
Various harmonization approaches to standardize regulatory requirements and streamline regulatory processes have been initiated. There are regional and subregional approaches and global initiatives that are considered for pooling resources to deal with capacity challenges. None of these initiatives and harmonization models are a complete solution for resource constrained settings, and adaptation is suggested to help developing countries to deal with technical complexities and capacity challenges they are facing. Even with this level or regulation, harmonisation of regulatory requirements has been initiated to reduce duplication of effort and achieve uniformity of standards. As a way to achieve access to essential medicines and newer technologies, stimulate research for medicines that are used to treat diseases affecting developing countries, and facilitate movement of safe and quality products, certain considerations are made for countries with limited capacity.

Some tools for decision making, exchange of regulatory reports between different assessors in different geographies may facilitate communication and improve regulatory approval processes through the use of modern Internet based technology to exchange regulatory information among national DRAs in view of efficiency gains and information sharing/harmonization. Lessons learnt from harmonization efforts of countries with resources and developing countries regional efforts, are that the regulatory frameworks created and approaches followed have overcome some of the barriers, but progress has been relatively slow. There are several initiatives from the SADC, EAC, ECOWAS, regions, The achievement has been standardization of regulatory requirements, in SADC and EAC. ECOWAS and UEMOA has similarly embarked on harmonisation efforts. Standardization benefits, regulators, the industry, researchers, and the end results are benefits to the public for improved access.
The Millennium Summit recognized the importance of good health as a prerequisite for reducing poverty and adopted the Millennium development goals as benchmarks for initiatives and partnerships aimed at promoting sustainable development.

The European and Developing countries Clinical Trials Partnership (EDCTP) is a true partnership between the European member states and developing countries in the sub-Saharan Africa. It was established to step up cooperation and networking of European national programmes, accelerate clinical trials of new products, in particular drugs and vaccines, in developing countries, help to develop and strengthen capacities in developing countries, including the promotion of technology transfer where appropriate and encourage the participation of the private sector and mobilize additional funds to fight HIV/AIDS, malaria and tuberculosis, including funds from the private sector. A significant part of the funding would be spent in the developing countries.

An assessment of EDCTP three years experience shows that a lot has been done implementing its joint programme of action. The governance structure and secretariat are already established, several projects have been approved and are being implemented in developing countries, including clinical trials, senior fellowship grants and training awards, and capacity development in sites has started.
Abstracts

The third forum offers the opportunity for renewing commitments made, discuss challenges and opportunities and make recommendations for the way forward.

As research on new clinical interventions to control effectively HIV/AIDS, tuberculosis and malaria advances, the need for additional sites to conduct clinical trials in endemic countries will increase sharply. For malaria alone the portfolio of new artemisine combination therapies and vaccine candidates overpass largely the already established sites and for HIV/AIDS and tuberculosis more candidates are undergoing preclinical investigation.

While calling for accelerating capacity to conduct trials in order to expedite development and testing of promising new interventions, I recommend we build on the achievements made and the ownership demonstrate by participating countries to move forward the implementation of our genuine partnership creating synergies to address the commonly agreed needs and priorities. From the established sites, EDCTP can maximize benefits by coordinating the development regional nodes of excellence, build scientific African leadership and find appropriate solutions to ethics and regulatory issues in developing countries; thus providing the appropriate environment for sustained interventions.
Abstracts

Peter Ndumbe

Title: Professor

Affiliations / Organisations:
Faculty of Medicine and Biomedical Sciences,
University of Yaounde I, Melen Street, BP 8445,
Yaounde

Research interest:
HIV, Malaria, Control of Vaccine preventable Diseases, Ethics

Capacity building for the conduct of clinical trials in training institutions

Introduction
The EDCTP initiative purports to ensure that quality clinical trials are conducted in the diseases endemic countries in Africa where HIV, TB and Malaria are rife. However, the current state of affairs in these countries requires an urgent rehabilitation of the clinical research environment if these aspirations are to be realised. This rehabilitation may be termed “capacity building”, and should be primarily done in training institutions in order to ensure sustainability.

Components of capacity building
1. Training in research: methodology, ethics, the institution of institutional review boards, role of communities, the administrative structure and superstructure
2. Training of staff in the specialised areas of clinical trials: both principal and support staff at the different levels
3. Equipment of laboratories and field stations with adequate materials and the institution of viable maintenance policies
4. Policy for the validation and utilization of the results of research
5. Policy for the financing and evaluation of the process

Conclusion
Preference should be given to the building/strengthening of capacity for the conduct of clinical trials within training institutions. They should in turn ensure the initial and continuing training of health professionals in this area.
Abstracts

Sodiomon Bienvenu Sirima

Title:
MD, BA, PhD

Affiliations / Organisations: Centre National de recherche et de Formation sur le paludisme (CNRFP)

Research interest:
Clinical trial and malaria epidemiology

The most recent estimates suggest that *Plasmodium falciparum* causes 300 to 500 million of clinical episodes of malaria each year of which more than 90% occur in Sub-Saharan Africa. In 2000, approximately 100 million Africans children lived in areas where malaria transmission occurs and an estimated 800 000 died of malaria. The current global strategy for malaria control places most emphasis on the early diagnosis and prompt treatment of cases and the vectors control. However, the spreading of *P. falciparum* resistance to the affordable antimalarials and the mosquitoes resistant to insecticides represent major challenges to these strategies. Therefore, there is an urgent need to develop effective vaccines and affordable drugs. Usually the early development of new malaria drugs or candidate’s vaccines takes place in the North and the late one in the South. A partnership between Northern and Africans scientists is then necessary to develop the new drugs or vaccines. This partnership should be an opportunity for the emergence of African leadership. This could only be possible if the African scientists are well trained, have their institutions well equipped and if they have been given the opportunities to be involved at all steps of the clinical trials, preferably as principal investigators. The funding agencies like EDCTP should play a major role to make it happen.
Abstracts

Steven Wayling

Title:
Manager - Research Training and Fellowships

Affiliations / Organisations:
World Health Organization
Special Programme for Research and Training in Tropical Diseases (TDR)

Framework for career development in clinical trials

People are the foundation of research, and TDR continues to invest in developing the skilled human resources needed to address the prevention, treatment and control of tropical diseases. The Career Development Fellowships which TDR initiated in 2000 are intended to better target training to priority areas and to develop local resources that TDR could draw upon in the future. The goal of these fellowships is to train individuals in situ with relevant partners in order to develop specialized skills not readily taught in academic centres. On completing their fellowships, the individuals return to their home institutes to add to the local capacity and become a valuable resource for TDR and their region. TDR has now completed five years of collaboration with Glaxo-SmithKline Biologicals in training, through doing, in clinical research and development. In addition, TDR has partnered with other groups as placement for career development fellowships including Serono Biotech, Wellcome-Trust and the WHO Regional Offices.
Abstracts

Tumani Corrah

Title: Professor

Affiliations / Organisations: Medical Research Council, The Gambia

Research interest: TB/HIV

The key question for science in Africa is why good people are lost; the key challenge for the continent is how to reverse this. “……The science gap between Africa and the rest of the world is widening and under business-as-usual this gap will continue to grow”. A significant number of “centres of research excellence” in Africa are largely expatriate-run organizations. Whilst the commitment, output and contribution of the expatriate scientists at these centres to the African development agenda are evident, the long-term sustainability of these institutions will require leadership from within the continent.

In most cases, the prospects for a talented, young African physician or scientist returning to Africa with a postgraduate degree from a prestigious foreign university are bleak; low and insecure salaries from weak, under-equipped institutions and few prospects for obtaining sufficient internal or external resources to conduct competitive research. Not surprisingly, many do not return home.

A two-pronged approach is suggested to address some of these problems:

1) Identify, nurture and develop talent from the earliest possible stage, through an attractive and well-supported development and professional pathway.

2) Remove economic and career obstacles to re-entry for expatriate African researchers wanting to return to the continent.
Presentations: Abstracts and Pragsters

Pragsters

Abdullrahman Orosanya
Creating for Life Initiative (CFLI), Nigeria

1. **Creating visual tools for low literate audience on New Preventive Technology (NPT) “microbicide” awareness and advocacy**
   - Abdullrahman Orosanya, Rose Ogbonna
   - Creating for life initiative (CFLI)
   - Acknowledgements
     - Nigeria HIV Vaccine and Microbicide Group (NIV/MG)
     - Africa Microbicide Advocacy Group (AMAG)
     - Global Campaign For Microbicides (GCM)

2. **Objectives**
   - To know the level of community awareness on Microbicides
   - The acceptability level of Microbicides in the rural communities
   - Community knowledge and involvement Microbicides trial
   - Prepare low-literate communities for Microbicides use and acceptance

3. **Focused group discussion**
   - Six (6) FGDs were conducted in three (3) highly populous rural communities of Ikorodu Lagos Nigeria to determine their knowledge about Microbicides trials.

4. **In-depth interview**
   - Forty (40) selected women and men of high risk behaviours and attitudes were interviewed within the communities to determine their type, colour, price and mode of application of referred Microbicides and their options on communication

5. **Focused group discussion**
   - 80% had no knowledge about Microbicides
   - All Not aware of trails in Lagos State
   - Knowledge about HIV/AIDS Prevention, care and support was high
   - 98% were willing to be part of trials result dissemination when available
   - 45% wants their community to be a trial site

6. **In-depth interview**
   - All wished Microbicides were available
   - 80% preferred get Microbicides
   - 45% Suppository
   - 25% Indeterminate
   - All preferred visual materials for communication and advocacy
   - Indeterminate about colours
   - 100% wants Microbicides to be lower that male condoms

7. **Discussion & Conclusions**
   - More visual communication and educational materials should be used to create awareness about Microbicides
   - Low-literate audience should be included in trails and other reach works since the constitute majority of the population

8. **Future perspectives**
   - Our Visual material can should be use as a behavioural Change tools for advocacy and community mobilization
   - Funding should be allocated to rural community sensitization for trials and when products are available for use
Pragsters

Abraham Alabi
MRC Laboratories, Gambia

Viral load dynamics as an insight to therapeutic vaccine efficacy in HIV dual infections

Abraham S. Alabi 1,2, Clayton Onyango 2, Mathew Cotton 1, Sarah Rowland-Jones 1
1. Viral Load Group, Viral Diseases Programme, MRC, Laboratories, Banjul, The Gambia
2. EDCTP Senior Fellow

Objectives

- To investigate viral load (VL) dynamics in HIV-1 and HIV-2 dually infected individuals
- To examine the effect of HIV VL on efficacy of therapeutic vaccines in individuals dually infected with HIV-1 and HIV-2

Methods

- Patients: Individuals in our clinical cohort infected with both HIV-1 and HIV-2
- Follow-up: Patients infected with a single HIV type (HIV-1 or HIV-2) were identified and followed up quarterly by acquisition of a second HIV type (D infection).

Discussion & Conclusions

- Viral load dynamics in HIV-dually infected patients appear complex and possibly depend on a number of factors such as virus strain, virus fitness, etc.
- Efficacy of HIV therapeutic vaccines may depend on the susceptibility of the different virus types in patients dually infected with both HIV-1 and HIV-2.

Results

- Viral load dynamics and efficacy of therapeutic vaccines in dual-infected individuals.

Future perspectives

- Enrol more HIV-1 & HIV-2 dually infected patients for follow-up studies
- There is a need for more virological and immunological studies focusing on such patients to better understand the viral dynamics and possible implications for future vaccine trials.
# Pragsters

**Adebola Orimadegun**  
University College Hospital, Nigeria

## An Evaluation of Pyrimethamine and Proguanil Prophylaxis in Sickle Cell Disease

A. E. Orimadegun, O. Sodeinde  
Department of Paediatrics  
University College Hospital, Ibadan  
Nigeria

### BACKGROUND
- Sickle haemoglobinopathies are associated with severe clinical symptoms with onset from early childhood.
- The sickle cell haemoglobinopathy is common among Africans; about 25% of Africans are carriers of HbS gene, but only 2.9% of Africans are homozygous.
- It was estimated that in Nigeria alone, about 000 000 children are born each year with sickle cell disease.
- Though infection with Plasmodium falciparum is less prevalent in children with sickle cell disease, it is one of the most common causes of morbidity and mortality in this group of children.

### METHODS
- **Design:** We conducted a prospective, cross-sectional study in children, five years and below. Neither blood nor haematology data was analyzed.
- **Subjects:** The patients were divided into two groups: group A (prophylactic) and group B (controls). Each patient was followed up for two years.
- **Data:** The results of clinical, parasitological and laboratory examination were recorded. Data was entered and analyzed using Epi Info version 6 software. The chi-square test was used for statistical analysis, while the t-test was used for continuous data.

### RESULTS
- There were 717 sickle cell disease patients and 680 controls with a diagnosis of malaria.
- Ages (mean±SD) were 34±15.9 and 33.5±18.5 in SCD patients and controls, respectively.
- The parasites prevalence among SCD was 5.1%, significantly lower than 20.3% in control group (X<sup>2</sup>=40.56; OR=0.21; 95% CI:0.14-0.30; p<0.000).
- However, among SCD patients, parasite prevalence was 2.4% in those on weekly prophylaxis compared with 11% among those on daily prophylaxis (OR=23.9; 95% CI:22.22-237; p<0.000).
- Also, the haemoglobin levels were similar in both groups.

### DISCUSSION
- Chloroquine and pyrimethamine are the mainstay of the current policy for the control of malaria in sickle cell disease patients in Nigeria.
- The finding of 20.3% parasite rate in the recent study is comparable to previous report by Hedrick in the same hospital. A higher malaria parasite rate occurred in non-SCD cases, but this finding was not previously reported.
- Although there is very little direct evidence to support or refute giving routine prophylaxis in sickle cell disease in areas where malaria is endemic from published works, but there was increasing evidence, in the literature, of the association of malaria with anaemic crisis in sickle cell anemia.

### CONCLUSIONS
- Our data suggested that weekly Proguanil and pyrimethamine were equally effective in malaria prophylaxis in Nigerian children with sickle cell disease.

### FUTURE PERSPECTIVE
- Our findings need to be demonstrated with a randomized-controlled study design.
- The cost benefit and tolerability of a once-daily regimen compared with a once-weekly regimen of pyrimethamine also needs to be further investigated.
Pragsters

Adenike Olaogun
College of Health Sciences, Obafemi University, Nigeria

Objectives
1. To assess the process of parental decision making in the care of febrile children under five years.
2. To investigate the treatment behavior of parents in the care of their sick under five children.
3. To highlight the implications of the study to ethical issues in clinical trials of anti-malarial drugs in the under fives.

Methods
- Design: a cross sectional study.
- Target population: parents of under 5 children sick in a timeframe of 4 weeks prior to study.
- Location: Osogbo (urban) and Ilesa (rural) in southwest Nigeria.
- Sample: 330 pairs of fathers and mothers (330 pairs- Osogbo, 220 pairs- Ilesa) selected through a multistage sampling method.
- Instrument: interviewer administered questionnaire.

Results
- 86% fathers and 80% mothers agree that mothers first discovered child was sick.
- Only 44% parents took joint decision on the first action taken in child care.
- Fathers were less involved in child's care.

Discussion & Conclusions
- Confirms recent studies that parents in developing nations give biomedical facilities' orthodox drugs for the care of under 5 sick children.
- Mothers are very important in discovering child is sick, initiating care and sustaining care.
- There is a shift in the decision making process at the home even from fathers to mothers.
- In clinical trials of anti-malarial drugs, mothers are very important in the areas of informed consents, correct use of drugs (dosage and duration) and in the report of effects of drugs.
- There is need for empowering women on the early detection of malaria, appropriate drugs to be used and the report of effects of drugs during clinical trials and post that period.

Future perspectives
1. To understand better the shift in parental decision making on care of children that can influence clinical trials, there is need for further studies into socio-culture and psychological factors influencing women's and men's approach in the treatment of malaria particularly as it relates to the under five children.
2. Malaria management must be approached from a gender perspective.
3. Inter-sectional collaborations that will promote gender equity in health must be bifurcated and improved.
Pragsters

Alfred Tiono
Centre National de Recherche et de Formation sur le Paludisme, Burkina Faso

An open randomised controlled study to compare the safety and efficacy of artesunate and amodiaquine in fixed formulation versus loose combination for the treatment of acute, uncomplicated Plasmodium falciparum malaria in children in Burkina Faso

Objectives
- Primary objective: To demonstrate the non inferiority of artesunate and amodiaquine in fixed formulation versus the loose combination in terms of parasitological cure rate on day 28.
- Secondary objective: Safety of artesunate and amodiaquine in fixed formulation versus the loose combination.

Methods
- Open randomised controlled trial of amodiaquine and artesunate in fixed formulation (AS/AQ) vs loose combination (AS + AQ).
- Each subject is randomised to receive AS/AQ or AS + AQ in a ratio of 1:1.
- 750 children aged 6 to 59 months and weighing ≥ 10 kg presenting with acute uncomplicated P. falciparum malaria were recruited.

Results
- Parasite clearance (PPF) rate on day 28 was 89.2% in the fixed formulation group versus 95.3% in the loose combination group (not corrected by Poisson).
- Adverse events were mild to moderate.
- 9 Serious adverse events reported; one judged possibly related to the study drug (convulsions).

Discussion & Conclusions
- The cure rate at day 28 is comparable to what was obtained in previous studies with the loose combination in Kenya (86%), Senegal (82%) and Gabon (85%).
- In total, the fixed formulation of amodiaquine and artesunate (AS/AQ) has demonstrated a very good efficacy as compared to the loose combination.
- Easy to use.
- Well tolerated with good safety profile.

Future perspectives
- Pharmacokinetic study in children and adults planned for 2006.
- Preparation for the registration of the fixed formulation in process.
Pragsters

Alphonse Ouedraogo
Centre National de Recherche et de Formation sur le Paludisme, Burkina Faso

Impact of a pretreatment with Suladoxine-pyrimethamine or Artether-lumefantrine during the high transmission season on Plasmodium falciparum malaria infection and clinical episodes in children in Burkina Faso

Authors: OUEDRAOGO, Alphonse; KOTOKO, Issaka; SOUMAWO, Alain; GANSANE, Edith; BOODOU, Alassane; and BIRIBA.

Funding: This study was funded by a grant from the African Malaria Network Trust (AMNET).

Affiliation: Centre National de Recherche et de Formation sur le Paludisme (CNIRF)

Objectives

To assess the effects of an initial radical cure of Plasmodium falciparum infection with Suladoxine-pyrimethamine (SP) or Artether-lumefantrine (ACT), prior to the malaria high transmission season on the following:

1. Time to the first malaria infection
2. Time to the first malaria episode
3. Cumulative incidence density of P. falciparum infection
4. Incidence density of malaria episodes

Methods

A cohort of 589 children from 2 villages of the Health District of Sopone was enrolled for longitudinal follow up during 10 weeks.

Children received supervised curative therapy with SP (150) or ACT (66), a third group no treatment (296).

Actively followed up by study nurses by home visits twice a week.

Results

The mean time for the first malaria episode was 22.4 days (IC95% 20-24.4) in ACT arms (P=0.008).

The mean time for the first malaria episode was 22.4 days (IC95% 20-24.4) in the SP group and 27.3 days (IC95% 24-30.5) in ACT group (P<0.1).

Cumulative incidence of P. falciparum infection

The incidence rate was 88.9% (160/178) in SP treatment arm and 92.3% (82/88) in ACT arm (P=0.4).

Discussion & Conclusions

From our study it appears that the more children receive a preventive treatment with an effective anti-malarial drug the shorter is the time to the first malaria infection and highest is the clinical malaria density incidence.

Our findings also suggest that the radical elimination of parasitemia with ACT drug may increase the susceptibility to subsequent malaria infection and therefore clinical malaria episode.

Future perspectives

For blood stages malaria candidate vaccines trials where initial cure may be indicated when the efficacy of the vaccine is an endpoint, these findings should be considered in the protocol design.

We express our gratitude to the mothers and families of study children for their kind cooperation and support.
Pragsters

Amadou Konate
Centre National de Recherche et de Formation sur le Paludisme, Burkina Faso

**Objectives**

- Primary Objective
  - To assess the reactogenicity and the safety of 3 doses of 30 μg MSP5 adsorbed on alumina hydroxide or 3 doses of vaccine tested in 15 male adults fully exposed to Plasmodium falciparum.

- Secondary Objectives
  - To assess
    - the humoral immune response to the candidate vaccine antigen,
    - the cellular immune response to the candidate vaccine antigen.

**Methods**

- Trial Phase 1b, single centre, single-blind, randomised and controlled
- Sample size: 30 male adults volunteers aged 18 to 40 years.
- Trial vaccines: MSP5/181,276 (reference); Dosage: 30 μg.
- Subjects: 15.
- Tetanus toxoid (control): Formulation of 0.5 ml.
- Subjects: 15.
- Route of both vaccines: Sub-cutaneous.

**Results**

- No serious adverse events were observed in either vaccine group.
- Local reactions at the injection site were reported.
- Only one immediate systemic reaction: a tachycardia, reported in a male vaccinated with the control vaccine, which lasted for 2 days.
- No clinically significant biological abnormalities following vaccination were observed.

**Discussion & Conclusions**

- Both vaccines were well tolerated; no unexpected adverse reactions were reported. No serious adverse events were observed.
- MSP5/LSP vaccine is able to stimulate cell-mediated immune response in individuals with some degree of preceding immunity.

**Future perspectives**

- MSP5/LSP vaccine is considered as safe in male African adults and the progression has been met according to the clinical development plan.

We express our gratitude to the volunteers and families of Bologun for their kind cooperation and support.
Pragsters

Bakri Nour
Blue Nile research and Training Institute, Sudan

Experiences of Blue Nile Research and Training Institute University of Gezira, in conducting clinical trials on malaria in Sudan

- Bakri Nour, Found of Pragster, University of Gezira, in conducting clinical trials on malaria in Sudan
- Blue Nile Research and Training Institute, University of Gezira, in conducting clinical trials on malaria in Sudan
- The Pragster project is funded by the USAID, USA
- The Pragster project is supported by the United Nations Development Programme (UNDP), Sudan

Methods

- The following clinical trials were conducted:
  1. Malaria Prophylaxis During Pregnancy in Hamar, Using Sulphadoxine-Pyrimethamine in Well-Medicated Sudanese Women
  2. Evaluation of CQ versus SP and combination therapy in the treatment of uncomplicated Plasmodium falciparum in Egypt
  3. Effect of Artemether plus Chlorpromazine versus Chlorpromazine alone in the treatment of uncomplicated Plasmodium falciparum malaria in Gezira State

Discussion & Conclusions

- SP is an effective prophylactic intervention for reducing malaria episodes during pregnancy and improving neonatal birth weight
- CQ/SP combination is not recommended to be launched in the drug policy, as it revealed high resistance
- The ACT used in these clinical trials were well tolerated and absorbed, and reactions of the expected were fast and brief and not of gastrointestinal side effects
- The ACT used in these clinical trials could play a role in the reduction of contraceptive use among pregnant women, in resistance and delaying of drug resistance

1. To formulate an effective malaria treatment policy aiming to promote the national control program

2. Assessment of efficacy and safety of non-artemisinin combined therapy (Malteco-ART) and artemisinin combined therapy (Malteco-ART) in the treatment of uncomplicated P. falciparum malaria in Sudan

3. To assess the safety and efficacy of using SP as a malaria prophylactic during pregnancy

4. To determine the sensitivity, specificity and reliability of RDTs in comparison with expert microscopy in the diagnosis of malaria and monitoring therapeutic efficacy of antimalarial drugs

Results

- SP use per episode during pregnancy
  - Intervention: 14.1%
  - Control: 29.7%

- Proportion of low birth weight to be: 3.50%

- Malaria parasitaemia: 10.0%

- Plasmodium falciparum: 24.5%

- CQ: SP and their combination:
  - Intervention: 30.7%
  - Control: 50.0%

- CQ (n = 61)
  - Sensitivity: 78.3%
  - Specificity: 61.0%

- CQ/SP combination (n = 100)
  - Sensitivity: 51.3%

Future perspectives

- ACT is an option for malaria treatment in Sudan
- SP is effective to be used as malaria prophylactic during pregnancy as it is recommended in Sudan malaria drug policy (MDP)
- The RDTs can be implemented in areas where lacking adequate malaria microscopy to diagnose malaria and monitoring antimalarial drugs efficacy
**Pragsters**

**Beatrice Namutangula**

Makere University, Uganda

**Methods**
- Sample size >78 per arm. Total of 156 patients
- Follow up until discharge, death or to day 7
- Clinical evaluation daily: coma, RR, pulse, BP, Blood sugar
- Monitored for adverse effects.
- Laboratory progress: RFTs on 3rd day, repeat blood film 5th day

**Results**

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<th>156 recruited</th>
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<td>31 excluded</td>
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<td>125 enrolled</td>
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<th>247 children with CM</th>
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<td>13 died</td>
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<td>98 no N/C</td>
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<td>62 no N/C</td>
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<td>3 N/C</td>
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**Discussion & Conclusions**

1. IV mannitol given as adjunct therapy in treatment of childhood CM did not significant improve the mean time to regain consciousness.
2. Mortality in the mannitol group < placebo group (not significant).
3. Mannitol was well tolerated, no adverse effects documented.

**Future perspectives**

1. The use of mannitol as adjunct therapy in the treatment of cerebral malaria cannot be recommended by this study.
2. Studies with higher doses and more than one dose of mannitol should be undertaken to determine if there is any role of mannitol as adjunct therapy in treatment of childhood cerebral malaria.
Pragsters

Bornwell Sikateyo
Central Board of Health, Zambia

**Objectives**

- To make an assessment of the knowledge, attitudes and practices of research ethics of the health researchers in Zambia
- To identify the experiences of research ethics of health researchers in Zambia
- To determine the knowledge and attitudes of research ethics regulations by health researchers in Zambia
- To describe the practices and experiences of the ethical review process of health research in Zambia

**Methods**

- Cross sectional study with a national coverage of all active health researchers
- Survey instrument obtained approval from JHSPH CHR in USA and TDRC REC in Zambia
- Identification of health researchers
- Attempted to reach all health researchers listed in the Annotated Bibliographies Of Essential Health Care Package in Zambia
- Determination of the state of research ethics
- Exploration of various research ethics issues

**Results**

- All data entered in Epi-Info 3.2 and subjected to double entry and confirmatory cross checks
- Descriptive statistics computed for all the variables to give meaning to the several pieces of information that can be useful to understanding the descriptive qualities of the data.
- Out of 600 questionnaires sent out, 144 were returned giving an overall survey response rate of 24%.
- 69% were male and 31% were female.
- 48% have had some formal training in research ethics or bioethics.

**Discussion & Conclusions**

- International partners have too much authority in the research conducted in the country with the potential danger of weakening and compromising the IRB process each time they feel uncomfortable.
- Funding does have a very significant role given the low socio-economic status of the studied populations.
- There were a few cases where people remained uninformed or uncares for so they could be studied.
- There is a need for home grown ethic regulations and solutions and not necessarily dictated by international ones.

**Recommendations**

- Conduct a national level study to make an assessment of the ‘real’ understanding of the informed consent process by research participants involved in various experimental and even observational studies.
- Establish a register of all researchers in Zambia and dynamically capture all research studies in a national database of research studies.
- Conduct ongoing training and orientation of health researchers to research ethics.

**Future perspectives**

- The establishment of a ‘Zambian’ national Research Ethics Committee driven by a Zambian initiative giving more relevancy and appreciation instead of subconsciously external or funding pressures.
- Strong view that research ethics regulations must be driven by local needs and not driven by external needs or requirements.
- Establishment of mechanisms to monitor research and to check malpractices and unethical research.
Pragsters

Britta Wahren
Karolinska Institute, Sweden

How to design an effective HIV vaccine

Andreas Brogren, Linde Gustavsdotter, Andreas Brogren, Bo Brekelmans, Christina Johansson, David Engstrand, Katarina Hakevall, Jonas Hvidt, Maja Haglund, Gunnar Alborn, Erik Sandhagen, Margareta Lin, Brita Wahren

Karolinska Institute and Swedish Institute for Infectious Disease Control, Stockholm, Sweden

Objectives
- To design a multigene, multisubtype HIV vaccine for use in many populations
- New concepts include design, composition, route and adjuvant
- To perform clinical trials for prophylaxis and therapy

Methods

Results

Discussion & Conclusions
- Strong immunogenicity is induced in preclinical and clinical studies.
- This warrants clinical phase II studies with the same and developed genetic vaccines.
Pragsters

Bruno Kilunga Kubata
Bioscience Eastern and Central Africa, Kenya

**BecANet: An opportunity for capacity building in East and Central Africa**

Kubata Bruno Kilunga
Bioscience Eastern and Central Africa

**Vision**
To create a platform of centres for excellence in East and Central Africa where African scientists and institutions can address specific problems related to Africa through the use of cutting edge technologies and modern facilities.

**Mission**
Improve human health, sustain agricultural production, conserve the environment, and develop and use new bioscience technologies and strategies. Improve livelihoods of resource poor people.

**BecA Design**
- BecA Hub and Secretariat
  - Located on the campus of ILR in Nairobi, Kenya
  - Provide common biosciences research platform
  - Deliver research related services
  - Facilitate capacity building and training opportunities
- Network of regional nodes, National Programs and other laboratories
  - Distributed throughout institutions in eastern and central Africa
  - Conduct research on priority issues affecting Africa’s development

**Scientific & Technical Competencies at Hub**
- Bioinformatics
- Biometrics
- Diagnostics
- Genomics
- Functional genomics
- Molecular breeding
- Transformation
- Tissue culture
- Vaccine technology
- Vectors

**Non-Scientific Competencies**
- Laboratory management
- Equipment maintenance
- Bioethics policies and practices
- Communication and knowledge management
- Information technology
- Intellectual property management
- Regulatory management
- Partnerships for technology
- Science writing
- Proposal preparation

**BecA Network Core Competencies**

**Way forward**
- BecANet institutions provide a means that EDCTP may well use to share experiences in conducting clinical trials in other countries of the region.
- EDCTP may well partner with existing structures on the continent to achieve its goals.
Pragsters

Bulabula Mugambwa Ali
Universite Officielle de Bukavu, Congo

**URBAN AREA ADULTS MALARIA IN LUBUMBASHI, D.R. CONGO**

BULABULA.A.B, MALA KANEH, MAIZUMA R.E., EBENDA S.M.,
LOUBADA, KAMBA B.
(C) UNIVERSITE OFFICIELLE DE BUKAVU DOHA & CRESPIN

Acknowledgements and affiliations to:
EDCTP
The Swedish Society of Medicine

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**Objectives**

- To determine malarialometric indexes
- To assess the impact of Malaria

---

**Methods**

- A prospective study, case-controls
- Places: Sendwe Hospital and the Teaching Hospital of Lubumbashi, in Lubumbashi, D.R.Congo
- Sample:
  - 154 patients (cases)
  - 202 controls
- Period: March – July 1994

---

**Results**

- Mean age: 29 ± 11 years old
- 38.6% of patients are 15 to 19 years old
(P=0.001)
- Prevalence:
  - Patients: 31.1% (CI at 95%, 23.3, 38.4)
  - Controls: 18.8% (CI at 95%, 14.3, 23.2)
- Gametocytic index: 3.8% (CI at 95%, 1.6, 9.2)

---

**Discussion & Conclusions**

- The malaria situation in Lubumbashi is mesoendemic (NGIMBI D. et al, 1986),
at 1200m of altitude, due to Plasmodium faliparum species,
contradicting to adult’s anaemia.

---

**Future perspectives**

- Malaria epidemiological researches
- Case studies on the treatment response to Artelinsin derivated products in Bukavu, South Kivu,
D.R.CONGO.
Pragsters

Catherine Falade
University of Ibadan, Nigeria

Experience with ethical issues in malaria clinical trials in Nigeria

By Falade CD and Ademowo DG
Department of Pharmacology and Therapeutics, University of Ibadan, Ibadan, Nigeria

Institutional review committees (IRCs) in Nigeria

- Unlike in the past, IRGs are more generally available in our health care and research institutions
- IRGs also demonstrate better adherence to international standards in composition, establishment and operations.
- National ethical advice now available
- Critical mass of investigators with training in biomedical ethics also growing
- Standard operation procedures established and regular continuing education training in ethical issues carried out by our institutional review committee

Objectives

To evaluate
Post Ethical approval issues and obtaining informed consent
- Understanding of consent critically
- Verbal? Written? Witnessed verbal?
- Who gives consent? Mother/Father/extended family head?

Case 1: Hospital case presentation - divorce resulting from informed consent

- 4 year old girl with confirmed falciparum malaria enrolled after 36 year old father gave informed consent
- Day 2 - Child vomits 14 hours, re-admitted successfully
- Home visit by research staff when child did not come on DT reveals signs of domestic violence
- Father sent away from home and told not to be seen or treated for malaria not being given informed consent and spending time in hospital
- Sister who now in charge of child kept at home (keep 39.9°C still vomiting)
- Child withdrawn from study, rescue therapy given and child followed-up
- Prophylaxis P1 and 2 other investigators lined up peace after 3 visits over 1 week
- Mother re-integrated into family

Case 2: Forceful removal of study participant from hospital ward by uncle

- 2 year old girl with falciparum malaria enrolled in a study
- Informed consent from 3 year old mother
- Study protocol demands hospital admission for 1st 3 days
- Child forcefully removed from ward 9pm to 09
- Child's father apparently dead, Mum lives in family house
- Uncle has traditional cultural authority over child
- A home visit by PI and another investigator was fruitful
- Child brought back to hospital and allowed to complete the study
- Uncle was very cooperative and supportive throughout study period

Case 3: Withdrawal of Consent by extended family head

- Case similar to case 2
- Informed consent given by 48 year old mother
- Father dead
- Family head came to hospital to tell mother off and demand release of child
- Intervention of hospital staff and PI unsuccessful
- Rescue therapy given and child withdrawn from study

Studies in the community

- Local government health department permission necessary
- Important to know if there are political/religious factions or power tussle in the community
- Community consent from community head, leaders, opinion makers
- Advocacy to include priests and imams
- Individual informed consent from the parent/guardian before enrolment

A community case situation

- Very critical and follow up refused after clinical improvement
- Children well so no need for subsequent bleeding
- Protocol split out during informed consent procedure
- Parental explanation not helpful
- Report goes to village head
- Reaches concerned about bleeding a recovering child
- Takes action
- - cultural belief that blood is the life so is being taken out of children
- Blood letting also associated with witchcraft
- Series of meetings with
- Village head, elders, opinion leaders and other segments of the community partially successful
- Objectives fended by mud before dying for community leadership
- Study ended in another community
Pragsters

Charles Makassi
National Institute for Medical Research, Tanzania

Verbal autopsy and neurological sequelae in children with malaria recruited in a clinical trial in rural Tanzania.

Marger Tanziwa, Division of International Health (HCIP), Karonga Institute, Tanzania.
Andrew Kibata, Director (aetiology, NMH, Dar es Salaam, Tanzania.
Zoheen Mabgachi, co-investigator (aetiology, project manager, NMH, Kenya.
Ton Peo, co-investigator (aetiology, project manager, NMH, Kenya.
Charles Bwana, co-investigator (aetiology, NMH, Dar es Salaam, Tanzania.

We would like to thank the study doctors, Dr. Melissa Jones, and the study monitor, Dr. Isabatai Kivuga. This study was a collaboration between NMH and WHO/TDR.

Methods for verbal autopsies

• Field supervisors visited villages on motorcycle and brought information of follow-up of recruited children (after 7-30 days) back to the hospital.
• A medical doctor then visited the village and conducted a pre-test verbal autopsy questionnaire with the parent/guardian.
• Particular focus was made on the health seeking behaviour leading up to the death.
• The same medical doctor also collected information from original case record forms, blood slides taken at recruitment and hospital records.
• Verbal autopsy narratives were sent to an end-point review committee to determine if the appropriate supportive care had been realistically expected to make the difference between life and death at the point it was given in the child’s disease.

Provisional results of verbal autopsies

• FINAL DATA TO COME EARLY AUGUST 2006
• Total deaths: 300
• Main symptoms at recruitment:
  - Convulsions, altered consciousness, repeated vomiting, prostration
• Manifestations of neurological sequelae
  - Hemiparesis
  - Cerebral palsy
  - Behavioral changes
  - Speech disorder
  - Sciatric nerve injury
  - Blindness
• Median age at death 1 year 10 months
• Median age of children with neurological sequelae 5 years

Discussion & Conclusions

• Verbal autopsies have provided a lot of information to help us understand what happened in cases where something went wrong. One major finding was that children often died soon after recruitment, and perhaps that is what we needed to do.
• We greatly increased the sensitivity, and therefore the power of the study by this stratification of deaths.
• Neurological sequelae cases were fewer than in earlier studies.
• We investigated the case outcomes to determine if the sequelae were improving, worsening, transient or permanent.

Future perspectives

• High rates of sciatric nerve injuries caused by injections at health facilities and in villages were found – possibly supporting the wider use of supplementary instead of parental treatment at distant levels.
• We attempted a simple intervention to improve injection practices among clinic staff in dispensaries (rural clinics) where we discovered problems, and this could be appropriate in other similar contexts.
Pragsters

Charles Obonyo
Kenya Medical Research Institute, Kenya

1. My First Experience as a Principal Investigator in a Clinical Trial evaluating combination therapy for uncomplicated malaria

Charles Obonyo
Kenya Medical Research Institute

2. Objectives

- Share my first experience as a Principal Investigator in the design and conduct of a randomised clinical trial

3. What was the Project?

- A randomised, double-blind, placebo controlled trial of the efficacy of artesunate plus sulfadoxine-pyrimethamine versus sulfadoxine-pyrimethamine alone in the treatment of uncomplicated malaria in western Kenya
- Dates: October 1999 to March 2000 (5 months)
- Enrolled 600 children below 5 years with uncomplicated malaria
- Workforce of 20 people (clinicians, nurses, lab, data, field, driver)
- Funded by WHO/TDR

4. How were you prepared?

- Masters degree in Clinical Epidemiology
- Attended a workshop on research ethics
- Training and worked as a Clinical Officer
- Managed hospital-based epidemiological studies before
- Familiar hospital environment

5. Tasks

- Literature review
- Data collection
- Data entry
- Data analysis
- Presentation
- Particle

6. Results

- Successfully completed the trial
- Main results written up and published
- Technical and financial reports submitted
- Results presented at:
  - Malaria conference
  - Ministry of Health
  - Hospital
- Promoted
- Received other research funding

7. Discussion & Conclusions

- Besides the education, I felt poorly prepared for the practical aspects of conducting a trial
  - Human resources management
  - Financial management
  - Purchasing and supplies management
  - Plenty of learning on the job
  - The tasks were overwhelming
  - I had no role model, or someone to consult on a daily basis

8. Future perspectives

- STRONGLY RECOMMEND:
  - Better preparation of potential Principal Investigators
  - Mentorship programme
  - Apprenticeship/internship programme
Pragsters

Charles Obonyo
Kenya Medical Research Institute, Kenya

Malaria and HIV immune suppression: Efficacy of sulfadoxine-pyrimethamine in the treatment of uncomplicated malaria in HIV-infected adults

Shah SN, Smith ES, Obonyo CO, Bioland PR, Shikonen I., Hamek MM

1

Objectives

- To compare the clinical and parasitological responses of HIV-infected vs. HIV negative adults with uncomplicated malaria to Sulfadoxine – pyrimethamine treatment

2

Methods

- Study dates: Sept. 2002 to July 2004
- Non-pregnant adults presenting with fever or recent history of fever were screened with a blood smear
- Consenting patients with ≥ 400 parasites/μl were provided pre- and post-test counseling and tested for HIV
- All participants treated with SP according to Kenya’s national malaria guidelines
- Follow up for 28 days

3

Methods 2: Study protocol

- CD4 count and hemoglobin (Hb) Day 0
  - Low CD4 group: CD4 count ≤ 200 μl
  - High CD4 group: CD4 count > 200 μl
- Missing, unplanned exams and malaria lifelines smear on days 0, 7, 14, 21, and 28
- Treatment failure defined according to WHO protocol for evaluating antimalarial treatment efficacy

4

Results: Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>HIV neg n=130</th>
<th>High CD4 n=256</th>
<th>Low CD4 n=122</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age in yrs</td>
<td>31</td>
<td>30.9</td>
<td>32.9</td>
</tr>
<tr>
<td>% female</td>
<td>61</td>
<td>61.5</td>
<td>66.5</td>
</tr>
<tr>
<td>Geometric mean</td>
<td>12,742</td>
<td>10,784</td>
<td>30,016</td>
</tr>
<tr>
<td>Parasite density/μl</td>
<td>14.2</td>
<td>11.9</td>
<td>33.5</td>
</tr>
<tr>
<td>Mean Hb (g/dl)</td>
<td>13.4</td>
<td>11.5</td>
<td>10.7</td>
</tr>
</tbody>
</table>

5

RESULTS 2

Clinical and parasitological response to SP treatment

<table>
<thead>
<tr>
<th></th>
<th>HIV neg n=130</th>
<th>High CD4 n=256</th>
<th>Low CD4 n=122</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETP</td>
<td>2 (15.4%)</td>
<td>11 (4.3%)</td>
<td>10 (8.3%)</td>
</tr>
<tr>
<td>LCF</td>
<td>5 (3.8%)</td>
<td>9 (0.5%)</td>
<td>10 (8.2%)</td>
</tr>
<tr>
<td>LPF</td>
<td>9 (6.9%)</td>
<td>25 (9.8%)</td>
<td>19 (15.6%)</td>
</tr>
<tr>
<td>ADRP</td>
<td>114 (87.8%)</td>
<td>212 (82.4%)</td>
<td>83 (68.0%)</td>
</tr>
</tbody>
</table>

6

Discussion & Conclusions

- HIV-infected adults with low CD4 count are more likely to present with fever, higher mean parasite density and lower mean haemoglobin
- HIV-related immune suppression when associated with anaemia increases the risk of SP treatment failure

7

Future perspectives

- Prevention
  - Collaboration between HIV and malaria programs
  - Incorporate effective malaria prevention strategies into the care of HIV-infected individuals
  - Emphasize malaria prevention
  - Distribute insecticide treated bed nets
- Antimalarial treatment of HIV-infected individuals
  - Determine the optimal antimalarial therapy for immunocompromised HIV-infected individuals
- Treat HIV-infected persons with the most effective antimalarials available

8
Pragsters

Chifumbe Chintu
School of Medicine, University of Zambia, Zambia

1. Retention of Researchers in Developing Countries.
   Professor Chifumbe Chintu
   School of Medicine, University of Zambia
   P.O. Box 50110
   Lusaka, Zambia

2. Objectives
   • To identify reasons for non retention of Researchers in Developing Countries.
   • To offer suggestions for retaining Researchers in developing countries.

3. Methods
   • Review literature on research in developing countries.
   • Review literature on human resource for research in Health.
   • Review Established links Between North and South

4. Results
   • To be communicated later.

5. Discussion & Conclusions
   • Discussion will follow after the relevant review has been done

6. Future perspectives
   • Will follow the presentation
Pragsters

Chukwuemeka Nwachukwu
Institute of Tropical Disease Research & Prevention, Nigeria

ANTIMOTILITY AGENTS FOR CHRONIC DIARRHOEA IN PEOPLE WITH HIV/AIDS
(A Cochrane Systematic Review)

NWACHUKWU, CHUKWUEMEKA
OKEBE, JOSEPH

ACKNOWLEDGEMENTS:
South African Cochrane Centre
Kate Grimwade (Review mentor)

Objective
To assess the effectiveness of antimotility agents in controlling chronic diarrhoea in the immunocompromised states caused by HIV/AIDS

Search Strategy
  - The Cochrane Library Controlled Trials Register (2005 issue 4) (14 records, non-selected)
  - Embase (1980 to Dec. 2005) (10 records, non-selected)
  - AIDS-Search (1980 to Dec. 2005) (51 records, 1 selected)
  - WHO, CDC, Plos, Jansen-Claeg (No relevant trials)
  - Reference list of identified trials (No output)
  - Two authors independently undertook study selection.
  - Full articles of potentially eligible studies were also examined by both authors.

Result
- No study met our inclusion criteria

Discussion
- No RCTs identified, review articles propose efficacy
- RCT comparing Ondansetron & Loperamide
- Ondansetron in HIV positive people shows Ondansetron as more effective.
- RCT comparing Loperamide & Rifaximin in HIV negative people shows comparable effect.
- Use of antimotilitys has been based on expert opinion and studies on HIV negative people.
- Need to search for evidence applicable to resource-limited settings: comparing antimotilitys with other antidiarrhoeal, weighing benefits against cost while awaiting HAART.

Conclusion
- No evidence available from RCTs
- Caution in use of evidence from expert opinion, review articles and studies on HIV negative individuals.
- Consider different etiologies in HIV positive and negative people in deciding treatment options.

Future Perspective
- Need for trials to assess effectiveness of antimotilitys both in areas where AIDS are not yet available and in persons on ART.
- Systematic review to compare antimotilitys with other antidiarrhoeal, weighting benefits against cost.
- To add meaningful evidence to practice and improve QOL of HIV positive persons.
Presentations: Abstracts and Pragsters

Pragsters

David Olufem Olaleye
University of Ibadan, Nigeria

EVALUATION OF HIV LABORATORY SYSTEM IN NIGERIA

OLALEYE O.O. and ODARO O.N.
Department of Biostatistics, College of Medicine,
University of Ibadan, University College Hospital, Ibadan, NIGERIA

Background
HIV/AIDS situation in Nigeria
- Nigeria is the tenth largest country in the world and the most populous country in Africa. The estimated population of the country in 2003 stood at 136.2 million.
- There are more than 350 ethnolinguistic groups. Currently, it is estimated that about 35% of the population live in urban communities.
- The mother rate of infection among the general population and in different parts of the country has increased from
- 1.4% in 1991 to
- 4.5% in 1995
- 5.4% in 1999 and
- 5.6% in 2001 and a decline to
- 5.0% in 2003. The prevalence however varies across areas and groups.

Prevalence varies across areas and groups

Objective
This study was commissioned by the National Action Committee on AIDS in Nigeria to evaluate the entire national HIV laboratory system in Nigeria

Methodology
- Records from the Federal and State Ministry of Health
- Site visitation
- Hospital and Site Laboratory Records
- Used Structured Questionnaires
- Observation and Physical Inspection

Results

Recommendations for Implementation
- Laboratory Capacity (Personal and Facilities)
- HIV Testing Centres
- Referral and Networking
- Communication between laboratories
- Transportation of Specimens
- Monitoring and Evaluation
- Supervision
- Transportation of Specimens
- Funding Mechanisms
- Funding Mechanisms and all stakeholders

Challenges
- Recommendations from the New National Strategic Framework for Action
- Scale-up HIV testing in the country with emphasis on VCT + PMTCT,
- universal access to treatment, care and support for infected persons
- Expansion of the Prevention efforts.
- Presidential mandate to enroll 250,000 HIV infected persons on treatment by year 2007.
- National PMTCT program has proposed to
- increase access to pregnant women to HIV testing and PMTCT from the current rate of less than 1% to over 50% by year 2010.
- On transmission
- promote access to safe blood

Results map 1

Results map 2
Pragsters

Dominic Dery

Kintampo Health Research Centre, Ghana

Site specific malaria transmission indicators: patterns for clinical and vaccine evaluations in the endemic belt of Ghana-Kintampo

DB Dery1, S Owusu-Agyei1, KP Asante1, MA Adams1, OK Dosso2, C Brown2, B Greenwood2

Acknowledgements and affiliations:

1 University Health Research Centre
2 Institute for Research in Tropical Disease
3 Liverpool School of Tropical Medicine and Liverpool University

Methods
- Sixteen (16) clusters or communities depicting micro-ecology of the area selected as study sites
- Study in two parts
  1. Seasonal prevalence of P. falciparum parasitemia (320-400 & 80 all age groups)
  2. 20% /in each community
  3. 3 echos with week (Monthly surveillance)
  4. 24 group community
  5. 6 months/period
  6. An entomological survey
- Eligible participants in 1st part of study consented to

Results
- A yearly EIR of 211/kb was calculated for the second period (Jan-Dec, 2008)
- Molecular identification revealed that Plasmodium falciparum is as dominant in complex
- Exercise diurnal revealed the D. stephensi form on the prevalent molecular form in the midday's infection
- Intensity (MS) forms detected in gametocyte's samples
- K1 (KDR) genes prevalent in the K form of An. gambiae (5.4%)

Discussion & Conclusions
- An annual round transmission was clearly observed from these results
- Major malaria vectors (Ag. & AK) contribute in phase and hypothesis at different times of the year to malaria transmission
- An. gambiae s.s (M-form) remains the main vector contributing immensely to transmission despite its low numbers
- High prevalence of hybrid/MS forms, suggest that there is probably interbreeding between these two distinct molecular forms and therefore further work is needed to confirm this observation
- Molecular characterization revealed KDR resistant gene (K10) highly prevalent in the An. gambiae s.s form

EDCTP Third Annual Forum 2006 - Partnership and African Leadership: Challenges and Opportunities 61
Pragsters

Ediang Okuku
Nigerian Meteorological Agency, Nigeria

**RESEARCH AND CAPACITY BUILDING IN future of Clinical Trials IN NIGERIA.**

Dr. Ediang Okuku Archibong
Research Officer, Nigerian meteorological agency

**Introduction**

- Air Introduction to Clinical Trials
- What is a clinical trial?
- Phases in a clinical trial.

**Methodology**

- What are the different types of clinical trial?
- Treatment trials.
- Prevention trials.
- Diagnostic trials.
- Screening trials.
- Cessation trials.

**Result**

- Research
  - Research deals with issues, activities and strategies relating to epidemiology, documentation, conservation, improvement, sustainable utilization, processing, marketing, valorization, marketing and exportation of meteorological data. In addition, the research conducted in this presentation will include the consideration of the role and value of indigenous knowledge and Indigenous participation.
  - Literature search
  - This field is the need for in-depth training and back-stopping support to Screnyo growers, staff and research managers of partner organizations.

**Conclusion**

- Research
  - The different types of clinical trials.
  - Application of clinical trials.
  - Conclusion
  - The different types of clinical trials.

**Recommendations**

- Developing a national agenda for local and national meteorological organizations.
- Strengthening the research capacity of meteorological organizations.
- Promotion of indigenous knowledge and Indigenous participation.

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**Presentations: Abstracts and Pragsters**

**Pragsters**

**Research**

- Location and Contact Information
- Purpose and the study by Clinical Trials in Nigeria
- Methods and Statistical Information
- Results and Discussion
- Conclusion
- Recommendations

---

**Presentations: Abstracts and Pragsters**

**Pragsters**

**Research**

- Location and Contact Information
- Purpose and the study by Clinical Trials in Nigeria
- Methods and Statistical Information
- Results and Discussion
- Conclusion
- Recommendations
Pragsters

Egeruan Babatunde Imoukhuede
European Malaria Vaccine Initiative, United Kingdom

Progress Towards a Malaria Vaccine: A European concerted effort
Egeruan Babatunde Imoukhuede
Clinical Affairs Manager, EMVI

EMVI Mission
- To contribute to the global efforts to control malaria by:
  - providing a mechanism for accelerated development and the clinical trials of malaria vaccines in Europe and Developing Countries
  - promoting affordability and accessibility of malaria vaccines in Developing Countries

Organisation of EMVI Projects

EMVI Partnerships

Vaccine Development
INDUSTRIAL INTEREST

Clinical Plan Strategy

EMVI Completed Trials
- Phase 1a trial of GLURP (LSP) – Nijmegen – Accepted for publication in Vaccine
- Phase 1b trial of MSP3 (LSP) – Burkina Faso 2003 – 2004 - Accepted for publication in Vaccine

Planned Clinical Trials 2006 – 2007
Elizabeth Wala
Kenya AIDS Vaccine Initiative, Kenya

Integration of an ART program in an HIV Vaccine Trial Site: Lessons learned
Dr. Wala, Dr. Anzala et al
Kenya AIDS Vaccine Initiative (KAVI) – Kangemi University of Nairobi, Kenya

Objectives
- To establish the HIV prevalence in a high risk cohort who have been recruited in preparation for Phase Ib AIDS vaccine studies
- To offer optimum care and treatment to volunteers of HIV vaccine trial studies who were found to be HIV positive
- To establish networks with other

Methods
- Under KAVI a high risk cohort of 1500 volunteers was established in 2004 in one of Nairobi’s slum areas. This included commercial sex workers and their male partners.
- Volunteers were then screened for HIV using approved rapid tests after counselling

Results
- Of all the 1000 high risk volunteers screened initially in 2004 the prevalence was approximately 16% i.e a total of 164 volunteers
- Out of these, only 20 went to the referral hospital at the time of referral in 2004
- Those who have since been transferred in are 12

Discussion & Conclusions
- Despite intensive mobilization and awareness campaigns there is apathy amongst the volunteers in follow-up at the ART program at the research site
- Those who have been counselled on ART and are still reluctant to start are citing issues to do with food security, stigma, non-disclosure, issues about ARVs (including suspension in terms of supply, pill burden and the life long therapy) and a false feeling of well-being
- It seems like the volunteers have not owned the

Future perspectives
- A monthly support group has been started to help improve HIV/AIDS and its treatment through turnout is improving
- Plans are underway to integrate the ART program offered at KAVI and that offered by the local city council health clinic where KAVI is located (to avoid duplication of roles and also standardize the research arm of KAVI to offer quality care)
- Efforts are being made to network patients with organizations that offer food, employment, school fees for the children etc.
- The question as to why there is general apathy amongst the clients despite everything being offered free of charge requires further research

Acknowledgment
- The volunteers at KAVI – Kangemi
- KAVI
- NASCOP
- FHI/UNITED

Presentations: Abstracts and Pragsters
Pragsters

Franklin Weria Mosha
Kilimanjaro Clinical Research Centre, Tanzania

1. Title: Regulatory and Ethical Issues in Clinical Research

Topic: Ethical Impact of Cultural Practices in Multilateral Research

Dr. F. W. Mosha
Kilimanjaro Clinical Research Centre
KCMC
Moshi
TANZANIA

2. Research involving human subjects conducted in Africa mainly during and after colonial rule.
3. Most research involved few researchers within one or two institutions.
4. Research proposal review and monitoring mechanisms were hardly in place.
5. With the adoption of Global Guidelines for clinical research especially in multilateral/collaboration research during the past three decades Ethical Principles are now considered within the context of GCP

4. Social cultural practices that need to be taken into account during implementation of “Informed consent” procedures include:
   - spheres of influence – family/community
   - oral versus written consent
   - confidentiality during filling consent forms and filing collected information
   - information disclosure

5. KCMC – Tanzania experience

   - We have over 20 ongoing multilateral clinical research, mainly in the area of HIV/AIDS and TB.
   - Ethical issues related to cultural practices that are being addressed by our local institutional ethical committee include:
     - Consent procedures
     - Sample collection, preservation transportation and disposal
     - Adverse effects reporting

6. Violation of principles of “Justice”

   - Global ethical requirements are usually viewed as general statements of value that must be elaborated by traditions of interpretations.
   - There is need for collaborative partnership as outlined by Emanuel et al., (2004) - This includes recognition and respect of Host country distinctive cultural values and social practices
Pragsters

Friday Odey
Institute of Tropical Disease Research and Prevention, Nigeria

**Objectives**
- The main objective was to compare the safety and efficacy of Guanamine Kit (Artesunate + Amodiaquin) for treating uncomplicated malaria in children and adults in Calabar, Nigeria.
- The specific objectives will be:
  - To measure the proportion of early treatment failures, late treatment failures and adequate responses to treatment for these trial drugs.
  - To obtain measures of Artesunate and Amodiaquin efficacy such as fever and parasite clearance by Day 3, and mean improvement in haemoglobin by Day 14.

**Methods**
- This was an open-label, non-comparative trial of Artesunate Kit for efficacy, safety and tolerability in vivo/14-day study.
- Inclusion criteria:
  - Age > 6 months.
  - Weight > 15 kg.
  - Fever in the past 24 hrs or temp ≥37.5°C Parasite density of 1000-2500 parasites/μl of blood.

**Results**

<table>
<thead>
<tr>
<th>Treatment Outcome</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number enrolled (N)</td>
<td>99</td>
<td>100</td>
</tr>
<tr>
<td>Loss to follow-up</td>
<td>6</td>
<td>6.1</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>1</td>
<td>1.0</td>
</tr>
<tr>
<td>Number of evaluable participants</td>
<td>92</td>
<td>92.9</td>
</tr>
<tr>
<td>Therapeutic efficacy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adequate clinical and parasitological response (ACPR)</td>
<td>92</td>
<td>100</td>
</tr>
</tbody>
</table>

**Results**

<table>
<thead>
<tr>
<th>Follow-up Days</th>
<th>Number with parasitaemia</th>
<th>% with parasitaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>D0</td>
<td>99</td>
<td>100</td>
</tr>
<tr>
<td>D1</td>
<td>98</td>
<td>91.9</td>
</tr>
<tr>
<td>D2</td>
<td>20</td>
<td>20.2</td>
</tr>
<tr>
<td>D3</td>
<td>1</td>
<td>1.0</td>
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<tr>
<td>D7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>D14</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Discussion & Conclusions**
- Guanamine Kit is highly effective against uncomplicated Plasmodium malaria in Calabar.
- The combination was tolerated by Nigerians living in this part of the country.
- This ACT has potential value to play in reducing morbidity and mortality due to falciparum malaria in Nigeria.
- This was a 14 day study (not 28 day as currently recommended by WHO) and the study period could have affected the results.

**Future perspectives**
- To conduct 28 day study as being currently recommended by the WHO when more funds are available.
Pragsters

George Ademowo
Institute for Medical Research and Training, Nigeria

**Presentations: Abstracts and Pragsters**

**Pragsters**

**George Ademowo**
Institute for Medical Research and Training, Nigeria

1. The question of rational treatment of acute uncomplicated malaria with chlorquine or artemether-lumefantrine and severe malaria with quinine or artemether.

- Ademowo OD, Njeh CJ, Adebayo AJ, Osunuga OY, Falade CO.
- Postgraduate Institute for Medical Research & Training, Department of Pharmacology, College of Medicine, University of Ibadan, Ibadan, Nigeria.

2. The objectives of the study are:

1. To evaluate the efficacy of chlorquine in acute uncomplicated malaria.
2. To evaluate the efficacy and safety of artemether-lumefantrine in the treatment of acute uncomplicated malaria.
3. To determine the efficacy of artemether and quinine in children with severe malaria.
4. To evaluate the relative safety of artemether and quinine in the treatment of malaria.

3. Methods:

- Children (1-12 years) with microscopically proven malaria were recruited as follows:
- 71 children with acute uncomplicated malaria were recruited for chloroquine study.
- 93 children with acute uncomplicated for artemether-lumefantrine (western) study.
- 32 children with severe malaria who met with the inclusion criteria were recruited. Fever (temperature >37.5°C) within the last 24 hrs, presence of convulsion, hypoglycemia, anemia, and hyperparasitemia were recruited for quinine and artemether.

4. Exclusion criteria

- History of blood transfusion in the last 2 months.
- Concomitant illness.
- History of allergy to quinine or Artemether.
- Antibacterial drug intake in the past 7 days.
- Lack of informed consent.

5. Withdrawal criteria

- Development of concomitant illness.
- Protocol violation.
- Withdrawal of consent.

6. Results:

- 33 of the 71 (46.3%) patients administered chloroquine were resistant to chloroquine at various degrees (R0-6, R6-20, R20-7) after PCR correction.
- In the cohort group, the PCR corrected cure rate at day 28 was 100% for coartem. Fever and parasite clearance rates were 19.2 ± 1.3 and 25.1 ± 1.1.
- The drug was well tolerated as there was no serious adverse events documented.

For the quinine and artemether study, the presenting clinical features were similar in the 2 treatment groups.
- Fever clearance time for quinine (46.8 ± 26.0 hrs) was significantly lower than with artemether (72.0 ± 27.7 hrs) (p < 0.001).

7. Discussion

- Resistance to chloroquine was very high. This necessitates the use of alternative drugs for treatment of malaria.
- Coartem, an ACT was very effective parasitologically and clinically in the treatment of malaria and it was well tolerated.
- Quinine had a shorter fever clearance time than artemether.
- Artemether had rapid malaria parasite clearance, faster and sustained recovery from anemia, shorter coma and jaundice resolution time. It is better tolerated and appears safer.

8. Future Perspective

- It would be necessary to:
  - monitor the efficacy and safety of the various ACTs that are in the market.
  - Evaluate the relative disposition of artesinime derivative and other combined drugs in the ACTs in Africa.
  - Educate and train health care workers on the correct and effective treatment of malaria especially in the rural areas.
  - Determine the effect of nutrition on malaria and efficacy and distribution of ACT.
  - Special focus should be directed at children under 5 years and pregnant women.
  - Appropriate treatment for malaria patients with co-infection with HIV needs to be determined.
Pragsters

Georgina Odaibo
University of Ibadan, Nigeria

HIV VARIABILITY AND RELIABILITY OF LABORATORY DIAGNOSIS IN AFRICA

BY

GODABO EN, OYEBAMI E, ADERRU MG, SAURENY A, OLUYEDE E
Department of virology, College of Medicine, University of Ibadan, University College Hospital, Ibadan, NIGERIA

Background

- Accurate and reliable testing for evidence of infection with HIV is a critical factor towards the implementation of effective control of the spread of the virus and care of infected individuals.
- HIV testing is a key strategy for ensuring that individuals learn their status and receive referrals to appropriate services based on that status.
- Uninfected persons may benefit from HIV testing if knowing their HIV status assists them in modifying or reducing risk behaviour.

Objective

This study was planned to evaluate the reliability of some HIV rapid test kits that are commercially available for HIV-1/2 testing in Nigeria using the Western immunoblotting technique as reference.

Methodology

- 78 sera were selected based on confirmed symptomatic or asymptomatic HIV-1 infected persons.
- 88 seronegative patients from those referred for testing in our laboratory were used for this study.
- Each sample tested with 16 HIV-1/2 rapid test kits commercially available at one time or the other for HIV-1/2 testing in Nigeria.
- Each serum sample was tested with the HIV-1/2 test kits according to each manufacturer’s instructions.

Results

- The sensitivity of the rapid test kits ranged from 42.1% to 94.7% with specificity of 90.9% to 100%.
- Further analysis showed significant variation in the sensitivity and specificity of the same kit based on whether an individual had asymptomatic or symptomatic infection.

Conclusions/Recommendation

- The results of this study highlight the problem of diagnosis of HIV infections in Africa.
- The implications of possible misdiagnosis on the various intervention strategies such as treatment and vaccine trials that rely predominantly on correct HIV status of an individual are enormous.
- Thus the need for better understanding of the molecular epidemiology of HIV in relation to diagnosis, treatment and future vaccine trials in Africa.
**Pragsters**

**Gernard Msamanga**  
Muhimbili University College of Health Sciences, Tanzania

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**Vitamins and HIV infection**

**Objective**

- To examine the effect of vitamin A and or multivitamin supplementation on birth outcomes, vertical transmission and disease progression of HIV infected pregnant women.

**Methods**

- Randomized double-blinded, placebo controlled study design.
- 14,000 consenting women were tested for HIV with prenatal and post-natal care.
- At 20-27 wk of gestation 1078 women were randomized into Vitamin A alone, multivitamin without vitamin A, multivitamin or placebo.

---

**Results**

- Multivitamin supplements reduced fatal deaths (abortion and stillbirth) by 40% compared to no multivitamin.
- Reduced low birth weight (less than 2500g) and small for gestation age by >50%.
- Increased CD4, CD8 and CD3, Hemoglobin and maternal weight.

---

**Conclusion & Recommendation**

- High doses of vitamin supplements are simple, and effective in reducing adverse pregnancy outcomes and AIDS related morbidity and mortality.
- Multivitamin supplements should be given to all HIV infected pregnant women and those who are not yet eligible for antiretroviral therapy.
**Pragsters**

**Getnet Yimer**  
Addis Ababa University, Ethiopia

**Presentations:** Abstracts and Pragsters

**EDCTP Third Annual Forum 2006 - Partnership and African Leadership: Challenges and Opportunities**

**Methods**

- Baseline investigations and periodic LFT done at St. Peter's TB Specialised Hospital, Ethiopia
- CD4 count done at International Clinical Laboratories, Ethiopia
- Diastatation and urine processing at 4HPR, Ethiopia
- HIV and Drug Administration and Control Authority, Ethiopia
- Genotyping at Karolinska Institute, Sweden

**Results**

- The prevalence of Drug induced hepatotoxicity (DIH) is 17.3%
- 23.9% of those with DIH had discontinued their anti-TB
- Mean time for development of DIH is 2.8 weeks (Range 1.8 weeks)
- Percentage of slow acetylators = 53.5%
- Percentage of rapid acetylators = 46.4%

**Discussion & Conclusions**

Anti-TB drug induced hepatotoxicity is an important clinical problem in TB management (17.3%)

- **Exacerb**
  - Rapid acetylator status
  - Concurrent drug intake
  - Hepatic fibrosis
  - HIV infection
  - Low CD4 count (≤500/μL)?

- **DIH in patients taking ARV and anti-TB drugs at the same time**
- Study association of DIH and female sex further
- Assessing underlying mechanisms of DIH
- A new follow up study on treatment outcome in patients who interrupted anti-TB drugs due to DIH

**Objectives**

1. To determine the prevalence of anti-TB drug induced hepatotoxicity (DIH) in TB-HIV co-infected and non co-infected patients
2. To identify other possible risk factors for DIH
3. To assess need for special follow up and management of patients at risk of DIH
4. To see the effect of acetylation status in DIH
Hannah Kibuuka
Makere University, Uganda

**USMHRP in Uganda**
Capacity building and Networking

LM Hannah Kibuuka
Makere University- Walter Reed Project.

**Objectives**
- General: To establish HIV vaccine testing capacity in Uganda
- Specific objectives:
  - Conduct preliminary laboratory studies in preparation for HIV vaccine testing
  - To conduct phase I and II HIV vaccine trials
  - To conduct a population based cohort for potential phase III testing
  - Networking

**Preliminary laboratory activities**
- Capacity building activities
  - Infrastructure, staff and certification
- Laboratory studies (blood bank study)
  - Anonymous samples from 6000 blood donors.
  - 1000 samples to establish reference ranges for haematology, chemistry and lymphocyte subsets
  - 5000 samples to
    - Validate HIV rapid tests.
    - HIV subviral analysis (HIV positive samples).
    - Determine prevalence of antibodies to vectors used in vaccine designs

**HIV Vaccine Testing Activities**
- RV 156
  - Phase I Trial to test the safety and Immunogenicity of Multiclude DNA-Plasmid vaccine in 30 adult Ugandans
  - Follow up for one year.
- RV 172
  - Phase I trial to test safety and Immunogenicity of Multiclude DNA-Plasmid vaccine inoculated by Recombinant Adenovirus 5 Vector vaccine in East Africa
  - Enroll 33 HIV uninfected adults at 3 sites
  - Follow up for one year after enrollment

**Cohort Development activities**
- Enroll 2000 volunteers in a rural Ugandan population
- Follow up monthly for 3 years
  - HIV incidence, population stability and willingness to participate in vaccine trials
- Provide care and treatment for cohort participants

**Results**
- Laboratory studies
  - Completed sample collection (n=6000)
  - Determination of reference range completed
  - CAP certification
- Vaccine trials
  - Completed enrollment and follow up of 31 volunteers
  - Enrollment for Phase I of RV 172 completed.
- Cohort development
  - Completed enrollment at baseline
  - ART program established

**Networking**
- USMHRP Africa investigator sites
  - Joint site investigators meeting
  - Conference calls
- Community involvement
  - CAI
  - Sharing CAI and Cross CAI network
  - Joint functions eg HIV vaccine awareness day

**Discussion and Conclusions**
- With sufficient financial and technical support, it is possible to build sufficient capacity for phase I, and II vaccine trials
- It is possible to plan and implement phase I and II trials in a developing country like Uganda
- It is important to develop cohorts now for phase III trials in anticipation that some constructs may proceed to phase III trials in the near future

**Future perspectives**
- Continue to fully enroll and follow up current phase III vaccine trial
- Continue cohort development activities in anticipation of phase III testing
- Join consortia (PVCE-100) for possible phase II B in the near future
- Conduct other laboratory studies that will inform vaccine development efforts
Pragsters

Hassan Mahomed
University of Cape Town, South Africa

Considerations with respect to the enrolment and follow up of adolescents in clinical trials

- Hassan Mahomed, T Hawking, F Kafar, WA Hassen, GD Hussey

Affiliations: South African Tuberculosis Vaccine Initiative, University of Cape Town, South Africa

Acknowledgements: Dept of Education, South Africa, Aeras Global Tuberculosis Vaccine Foundation

Background

- There are plans for tuberculosis vaccine trials in the future with Adolescents as one target group.
- The South African Tuberculosis Vaccine Initiative (SATVII) has set up a trial site 100 km from Cape Town in South Africa.
- SATVII are currently conducting an epidemiological study on tuberculosis in adolescents at this trial site in preparation for a TB vaccine trial

Objectives

- To determine what preparation is required for an adolescent vaccine trial.
- To determine the epidemiological profile of the target population that will be enrolled in a TB vaccine trial.
- To determine the main problems involved in enrolment

Methods

- A questionnaire and qualitative study was conducted on a sample of adolescents prior to the start of the study (preparatory study).
- An epidemiological study is being conducted to determine the incidence of tuberculosis in adolescents aged 12-18 at 11 high schools in the trial site.

Results

Epidemiological data to date

- Vaccinated with BCG: 96.9%
- BCG scar: 56.6%
- Currently on TB treatment: 0.4%
- Previously treated for TB: 0.0%
- Household member currently on TB treatment: 4.0%
- Lived with household member with TB: 22.9%

Discussion & Conclusions

- Knowledge of vaccines needs to be improved.
- Parental consent required for all adolescents of 12-18 years of age. Obtaining this consent is a major logistical issue. Parents may be approached more than once to agree to their children participating in the study. Once parents have agreed, only 4% of adolescents refuse to participate.
- The payment of incentives need to be more attractive as these could be quite costly.
- School infrastructure variable and related to socio-economic status.
- Blood draws a major reason for refusal to participate. Making blood draws more acceptable is important through the use of local anaesthetics, having a comfortable environment and adolescent friendly staff.

Future perspectives

- Trials in adolescence are feasible.
- Population diversity would be important to multicentre studies would be needed.
- There is a general need to improve the public’s knowledge and understanding of the value of vaccines.
Pragsters

Hulda Swai

Council of Scientific Industrial Research, South Africa

Potential for treating tuberculosis with nano drug delivery system

Seali H. Shoba L, Kalombo L, and Semete T

Council of Scientific Industrial Research (CSIR) South Africa

Methods

• Preparation and characterization of polymeric nanoparticles
  • In vitro
    • Slow release
    • Cell culture
    • Intracellular delivery
  • Drug targeting
    • in vivo
      • Animal tests (healthy and TB models: mice, guinea pig and primates)
        • Efficacy assays
        • Release profile
        • Pharmacokinetics and Pharmacodynamics
        • Bioavailability and biotransformation
        • Toxicity
  • CSIR facilities
    • Phase I and phase II

Results

• Polymeric Nanoparticles (PNP) of 500-2000nm prepared by the multiple emulsion spray drying and self-assembling block polymers techniques:
  • Drug encapsulation efficiency for rifampicin/isoniazid (RIF/INH) ranged from 64-65%.
  • Slow release up to 8 days was achieved both in vitro in our lab and in vitro by our collaborator, Prof. Khulere from South Africa.
  • PNP was able to release drugs from degradation in the stomach was achieved.
  • Drugs detectable in the plasma for 8 days and in the organs for 10 days following a single oral administration of ATD-loaded PNP to mice.
  • No toxicity detected in mice and guinea pig (Khulere et al., 2006, 2007, and 2008).
  • PNP loaded with INH resulted in complete clearance of bacilli in TB-infected mice (Khulere et al., 2006, 2007, and 2008).

Conclusions

By employing polymeric nano drug delivery carriers, drug dosage, toxicity, bioavailability, efficacy, as well as dosing frequency can be reduced, which can aid in improving patient compliance in the management of TB.

Future perspectives

• Perform in vivo studies
  • Healthy mice and non-human primates
  • Toxicity study
  • Bioavailability
  • Determination of drug absorbed per kg weight
  • Determination of liver function test
  • Mechanism of PNP absorption
  • Animal models
    • Efficacy assays
    • Release profile
  • Clinical trials
  • Target drug delivery
**Pragsters**

**Issa Nebie**

Centre National de Recherche et de Formation sur le Paludisme, Burkina Faso

---

**Background and objectives**

- Merozoite surface protein 3 (MSP3) as a promising candidate vaccine, has been tested in many volunteers and was shown to be highly immunogenic.
- A phase II trial was then performed to assess the safety and the immunogenicity of the MSP3 long synthetic peptide (MSP3-LSP) in adults living in malaria endemic area of Burkina Faso. We thus used this opportunity to assess the humoral and cellular immunity to MSP3-LSP and overlapping by measuring:
  - The level of IgG, IgM and IgG subclasses;
  - T-cell proliferation and level of IFN-γ.

**Methods**

- The study was a single-blind randomized trial.
- 18 volunteer adults, 15 to 40 years old were eligible. 19 received MSP3-LSP, 18 received saline as control and 15 received Tansias vaccine.
- The vaccination schedule: 0, 6, 9, 15 and 21 months.
- Malaria, tsetse and trypanosoma haemagglutination, latex agglutination and titres were measured by ELISA (20, 25, 40, 70, 140, 280 and 560).
- Lymphocyte proliferation and IFN-γ production were measured on samples obtained on days 7, 14, 22 (days after the 2nd injections) and 30, 90 days after the last injection.

**Results**

- IgG, IgM and IgG subclasses levels were similar in both vaccine groups before and after the vaccine administration.
- The opsonic activities (IgG1 and IgG2) to MSP3-LSP were predominant and similar in both vaccine groups before and after the vaccination.
- IgG levels to the 4 overlapping MSP3 peptides were also similar in both vaccine groups.
- Lymphocyte proliferation index and interferon gamma production to MSP3-LSP and to the 4 overlapping MSP3 peptides were similar before the vaccine administration in both groups but increased in MSP3-LSP vaccine group after the second and the third doses.
- Lymphocyte proliferation index and IFN-γ kinetics levels to vaccine trace were also higher in the vaccine trace vaccine group after the third dose compared to MSP3-LSP vaccine group.

**Discussion and conclusion**

- The IgG, IgM and IgG subclasses levels were similar in MSP3-LSP and tansias trial vaccinated group, this may be due to pre-existing humoral response of these 18 to 40 years old volunteers.
- The cell mediated immunity: Lymphocyte stimulation index and IFN-γ was high in MSP3-LSP vaccinated compared to tansias vaccine group.
- These data suggest that MSP3-LSP is able to boost cell-mediated immunity in individuals with some degree of pre-existing immunity.

**Future perspective**

- A randomized controlled age de-escalation trial Phase 1b with MSP3-LSP is planned for the end of 2006.
- Assessment of:
  - Cell-mediated and humoral immunity
  - Immunogenic functional assays (MSP3) and native protein recognition by Western blot.

We are grateful to the trial volunteers and to the village of BoboDioulasso/Burkina Faso.
Pragsters

Janneke van de Wijgert
Academic Medical Center, The Netherlands

**Objectives**

- To establish a microbicide trial site in Kigali, Rwanda

**Methods**

- An international non-governmental organization (Projet Ubuzima) was established in Kigali in early 2004, as a partnership between three public Rwandan institutions, a Dutch academic institution and IPM.
- Projet Ubuzima is governed by a management team and a governing council, consisting of stakeholders from Rwanda’s medical and public health community.
- A memorandum of understanding was signed with the Rwanda Ministry of Health.

**Establishing a new microbicide trial site in Kigali, Rwanda**

Janneke van de Wijgert, Jan Joosten, Jozef Vuyk-Jan et al. 2006

**Results**

- In November 2005, a double-blind, randomized, clinical trial of Dapivirine (TMC120) vaginal gel among healthy HIV-negative, non-pregnant women was successfully initiated. Data collection will be completed by August 2006.

**Conclusions**

- After two years of preparations related to networking, capacity-building, and infrastructure development, Projet Ubuzima successfully conducted its first microbicide trial.

**Future perspectives**

- Further capacity-building is needed at Projet Ubuzima to scale up large Phase III microbicide trials. An HIV incidence/Phase III readiness study is planned.
- Projet Ubuzima plans to expand its community outreach activities beyond the CAG.
- Further capacity-building is needed at the national reference laboratory and referral clinics to enable local laboratory testing and good clinical care for trial participants and their communities.

**Presentations: Abstracts and Pragsters**

EDCTP Third Annual Forum 2006 - Partnership and African Leadership: Challenges and Opportunities
Pragsters

Jenny Allen
Medical Research Council, South Africa

1. TB surrogate markers

Jenny Allen: Rosana Rustomjee
The Unit for Clinical and Biomedical TB Research will be validating SSCC methodology as a surrogate marker of resistance as a substudy within the UCL Pi funded study “Controlled comparison of two moxifloxacin containing treatment shortening regimens in pulmonary tuberculosis” (REMaxTB)
Professor Stephen H. Gillespie, UCL

2. Objectives

- Primary Objective
  - To compare the bactericidal and sterilising activities of two moxifloxacin-containing regimens and a non-fluoroquinolone-containing control regimen over the initial phase of 6 weeks of treatment, using methods which correlate with ultimate relapse.
- Secondary Objective
  - To determine the correlation of this serial sputum colony count methodology with the relapse rate.

3. Design

- Three arm randomised double blind placebo controlled study
- Newly diagnosed, previously untreated, sputum smear-positive patients presenting at TB clinics
- 400 patients

4. Methods

- Standard examination - spot and 15-hour overnight sputum collections at baseline, week 4 and 8. Spot collections will continue up to two year followup.
- Tests
  - sputum/cultures/first line resistance
  - ZN and Aureomycin smears
  - Plated onto TH11 dextrose agar medium and thioglycolate broth

  - A proportion sensitivity test to isoniazid, rifampicin, ethambutol, streptomycin and moxifloxacin with a 1% end point

5. Methods

- SSCC: pre-treatment and then after 2, 7, 14, 21, 28, 35, 42, 49 and 56 days of treatment.
- Counts of colony forming units (cfu) - sputum homogenised with dithiothreitol
- Range of 8-fold dilutions plated onto pairs of segments of selective TH11 plates.
- The limit of detection is 1.0 log10 cfu/mL sputum/day.

6. Discussion & Conclusions

- There is potential for the inclusion of molecular markers for relapse if funding allows
- In the process of sourcing funds for the project
Pragsters

John Kebaso
African Population and Health Research Centre, Kenya

The uniqueness of the DSS for conducting Clinical Trials in urban informal settlements in Africa. John Kebaso and Zwezu Vwoulwe

- AFRICAN POPULATION AND HEALTH RESEARCH CENTER - Promoting the well-being of Africans through policy-relevant research on population and health

Objectives
- This paper examines the opportunities that are provided by an urban DSS setting in conducting Clinical Trials.
- Since Clinical Trials require maximum follow-up to evaluate safety, tolerability and effectiveness of a trial product, the DSS is able to provide a longitudinal setting where such follow-up can be conducted effectively.

Methods
- This paper uses mainly the observation method and the review of literature available on the subject.
- The Nairobi Urban Health and Demographic Surveillance System (NUHDDS) is located in two informal settlements (Kongowea and Viwandani) in Nairobi, Kenya.
- It covers about 60,000 people in about 24,000 households. The NUHDDS was set up to serve as a platform for monitoring the impact of environmental, health and livelihood interventions aimed at improving the wellbeing of populations in the vast Nairobi’s informal settlements commonly dubbed as slums.
- It monitors three primary subjects (individuals, their households, and their dwelling units) as well as events occurring to the subjects.

Results
- On critical review of the NUHDDS and how the system monitors the subjects as well as events occurring to the subjects, and the ways in which longitudinal data is collected and the follow-up processes presents a great platform on which HIV intervention trials can be conducted within the urban setting.

Discussion & Conclusions
- The DSS framework is an important setting for conducting Clinical Trials. The DSS provides a superb context for good longitudinal data collection procedures.
- The contributions of the DSS in accurately documenting longitudinal data can be used in implementing clinical trials and other HIV interventions trials.
- Since Clinical Trials require maximum follow-up to evaluate safety, tolerability and effectiveness of a trial product, the DSS is able to provide a longitudinal setting where such follow-up can be conducted effectively.

Future perspectives
- Resistance evaluation studies of Drugs for malaria and HIV/AIDS e.g. AFRIVARTS
- Re-evaluation of drug toxicity and side effects studies
- Studies on effectiveness of different combinations of ARTs
- New inventions in the Malari and HIV Rx e.g. Microbicides products, New molecules etc.
- Non RCT intervention studies in DSS sites Lacking
**Pragsters**

**John Shao**

Kilimanjaro Christian Medical Centre, Tanzania

**1. Introduction**

- One component of the Ethical Principle of “Justice” is improvement of countries, institutions or communities which have supported the research or assumed certain amount of risk, to effectively participate in future clinical research.
- Capacity building as one form of empowerment may include:
  - Physical infrastructure development

**2. Ongoing collaborative research projects at KCMC**

- HIV/AIDS & Reproductive Health ..............15
- Tuberculosis ........................................... 8
- Malaria .................................................. 7
- Ophthalmology ........................................... 5
- Non-Communicable Diseases ..............5
- Parasitic diseases (Other than Malaria) ...2
  - Total .................................................... 42

**3. HIV/AIDS Collaborative Projects**

- Human capacity strengthening through training, staff retention or attachment to well supervised multilateral research.
- Fair distribution of research rewards, both tangible and intangible

**2. Tuberculosis**

<table>
<thead>
<tr>
<th>Project (and duration)</th>
<th>Funding Agency</th>
<th>Collaborating partners</th>
<th>Capacity building</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Surrogate markers of drug efficacy, disease activity and replace in TB (RxM)</td>
<td>EDCTP</td>
<td>• African partners Zambias, Tanzania (2x nodes), R. Africa, Senegal, Madagascar, Ethiopia, Gambia • 2 European (UK x 2 sites) Germany, Denmark, France</td>
<td>PhD &amp; MSc training +Infrastructure development</td>
</tr>
</tbody>
</table>

**3. Malaria**

<table>
<thead>
<tr>
<th>Project (and duration)</th>
<th>Funding Agency</th>
<th>Collaborating partners</th>
<th>Capacity building</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Consortium study of African Countries</td>
<td>Bill &amp; Melinda Gates Foundation</td>
<td>• Postgraduate training • Capacity strengthening of health facilities • Infrastructure improvement</td>
<td></td>
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</tbody>
</table>
Kamija Phiri
College of Medicine, Malawi

**Objective**

- To investigate if IPTpd with ACT in the post-discharge management of severe malaria anaemia, or a single (6-dose) treatment course of ACT on discharge, significantly improves haematological recovery over that with a single dose with oral SP.

**Methods**

- A three-centre double-blind randomized trial
- Children with severe anaemia who have received a blood transfusion, parenteral quinine and have sufficiently recovered to take oral medication will be randomized to receive either:
  1. **Group A**: 1 dose of SP
  2. **Group B**: 1 course of ACT (6 doses in 3 days).
  3. **Group C**: 3 courses of ACT: at discharge, at 1 month, and at 2 months post-discharge.

**Outcome Measures**

**Primary efficacy endpoint:**
Mean Hb at 3 months.

**Secondary efficacy endpoint:**
1. sick-child clinic visits due to clinical malaria
2. rebound severe anaemia (Hb < 50 g/L)
3. death by 3 and 6 months.
4. mean Hb at 6 months

**Safety endpoint:**
5. incidence of AEs by 3 & 6 months
6. mean QTc prolongation by day 3

**Results**

- Pilot study completed – February 2006
- Results show no QTc prolongation
- Pre-trial monitor visit complete – April 2006
- Study recruitment has commenced in 2 sites
- Study is on-going

**Discussion & Conclusions**

- Challenges of carrying out GCP compliant studies in developing countries
- From preliminary data, no signs of cardiotoxicity associated with use of ACT after quinine
**Pragsters**

Laurent Musango  
School of Public Health, Rwanda

**INTERACT**  
School of Public Health, TRAC, Centre Hospitalier Universitaire de Kigali, National Malaria Control Programme, National TB Control Programme, National Reference Laboratory (all in Kigali, Rwanda), and Center for Poverty-related Communicable Diseases (Amsterdam, the Netherlands)

**Objectives**  
- To organise and build sustainable capacity to perform trials of clinical and public health interventions, involving all stakeholders, in Rwanda

**Methods**  
- A consortium of Rwandan, Ugandan, Dutch, Belgian and Irish institutions and researchers has joined forces in the Infectious Diseases Network for Treatment and Research in Africa (INTERACT)

**METHODS**  
INTERACT refers to the interaction:  
- of the three infections malaria, TB and HIV  
- between the treatments directed against these infections  
- between research and capacity building, learning by doing  
- of technical laboratory investigations and clinical trials with implementation in the real world of clinical practice  
- between African scientists  
- between African and European scientists

**INTERACT** is a Programme funded by NWO-WOTRO (Netherlands) through the NACCAP subsidy scheme  
- Duration of INTERACT is 56 months  
- Expected outcomes in Rwanda:  
  - 6 Rwandan PhD's  
  - strengthened research infrastructure in participating institutions

**Methods**  
The Six PhD Research Projects:  
- Operational aspects of diagnosis and treatment of AIDS infection and tuberculosis at the district level  
- Evaluation of effect of HAART on reproductive health of Rwandan women  
- Incidence and risk factors for adverse effects of HAART in HIV-infected adults  
- Surveillance of HIV-1 drug resistance in HAART treated patients and in the general population  
- Malaria treatment and Intermittent Preventive Treatment in pregnancy, with and without HIV infection  
- HAART in Rwandan children 0-15 years: incidence, severity, risk factors and long-term outcome of adverse effects

**Results**  
- Treatment & Research for AIDS Center (TRAC) is the coordinating organisation in Rwanda  
- 6 PhD students in Rwanda are being selected  
- A Country Coordinator is being elected  
- Protocols for the 6 PhD projects are being drafted

**Future perspectives**  
- The aim of the INTERACT programme is a research setting where GCP-compliant trials of therapeutic or preventive interventions against HIV, TB, and malaria can be conducted
Evaluating the efficacy of treating children with uncomplicated malaria living in Limbe, Cameroon using Armodiaquine (AQ), Armodiaquine + Artesunate (AQAS) and Armodiaquine + Sulfadoxine-Pyrimethamine (AQSP).

Lem Edith Abongwa and Dr. Sul Magdelina

**Pragsters**

Lem Edith Abongwa

**Objective**
- To compare the efficacy and safety of Armodiaquine (AQ), Armodiaquine + Artesunate (AQAS) and Armodiaquine + Sulfadoxine-Pyrimethamine (AQSP) there by updating antimalarial drug policy in Cameroon.

**Methods**
- This study was carried out in Limbe from March 2005 to May 2005.
- Taking parental/guardian consent, 276 children between 6-60 months were recruited and had parasitemia ≤5000 parasites per microlitre of blood, hemoglobin concentration ≤10 g/dL and temperature ≤.
- 5°C were recruited.
- They were clinically examined and drug administration supervised based on WHO 2003 protocol on days 1, 3, 7, 14, 21 and 28.

**Results**
- The prevalence of fever at enrolment dropped significantly from 100% to 31.4% (P<0.001), 15.1% (P=0.04), 24.7% (P=0.007) respectively for AQ, AQAS and AQSP. (P=0.021).
- Cure rates were similar between AQAS and AQSP although AQAS had a higher cure rate 1A026, 61.8% (53/86) vs AQAS, 78.5% (73/95) (P=0.03) and AQSP, 78.5% (73/95) vs AQSP 73.2% (71/97) (P=0.23) at day 7.
- By day 14, AQAS recorded a 100% cure rate, while those of AQ and AQSP were 82.0% (69/86) and 90.7% (89/97) respectively.

**Discussion & Conclusions**
- Although the cure rates were similar for AQSP and AQAS, AQAS proved to be more efficient in increasing parasite clearance while decreasing gametocyteemia.
- This combined therapy has proven to reduce malaria transmission and therefore in line with current WHO recommendation for the use of Artemisinin based combination therapy (ACT) for the treatment of uncomplicated malaria.

**Future perspectives**
- To carry out antimalarial pharmacovigilance in terms of affordability, acceptability and tolerance with ACTs.
- To compare the same treatments in HIV positive and negative adults.
Pragsters

Maowia Mukhtar
Institute of Endemic Diseases, Sudan

1. Epidemiological patterns of pulmonary TB in Eastern Sudan
   Maowia M. Mukhtar, F. M. Elmi, F. M. Osman, S. M. Bashir, E. H. Almasary, Reem Elfikry, P. van der Stuyf
   Institute of Endemic Diseases, Sudan
   Institute of Tropical Medicine and Hygiene, Belgium

2. Objectives
   - To study the epidemiology of pulmonary TB in eastern Sudan
   - To identify a new site for future TB clinical trials
   - To determine the burden of TB in eastern Sudan

3. Methods
   - Cross sectional surveys to determine the cough rate
   - Clinical surveys for identification of TB patients
   - Observational surveys for identification of possible risk factors

4. Study site

5. Ecology of study site
   Kassala
   Gadaref

6. Cough rate and clinical surveys results

7. Discussion & Conclusions
   - Two epidemiological patterns exist in eastern Sudan.
   - Kassala state is inhabited by nomadic tribes with mobile lifestyle, different socio-economic structure, and weak health system.
   - Gadaref state is inhabited by tribes of seasonal farming, stable communities and better health system

8. Future Perspectives
   - Improvement of access to effective TB diagnosis and treatment
   - Strengthening of the health system
   - Effective TB control by vaccination and health education
**Pragsters**

**Martin Meremikwu**

University of Calabar Teaching Hospital, Nigeria

---

**Methods**

- **Treatment:** (Artesunate + mefloquine combination treatment for uncomplicated malaria in Calabar, Nigeria: 28-day in vivo study)
  - Patients ≥ 50 kg: 1 tablet each of artesunate 200 mg + mefloquine hydrochloride 200 mg daily x 3 days
  - Patients < 50 kg: 1 tablet each of artesunate 100 mg + mefloquine hydrochloride 125 mg once daily x 3 days
  - Treatment given under observation

- **Follow-up:**
  - Follow-up visits were scheduled on days 1, 2, 3, 7, 14, 21, and 28 (clinical and laboratory assessments)

- **Data Collection:** Collected in case record files/log books; entered and analyzed in EPI Info.

---

**Results**

<table>
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<tr>
<th>Treatment Outcome</th>
<th>Number</th>
<th>%</th>
<th>Remarks</th>
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<tbody>
<tr>
<td>Number enrolled (N)</td>
<td>108</td>
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<tr>
<td>Late lo (t)</td>
<td>10 (9.2)</td>
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<tr>
<td>Withdrawn (%)</td>
<td>1 (1.0)</td>
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<tr>
<td>Number of evaluable patients (%)</td>
<td>95 (92.3)</td>
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**Therapeutic Efficacy**

<table>
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<th>Failure</th>
<th>Remarks</th>
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<tr>
<td>Early treatment failure</td>
<td>0.0</td>
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<tr>
<td>Late clinical failure</td>
<td>1.0 Day 28*</td>
</tr>
<tr>
<td>Late parasitological failure</td>
<td>1.0 Day 14</td>
</tr>
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**ACTR:** adequate clinical and parasitological response: 94 (97.3)

---

**Discussion & Conclusions**

- 28-day in vivo cure rate of Artesunate + mefloquine combination treatment (97.9%) in this part of Nigeria with high prevalence of multi-drug resistance Plasmodium falciparum
- Few mild adverse events; no severe adverse events observed
- Both children and adults tested but the sample is small for each group.

---

**Future perspectives**

- Due to the long elimination half-life of mefloquine may increase risk of emergence of resistant parasites.
- ACTs containing mefloquine are preferably recommended for areas with low or seasonal transmission to minimize
- Artesunate + mefloquine is licensed for use in Nigeria
- In-vitro and in-vivo surveillance studies are required to monitor efficacy and detect early signs of declining susceptibility.
Pragsters

Mike Chaponda
Tropical Diseases Research Centre, Zambia

Impact of Transport Refunds on Research Participants Commitment to the Study: (Unpublished data)

Names of Authors
Dr. Mike Chaponda
Scientific Officer TDRC, Ndola, Zambia

Acknowledgements and affiliations
My special thanks go to Dr. Modest Mulenga for his support.

Objectives
• To compare the effect of transport refunds on the commitment of participants coming for scheduled visits in two malaria clinical trials done in Ndola, Zambia.

Methods
• The participants of one study was given an equivalent of a dollar each as transport refund for every scheduled visit made to the site.
• The other group of participants was receiving an equivalent of five dollars each for every scheduled visit made.

Results
• It was observed that the study whose participants were refunded a dollar had recorded thirty-three (33%) scheduled visit absentees compared to the study that refunded its participants an equivalent of five dollars for transport had a record of absentee as low as 3.4%.

Discussion & Conclusions
• On average a two-way taxi in Ndola, Zambia costs 4 dollars. The participants who were refunded 5 dollars for transport could thus afford to book a taxi to and from the research center.
• The group that was refunded a dollar for transport could only afford a bus to and from the research center.
• Easy accessibility to the research center increased the turnout for the scheduled visits.

Future perspectives
• Reasonable resources must be committed to the welfare of the research participants especially when it involves visiting the research centre from time to time.
• However, these transport refunds must not compromise good clinical practice.
Pragsters

Morenike Ukpong
Nigeria HIV Vaccine and Microbicide Advocacy Group, Nigeria

The development of the National document on the Standard of care for NPT clinical trials in Nigeria: the positive roles of advocates

Objective
To develop a national standard of care document that would guide researchers in the development of protocols for New HIV prevention Technology Research in Nigeria.

Methods
The development process entailed the facilitation of five stakeholders’ meeting. The meetings involved deliberations and development of recommendations at specific stakeholders’ meetings (ethicists, community activists and researchers separately) and through facilitated mixed national meetings (all stakeholders including policy makers and government).

Result
The final outcome is a consensus document on what is the national consensus on the minimum standard of care for NPT clinical trial participants in the country. The document is being prepared for adoption by the National Ethics Board.

Discussion & Conclusions
A defined national standard of care is critical for NPT trial conducts because of the increasing ethical concerns with the conduct of trials in developing countries.

Such a national document would serve as a legal reference document and reduces tendencies or trial disruptions due to concerns for care of participants.

Conclusion 2
Community advocates could and should be more active in policy and guideline development process – efforts that can fast track the national NPT research and development efforts.

Future perspectives
There is an increasing need to engage the community and national stakeholders in various forms in the NPT research and development process. Engaging the community in policy development can help facilitate this process and directly engage them in the NPT research and development process.
Pragsters

Muhammed Bakari
Muhimbili University College of Health Sciences, Tanzania

The HIVIS Project, a North-South collaborative study on safety and immunogenicity of a multigene, multiclade HIV-1 plasmid DNA prime and MVA boost

Bakari M.1, Ababu F.1, Abubu S.1, Pallangyo K.1, Wahren B.1, Heppner B.1, Nilsson C.1, Bräke A.1, Bratt G.1, Robb M.2, Michael N.2, Biberfeld G.2, Sandström E.1, et al.

1. Presentations: Abstracts and Pragsters
2. Background & Objective
   - DNA priming with MVA boosting has been reported to be poorly immunogenic in human HIV-1 vaccine trials, despite good results in non-human primates.
   - In 2001, a European Union funded HIV Vaccine Immunogenicity Study (HVIS), with a South-South (Tanzania & South Africa) and North-North (Sweden, USA, Germany) collaboration to develop and try out a DNA multiclade candidate vaccine with MVA vaccine boost was conceived within the EU INCODEV Programme.
   - The study seeks to optimize DNA delivery in a phase III trial in Tanzania.

3. Results, in Tanzania, 1
   - The Tanzania National Framework for the conduct of HIV vaccine trials has been in place since February 2005.
   - Clinical and laboratory capacity building including physical laboratory and clinical facilities, purchasing of necessary equipment, study population cohort and identification and training of staff has been achieved.

4. Results, in Tanzania, 2
   - Advocacy activities are continuing.
   - The study protocol incorporating advice and inputs from the WHO/UNAIDS and from the African AIDS Vaccine Programme (AAVP) has already received National as well as institutional ethical clearances.
   - Application for vaccine registration with Tanzania’s Food and Drugs Authority (TFDA) has been submitted and approval is expected soon.

5. Results, in Sweden, 1
   - By end of March 2006, 27 volunteers had received 3 DNA and one MVA immunizations of the preparations intended for Tanzania.
   - These immunizations have been well tolerated.
   - There were no safety laboratory abnormalities: rGMA-CSF was associated with influenza-like grade 3 adverse events in 2 subjects, one of whom only received one DNA injection. One volunteer defaulted after his first injection.

6. Results, in Sweden, 2
   - Two weeks after the 3rd DNA injection 11/38 had developed specific IFN gamma Elispot reactivity and two weeks after the MVA injection 22/24 so far analysed had new and/or boosted specific Elispot responses.
   - These results were supported by IL-2 Elispot and antigen specific lymphoproliferation assays.
   - The study is still blinded.

7. Conclusion
   - Preparations for the conduct of a Phase III trial in Tanzania are at an advanced stage, and the trial is expected to start in September, 2006.
   - Three injections with HIV-1 plasmid DNA or prime with a single HIV-1 MVA boost are safe and gave strong IFN-gamma Elispot reactivity 2 weeks after the last injection in over 80% of healthy Swedish volunteers.
Modest Mulenga
Tropical Diseases Research Centre, Zambia

1. Challenges impinging the translation of clinical trials results into practice: A Zambian historical perspective

2. Objectives
- Review historical perspectives of antimalarial drug research in the last two decades at the TDRC.
- Review antimalarial drug trials carried out in Zambia and trace their contribution to the evolution and formulation of drug treatment policy.
- Factors impinging on the translation of results of drug trials into general practice and the national malaria control programme.
- Meeting challenges for the future

3. Methods
- Review all peer-reviewed clinical trials carried out in Zambia during the last two decades.
- Reviewed unpublished records of antimalarial trials carried out by the TDRC and the National Malaria Control Centre during the last two decades.
- Interview key opinion leaders involved in the formulation and implementation of the current malaria control programme

4. Results
- A table of ethically approved clinical trials conducted at the TDRC and other research sites in Zambia will be compiled and displayed with the following headings: year of study, main objective, lead investigator or author, main finding(s) and comment.

5. Discussion & Conclusions
- Main historical factors that had a direct impact on the type of antimalarial drug research in Zambia.
- An analysis of the clinical trials which were carried out to address the national agenda with little regards to the global perspective.
- Emergence of drug resistance: what is seen as an immediate national health problem to guide future research on alternative treatment modalities and options.
- Unmet needs and lessons learnt from past research and results on the self

6. Future perspectives
- Factors in antimalarial drug research that should be elaborated to address specific national health problems, and take timely responses during the window of opportunity.
- The role of policy makers and other stakeholders in the generation of clinical trials concerning emerging global and national issues.
- Challenges facing future drug research in Zambia, and best ways of conducting research with a direct impact on the evolution of the national antimalarial drug policy.
Pragsters

Olivier Basenya
National Institute of Public Health, Republic of Burundi

**Methods**
- The seizure of the data has been made on Access and the treatment on Excel and SPSS
- The data collection had been made on March 2006

**Results**
- The mean cost of a tubercular patient hold in charge in ambulatory is about 200 USD
- This cost past to 235 USD for hospitalised tubercular patients
- At the health center level, the mean cost of a tubercular patient hold in charge is 88 USD while this cost is 222 USD at hospital level
- The cost of short course treatment is 12 USD: the reprocessing treatment cost is about 320 USD while the treatment of a multiresistance case is 2,465 USD

**Discussion & Conclusions**
- Even if tuberculosis treatment is free of charge for the patient, this one continue to support 96.9% of the cost.
- So we propose to review the tuberculosis financing in Burundi and support such us hospitalisation and complementary costs there.
- Also it will be efficient to accelerate the decentralization of national Tb program so that a part of the financing of treatment is ensured by peripheral structures nearer to patients.
- It will be also useful to make a feasibility study for implementing Community DOT in Burundi in order to alleviate the burden supported by Tb Patients

**Future perspectives**
- Subventions of some tuberculosis cost such as complementary exams
- Implantation of DOT at Community level

**Objectives**
- General Objective: To analyse the costs of a tubercular patient management in Burundi
- Specific Objectives:
  - To determine the cost of short course treatment, reprocessing treatment and multiresistance treatment
  - To calculate the cost of complementary exams
  - To determine the cost at national tuberculosis program level, Province level.
  - To estimate indirect and opportunity costs supported by patients
  - To estimate the annual cost of Tuberculosis in Burundi
  - To propose some alternative financing systems of Tuberculosis Management in Burundi

**Methods**
- Population targets: 23 Health Centers, 8 Hospitals and 53 Patients
- National Program against tuberculosis, Provincial Health Offices.
- Data collection used 3 questionnaires: 1 for health structures, 1 for national Program and Province level, 1 for patients
- The base of calculation is the year 2005
- The technique of imputation used is based on the volume of activities in relation with tuberculosis management cases.
Pragsters

Omari Kimbute
NIMR, Handeni and Kilosa, Kenya

Obtaining informed consent in community-based placebo-controlled trial in rural Africa

Objective
- We wanted to achieve the highest level of informed consent possible.
- Context-specific issues were:
  - Semi-literate, rural population (potential difficulty of comprehension)
  - Individual placebo-control in new study design to this population
  - Severe illness with rapid progression (an emergency situation)
  - Recruitment of children (parents had to give consent on their behalf)
  - Recruitment by village health workers (non-medical personnel)

Methods: community consent
- The process of sensitizing the population and their representatives had to be taken seriously.
- National, regional and district authorities were informed.
- A residential training workshop was held for all village leaders and village health workers (recruiters).
- Large public meetings were held in every village to educate the community about the trial and obtain community consent. The idea being that people would be familiar with the trial concepts before cases occurred.
- At each level we discussed the issues of randomization, placebo-control, double-blinding and the concept of voluntary participation.

Methods: individual consent
- Individual consent was obtained during recruitment.
- A written consent form containing the main study information in Swahili was used.
- A witness was required for parents/guardians.
- Who were under 18 years old.
- Males were incapable of understanding.
- Illiterate.
- For those who could not write, a thumb print was permissible instead of a signature.
- Close checks were made to ensure that the consent form was consistently read at recruitment.

Results
- Village meetings with attendances averaging 100 (between 30-250).
- Consent forms and case record forms were collected weekly and brought to the office to be checked and securely stored.
- In less than 1% of cases was there an issue with consent forms, a missing signature, a missing witness or discrepancy with names.
- These were investigated and in every case found to be because omissions due to the emergency situation at recruitment.

Discussion & Conclusions
- Trials of non-infectious diseases in developed countries commonly use individual placebo-control as it provides greater power to detect treatment effects than alternative designs.
- However, individual placebo-control for treatment in the circumstances we operated under is relatively new in developing countries and for infectious diseases.
- Before we began many people voiced concerns that this design was unethical and/or impractical as the study population would be unable to understand and/or would not consent.

Future perspectives
- We saw over five years that this design can be successfully implemented to international good clinical practice standards.
- There is increasing interest in running such trials among populations where the burden of infectious diseases is greatest – and this will benefit topical medicine, as long as standards of consent can be maintained.
- If future questions will be appropriately answered by community-based placebo-controlled trials, then we have demonstrated one model of how that design can work and obtain properly informed consent with the aid of prior community education.
Pragsters

Paul van Helden
Stellenbosh University and MRC, South Africa

**Surrogate markers to predict the outcome of antituberculosis therapy**

Paul van Helden, Hazel Dockrell, Jackie Cliff, Gerhard Wolz, Jan Verschoor, Rudo Beyer, Ken Duncan
Stellenbosh and Pretoria Universities, London School of Hygiene and Tropical Medicine, GlaxoSmithKline, MRC and NRF South Africa

**Objectives**

- To identify host biomarkers which predict successful cure or risk of recurrence during early treatment

**Methods**

- Recruit a cohort of uncomplicated Sm pts first episode TB patients and place them on Std DOTS treatment. Collect clinical info
- Follow them up carefully and collect variety of samples (>90 000) during repeat visits up to 30 months
- Sample analysis includes blood parameters, serology, immunology, bacteriology, genetics

**Results**

- 313 patients recruited, some excluded and 257 followed to 30 months, 21 visits each
- >90 000 samples collected, analysis begun
- At 2 months, only 75% smear conversion.
- 0.8% recurrence (remite+reapprx)
- Promising markers for slow or non-conversion or recurrence: smoking, certain VDR alleles, some blood parameters and soluble serum markers

**Discussion & Conclusions**

- We are encouraged that bacteriology and genotyping provides a basis for defining patients into well defined groups for further analysis
- Initial results suggest that this approach holds promise, as we are able to find markers with good predictive value.
- This needs further investigation, as no single marker has 100% sensitivity or specificity in large numbers yet

**Future perspectives**

- Analysis of the stored samples will lead to identification of candidate predictors of cure, which can then be tested in future trials on large numbers of smplea
Pragsters

Pembe Issamou Mayengue
Medical Research Unit of the A. Schweitzer Hospital, Gabon

Multiplicity of P. falciparum Infection and Humoral Immune Responses

P.F. Mayengue1*, A. Luty1, C. Roger1, B.F. Pane3, Kremsner2, G.P. F. Moumi4

Acknowledgement:
To the children and their families. To the staff of the Albert Schweitzer Hospital in Lambaréné, Gabon. DIAD, NAMRT.

Affiliations:
1. Catholic University of Lomé, Laboratory of Clinical Microbiology and Parasitology, Lomé, Togo.
2. Albert Schweitzer Medical Center, Department of Parasitology, Lambaréné, Gabon.
3. Medical Research Unit of the A. Schweitzer Hospital, Gabon.
4. Germany.

Objectives:
- To determine the multiplicity of P. falciparum infection (MOI) in children during sequential clinical episodes of malaria
- To evaluate the prevalence and levels of total IgG and IgM in serum samples at acute, convalescence and healthy phases in these children
- To determine if there is any relationship between MOI and humoral immune responses to the considered malarial antigens at the acute, convalescence and healthy phases.

Methods

Characteristics of patients at inclusion:
- MOI: 1 or more parasite genotypes
- MOI = 1: 73.4% (95% CI: 0.62-0.77)
- MOI > 1: 26.6% (95% CI: 0.23-0.30)

Results of laboratory examinations at acute phase:
- MOI = 1: 32.5% (95% CI: 0.30-0.34)
- MOI > 1: 67.5% (95% CI: 0.66-0.70)

Results of laboratory examinations at convalescence phase:
- MOI = 1: 71% (95% CI: 0.69-0.73)
- MOI > 1: 29% (95% CI: 0.27-0.31)

Future perspectives:
- To compare the MOI in asymptomatic and symptomatic phases of each individual during a longitudinal study in two areas with different level of malaria transmission.
- To compare the relationship between humoral immune responses and MOI during asymptomatic and symptomatic phases.
- To investigate on the relationship between MOI and cellular immune response in children with and without clinical malaria.

Discussion & Conclusion
- Higher proportion of children having one or two parasite genotypes during clinical episodes is in light with previous study in Lambaréné.
- The intra-individual fluctuation in the number of genotypes carriage may be due to the reactivation of some dormant parasite stages or the emergence of new strains recognized by immune system leading to clinical episodes.
- The intra-individual variation may reflect the qualitative difference in the host susceptibility.
- The carriage of high number of parasite xenoreactive during clinical infection is an indication of poor ability to control malaria symptoms and therefore loss acquisition of malaria immunity.

The simultaneous assessment of MOI and antibody responses to malarial antigens demonstrated that clinical malaria infection due to multiple parasite genotypes is associated with lower total IgG and IgM immune responses. The MOI may be a useful parameter to be considered in the evaluation of the malaria vaccine efficacy.

EDCTP Third Annual Forum 2006 - Partnership and African Leadership: Challenges and Opportunities
**Kotila Rachel**  
University of Ibadan, Nigeria

<table>
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<th><strong>Asymptomatic Parasitaemia In Semi-immune Adults: How Effective is Chemoprophylaxis</strong></th>
<th><strong>Objectives</strong></th>
<th><strong>Methods</strong></th>
</tr>
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</table>
| 1 | Kotila Rachel, Okeola Afolabi, Makarunje Obummi  
University College Hospital, Ibadan, Nigeria | - Determine the percentage of sickle cell disease (SCD) patient who use chemoprophylaxis  
- The types of chemoprophylaxis used  
- The percentage of SCD patients with asymptomatic parasitaemia between SCD patients and controls | - Thirty-five SCD patients in the steady state and thirty-seven healthy non-SCD patients were studied  
- A semi-structured questionnaire was administered to both groups  
- A thick blood smear was examined in both groups |

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<tr>
<th></th>
<th><strong>Results</strong></th>
<th><strong>Discussion</strong></th>
<th><strong>Conclusion</strong></th>
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</table>
| 4 | - Seventy-three percent of the patients use proguanil, 22% do not use chemoprophylaxis  
- Thirty-one percent of patients Vs 18% of controls were treated in the last month preceding the study  
- Twenty-four percent of patients Vs 43% of controls had a positive blood smear(p<0.1)  
- There was no significant difference in level of between patients on chemoprophylaxis and those not on chemoprophylaxis (p=0.3)  
- Only 10% and 2% of patients and controls respectively use bed-nets | - Cost and non-availability is a major reason why patients do not use chemoprophylaxis  
- Those who use chemoprophylaxis do not have an advantage over those who do not  
- Malaria is often over treated especially in these group of patients  
- What role can vector control play in this group of patients | - Is it economical to place patients on chemoprophylaxis with the high cost of the drug?  
- We suggest that patients should be encouraged to use bed-nets  
- Other modes of vector control should be considered in the fight against malaria |

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<th><strong>Future Perspective</strong></th>
<th><strong>Pitfalls of The Study</strong></th>
</tr>
</thead>
</table>
| 7 | - There is a need to look into why most of both the patients and controls do not use bed-nets | - Too small a sample size  
- Control group not ideal  
- A better method could be use to quantify the level of parasitaemia |

| 8 |   |   |   |
Ramatoulie Janha
Medical Research Council Laboratories, Gambia

Identifying inactive CYP2C19 alleles in adults and their effects on chlorproguanil pharmacokinetics


Acknowledgements: MRC & EDCTP, Louis-Marie Vindom, MRC Faraarins staff and Study participants

Objectives
- define the prevalence of inactive CYP2C19 alleles in the regulatory and exonic regions of the gene in Gambians.
- assess the effects of both known and newly defined alleles on chlorproguanil and chlorproguanil pharmacokinetic parameters such as T_max, T1/2 and AUC as compared with extensive metabolisers.
- examine association between variant CYP2C19 alleles and high plasma chlorproguanil levels and adverse effects.

Methods
- Genotyping of CYP2C19 alleles
  - Allele specific primers designed using Primer3 software
  - Primers put through a preliminary ARMS PCR run using DNA samples from Sota.
  - mRNAd1 and mRNA6 assessed using ABI 7500 real-time PCR system.
- Sample recruitment
  - 43 adult participants.
  - enrolled from Faraarins.
- underwent detailed pharmacokinetic studies on Lapdap.
- DNA from whole blood extracted.

Results

<table>
<thead>
<tr>
<th>Exonic region</th>
<th>mRNAd1</th>
<th>mRNA6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homozygous WR</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Heterozygous WR</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Homozygous MM</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Heterozygous MM</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>P-value</td>
<td>0.06</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Discussion & Conclusions
- CYP2C19 metabolises chlorproguanil to its active antimalarial metabolite, chlorproguanil.
- Polymorphisms in CYP2C19 gene give rise to a protein with a decrease in catalytic activity.
- The CYP2C19*2 mutation produces a non-functional CYP2C19 enzyme.
- 31% of Gambians are homozygous or heterozygous for

Future perspectives
- Define a SNP set to be used in other clinical trials of antimalarial biguanides.
- Determine pharmacokinetic parameters and any correlation with individual genotypes.
- Sequencing to find out novel polymorphisms in the population.
- Genotype children who had mild malaria and were treated with Lapdap for CYP2C19*2 mutation and assess any association with treatment failure.
Presentations: Abstracts and Pragsters

Pragsters

Rebecca Kivumbi
Makere University, Uganda

**Prevalence, Causes and Immediate Outcome of Non-Traumatic Coma among Children admitted to acute care unit**

Investigator: Dr. Rebecca Kivumbi

Acknowledgements:
Department Of Paediatrics and Child Health
Dr. Justice Byarugaba
Dr. Sarah Kigut

**Objectives**

1. To determine the prevalence of NTC among children aged 2months-144months admitted to ACU.
2. To establish the causes of NTC among these patients.
3. To determine the factors associated with adverse outcome of children aged 2months-12 years admitted with NTC in ACU of Mulago hospital.

**Methods**

**Study Design:** Cross sectional study design for determining prevalence and causes of NTC.

**Study Setting:** ACU of Mulago hospital, Uganda’s national referral and teaching hospital.

**Results**

The prevalence of NTC was 3.6% (95% CI = 0.65-6.30).

The causes of NTC among the study patients as shown below:

<table>
<thead>
<tr>
<th>Cause</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis</td>
<td>15</td>
<td>97.1%</td>
</tr>
<tr>
<td>Malaria</td>
<td>2</td>
<td>10.5%</td>
</tr>
<tr>
<td>Septic shock</td>
<td>2</td>
<td>10.5%</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>2</td>
<td>10.5%</td>
</tr>
<tr>
<td>Hypoglycaemia</td>
<td>2</td>
<td>10.5%</td>
</tr>
<tr>
<td>Hypovolemia</td>
<td>2</td>
<td>10.5%</td>
</tr>
<tr>
<td>Hypertensive encephalopathy</td>
<td>2</td>
<td>10.5%</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>2</td>
<td>10.5%</td>
</tr>
</tbody>
</table>

**Discussion & Conclusions**

1. The prevalence of non-traumatic coma among children admitted in ACU of Mulago hospital was 3.6%.
2. The main causes of non-traumatic coma among children admitted in ACU of Mulago Hospital were infections with meningitis being the leading cause followed by malaria, septic shock, encephalitis, hypoglycaemia, hypovolemia, hypertensive encephalopathy, poisoning and metabolic disturbances.
3. Factors independently significantly associated with death included incomplete immunization, dehydration, deep coma.

**Factors significantly associated with death on logistic regression analysis:**

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis</td>
<td>1.00 (0.50)</td>
<td>1.00</td>
</tr>
<tr>
<td>Malaria</td>
<td>1.00 (0.50)</td>
<td>1.00</td>
</tr>
<tr>
<td>Septic shock</td>
<td>1.00 (0.50)</td>
<td>1.00</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>1.00 (0.50)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hypoglycaemia</td>
<td>1.00 (0.50)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hypovolemia</td>
<td>1.00 (0.50)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hypertensive encephalopathy</td>
<td>1.00 (0.50)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>1.00 (0.50)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

**Future perspectives**

1. Children with modified Glasgow coma scale of 3 and below should be closely monitored and managed in the Pediatric Intensive Care Unit (PICU) not only for the first 3 days (as recommended standard of care for the unconscious patients).
2. All patients with NTC should be thoroughly investigated with thick blood slides for malaria parasites, cerebrospinal fluid for AFB, electrolytes, random blood sugar, and full blood examination as routine.
3. Larger studies with more investigations should be carried out to find more causes of NTC and follow these children for longer periods to find out the long-term outcome of these children.
Reem Bairam
Institute of Endemic Diseases - University of Khartoum, Sudan

The Role of IgE antibodies in protection against *P.falciparum*

Reem Bairam
Institute of Endemic Diseases
University of Khartoum, Sudan

Introduction

Malaria occurs in over 100 countries and territories. More than 40% of the people in the world are at risk of getting malaria.

Although drugs are available for treatment, malaria is still considered by many to be the most infectious disease of humans.

Malaria is caused by protozoa of the genus *Plasmodium*. Four species cause disease in humans: *P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae*. Of these, *P. falciparum* is the most dangerous. Malaria is spread to humans by the bite of female mosquitoes of the genus *Anopheles*.

Rationale

It is clear, however, that it includes both specific and non-specific mechanisms and that both cellular and humoral immune responses are involved.

Further, studies have suggested that IgE may play a role in the pathology of malaria (Perlman P. et al. 1987, Perlman H. et al. 1984). This supported by evidences from in vivo and in vitro studies, which have shown the ability of IgE to induce Tumor Necrosis Factor (TNF) cytokine, which has been shown to be strongly associated with *P. falciparum* pathogenicity.

On the other hand, it is well known that IgE mediates activation of various effector cells such as monocytes/macrophages, and subsequently contributes to anti-parasitic immunity.

Clinical Manifestations

Initially patients have fever, chills, sweating, headache, weakness, and other symptoms mimicking a "viral syndrome". Later severe disease may develop, with an abnormal level of consciousness, severe anemia, renal failure, and multisystem failure.

Malaria Immunity

Immunity to malaria is complex partly due to the complicated life cycle of the parasite with different antigens expressed at different times. Disple many years of research development of immune protection against malaria still remains largely unsolved.

Objective

1) To elucidate the possible role of IgE in protection to *P. falciparum* malaria in areas characterized by seasonal malaria.

Material and Methods

Study design:

Study areas: A programme of malaria surveillance will be established throughout the dry and wet seasons, and a cross-sectional study will be conducted each year for 2 years.

Study areas:

This study will be carried out in two villages:

1. KOKA
2. Um Elsieda

The area lies on the eastern bank of the Rahad River.

These studies include:

1. Processing of the blood samples
2. Blood sampling.
3. Microscopical examination: Polymerase chain reaction technology: It will be used to detect *P. falciparum*
4. Antibody measurement: ELISA method will be used to determine the plasma level of total IgE antibodies.
5. Cytokines measurement: Cytokines TNF, IL-4, IL-10, IL-12 and IL-15 will be measured by real time PCR

Tests of association will be carried out using standard statistical methods.

The sample size for a power of 90% is estimated for an African anti-malarial sensitivity study to be 200 individuals per country in a project.

Para-toxicological studies

Results

• The results will be analysed in one meta-analysis file.

For other epidemiological associations, the sample size will be calculated using the standard formula, considering the prevalence of malaria in each area.
### Presentations: Abstracts and Pragsters

#### Pragsters

**Roland Ndip**  
*University of Buea, Cameroon*

---

#### Objectives

- To determine the prevalence of TB and the susceptibility patterns of isolates to standard TB drugs.  
- Assess the genetic diversity of *M. tuberculosis* complex strains.  
- Determine whether the transmission of dominant clones contributes to the prevalence of TB.  
- Validate scientifically the use of plants by traditional medicine practitioners to treat TB.  
- Isolate active constituents from the plants as leads for new antibiotics.

#### Methods

- Sputum samples will be collected from patients presenting with cough and respiratory problems.  
- Demographic data as well as their HIV status will be collected.  
- Ethical approval and informed consent will be obtained.  
- Sequence will be performed and analyzed at VNAL and isolates identified by phenotypic and biochemical analyses.  
- Confirmed isolates will be subjected to DNA fingerprinting by PCR-based methods notably spototyping and RFLP based on IS6110 polymorphism to differentiate *M. tuberculosis* complex strains.

#### Results

- This study as described in the pre-proposal is expected to be carried out by my PhD student.  
- The major problem we face is that of funding. It is hoped that my attendance at the meeting will enable me to interact with scientists from Europe with whom we could collaborate and acquire funding from your scheme to undertake the study.  
- The long term goal would lead to capacity building and networking.

#### Discussion & Conclusions

- Results are expected to delineate *M. tuberculosis* complex strains circulating in Cameroon.  
- The incidence of TB in Cameroon stands at about 14%. Although there is a paucity of information regarding the distribution of *M. tuberculosis* strains, previous studies incriminated *M. tuberculosis* and *M. africanus*. In a recent study, Ndege-Ejogu et al. (2006) reported that 99.9% of TB isolates were *M. tuberculosis* complex. This could explain the requirements for sensitive and specific diagnostic tools revealing the need for proper strain characterisation.  
- Discover new lead molecules which could be potential sources for starting materials for the semi-synthesis of new drugs. Although this short course and TB regimens are effective, there is increasing resistance. Other limitations are their high costs and non-availability especially in rural areas.

---

#### Future perspectives

- I intend looking at some antigen molecules of *M. tuberculosis* which could be used to produce rapid diagnostic kits.
Pragsters

Roxana Rustomjee
Medical Research Council, South Africa

1. CONDUCTING TRIALS IN HIGH BURDEN COUNTRIES, FORGING COLLABORATIONS, AND BUILDING INFRASTRUCTURE
   - Dr. Roxana Rustomjee
   - The Unit for Clinical and Biomedical TB Research, Medical Research council
   - Durban, South Africa

2. Objectives
   - To highlight ways in which investigators can source funding and support for the conduct and completion of clinical trials
   - Information on available sources of funds
   - Joint applications

3. Funding
   - Share knowledge on formulating study budgets
   - Costs of paying for tests and procedures versus cost of buying and maintaining machinery
   - Capacity building costs

4. Monitoring
   - Cost of multi site monitoring
   - Uniform monitoring bodies across sites and studies
   - Planning monitoring visits
   - Possibility of sponsored monitoring

5. Communication
   - Need effective communication across sites with minimal site disruption and cost
   - Using skype
     - Teleconference
     - Website

6. Partnerships
   - Balanced partnerships
   - Avoid depletion of limited resources
   - Sharing of information
   - Exchange expertise

7. Conclusion
   - Collaboration should yield excellence in the type of trial conducted
   - Maintenance of links after completion of project
   - Encourage within country cooperation instead of competition
Pragsters

Sabrina Bakeera-Kitaka
Infectious Diseases Institute - Makerere University, Uganda

<table>
<thead>
<tr>
<th>Comprehensive Care of HIV-infected Adolescents in Sub-Saharan Africa: Monitoring Growth, Development and Recovery while on Antiretroviral Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sabrina Bakeera-Kitaka, Meda Mbidde, Cynthia Lusha, Ali Nkurunziza, Dorcas Mulindwa, Bilal Kulemuna, Merle Sande, Allan Ronait, and Ely Katabira</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Objectives</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) to evaluate treatment response prospectively for HIV-infected adolescent patients initiated on ARV every 3 months for 18 months; 2) monitor physical growth and sexual maturation while on treatment; 3) assess adherence with a visual analog scale, pill counts, 3 day pill re-call, and 4) to develop a social support network through peer support group meetings</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Methods</th>
</tr>
</thead>
</table>
| • A baseline intake assessment interview to ascertain the social demographic characteristics and previous medical history.  
• A physical examination was done to determine the CDC/WHO staging and the sexual maturity rating; baseline x-ray, followed up at requested intervals.  
• The laboratory evaluation included CBC, CD4 count, viral load, thyroid function tests (TSH, T4), ARTs, IRRs, and hormone levels (GH, LH, FSH, and testosterone). |

<table>
<thead>
<tr>
<th>Results</th>
</tr>
</thead>
</table>
| N=119, M:F=1:2, median age 13.5y (range 10-19), 80.6% (79.8%) completed follow-up of 12 months, 2 were lost to follow-up, and 8 (6.7%) died  
• 89% suppressed virus by 12 mo, and the mean CD4 rise by 6 mo was 360  
• Mean adherence rate was 98%, using visual analogue scale, 3-day pill re-call, and pill counts. |

<table>
<thead>
<tr>
<th>Discussion &amp; Conclusions</th>
</tr>
</thead>
</table>
| • Adolescents have a robust immune response to ARVs but must be supported to remain adherent to long term therapy  
• We have been able to recruit over 220 adolescents into the Peer Support meetings, and formed the Mulago Teen Club  
• We are yet to establish effects of long term therapy while promoting risk reduction. |

<table>
<thead>
<tr>
<th>Future perspectives</th>
</tr>
</thead>
</table>
| • Confirmatory evidence to show that the mode of transmission was mother-to-child; future aims include doing a sub-study on genetic testing, matched serology & genotyping for mother-child pairs.  
• Analyze the stored samples for the hormonal assays, efforts are underway to obtain funding for this purpose.  
• Long term follow-up, and implementation of model satellite clinics for adolescents with HIV. |
The ethics of research related to healthcare in developing countries

Sandy Thomas
Nuffield Council on Bioethics, UK
www.nuffieldbioethics.org

Presentations: Abstracts and Pragsters

Pragsters

Sandy Thomas
Nuffield Council on Bioethics, United Kingdom

2002 Report

There is an urgent need for healthcare related research in developing countries but there must be appropriate safeguards to avoid exploitation of participants

- The Council published the paper on 9 May 2002
- The Working Party was chaired by Professor Kenneth Calman, Vice Chancellor and Master of University of Aberdeen
- Sandy Thomas explains how the Council was set up for the task and the responsibilities of those involved in designing and conducting such research
- Sandy Thomas is available to discuss the paper at www.nuffieldbioethics.org/content/development/developmenresearch_discuss.htm

2005 Follow-up

- Sandy Thomas will be publishing a follow-up Discussion Paper in March 2005
- The paper will consist of an overview of the existing guidelines
- It will be available at www.nuffieldbioethics.org/content/developmenresearch_discuss.htm

Findings: Consent

- The primary purpose of the consent process should be to ensure informed consent
- The process of informed consent should be considered central to the relationship between scientists and the communities in which they work
- They must ensure that the patient is the focus of the local context and not merely a source of data
- It should provide for the protection of the patient's rights and autonomy
- It should be informed and continuous in all stages of research
- The ethics of research in developing countries have been addressed in previous reports
- The process of informed consent has been seen as problematic in many countries

Findings: Standards of care

The main area of treatment that should be provided to participants during research remains a concern
- In the United States, there have been numerous reports of unethical research practices
- A number of ethical guidelines have been developed to address these issues
- The Council has been involved in the development of ethical guidelines for research in developing countries
- The guidelines were developed in consultation with researchers, local officials, and community representatives
- The guidelines have been widely accepted and are used as a model for other countries

Findings: Ethical review

- All agreed that the ethical review of research should be guided by altruistic research
- The idea that the interests of the local and national community should be taken into account is a key theme
- The Council has been involved in the development of ethical guidelines for research in developing countries
- The guidelines were developed in consultation with researchers, local officials, and community representatives
- The guidelines have been widely accepted and are used as a model for other countries

Findings: Implementing guidance

- The Council has been involved in the development of ethical guidelines for research in developing countries
- The guidelines were developed in consultation with researchers, local officials, and community representatives
- The guidelines have been widely accepted and are used as a model for other countries

Findings: After the research is over

- The Council has been involved in the development of ethical guidelines for research in developing countries
- The guidelines were developed in consultation with researchers, local officials, and community representatives
- The guidelines have been widely accepted and are used as a model for other countries

EDCTP Third Annual Forum 2006 - Partnership and African Leadership: Challenges and Opportunities
Pragsters

Takafira Mduluza
university of Zimbabwe, Zimbabwe

1. Contemporary Ethical Issues and the Regulation of Biomedical Research in Africa
   - Is it ethical to do research involving children?
   - Are we willing to place a child at any risk or discomfort today for the sake of other children who might benefit in the future?
   - If so, how do we protect the children to assure they are not placed at undue risk?
   - Compensation?!

2. Research Involving Human Subjects
   - Are there any risks to the human subjects?
   - Are the protections adequate?
   - Are there potential benefits to the subjects and to others?
   - What is the importance of the knowledge to be gained?
   - Are the plans for inclusion of minorities, both genders and children adequately addressed?
   - Incentives – levels, form and frequency?

3. Inclusion of Minorities in Clinical Research
   - Dissemination of the study information: achievements and benefits at the end
   - Involvement of community gatekeepers.
   - Need to determine from the onset the level, form and frequency of incentives.
   - Harmonize disparity between developed and developing countries.

4. Contemporary Ethical Issues and the Regulation of Biomedical Research in Africa
   - Adolescent Consent in Research
     - Parental permission (or)
     - Adolescent consent/assent
     - Emancipated minor
     - Mature minor

5. Contemporary Ethical Issues and the Regulation of Biomedical Research in Africa
   - Institutional Review Boards
     - Expertise in the protocols dealing with the participants
     - Knowledge of regulations governing communities
     - Appropriate Community members
     - Credentialing/Monitoring/Accountability

6. Contemporary Ethical Issues and the Regulation of Biomedical Research in Africa
   - Child Assent in Research
     - Developmentally appropriate
     - Inform about study from perspective of child's experience
     - Elicit expression of willingness

7. Contemporary Ethical Issues and the Regulation of Biomedical Research in Africa
   - MRCZ Policy for the
     - Written parental permission
     - "If the MRCZ determines that a research proposal is ethical, then permission is granted for the opportunity to give responsible information to the subject.
     - If the minor is capable of understanding and making a decision, the consent or assent of a responsible person in the judgment of a responsible person is required.
     - "Compensation, benefits and incentives to study participants??

8. Contemporary Ethical Issues and the Regulation of Biomedical Research in Africa
   - Pediatric Informed Consent
     - Negotiating for incentives/compensation?
Pragsters

Tamirat Gebru

Addis Ababa University, Addis Ababa, Ethiopia

**Molecular Surveillance of Mutations in DHFR and DHPS Genes of Plasmodium falciparum in Ethiopia**

**Methods**
- DHFR and DHPS genes of the Plasmodium falciparum isolates have been assessed using capillary blood collected on filter paper from 124 uncomplicated malaria patients living in Ethiopia.

**Objectives**
- To detect and determine the prevalence of DHFR and DHPS gene mutation associated with SP treatment failure in P. falciparum in the blood specimen collected from patients with uncomplicated malaria in Jimma, Ethiopia.

**Results**
- There were 74 (60.3%) males and 50 (40.3%) females.
- 84 (67.0%) lived in Jimma town while the rest (24.6%) were from the surrounding rural villages.
- 70 (55.8%) were nonimmigrant and 55 (44.2%) were immigrants. The immigrant patients had a median age of 35 years (IQR 15-70) and the nonimmigrant patients had a median age of 42 years (IQR 19-68).
- 85.2% of the patients had been previously treated by doctors and they had been prescribed drugs repeatedly.
- 75% of the patients had been treated and these treatments failed, mainly due to 50% of the patients had been using antimalarial drugs without getting prescription from health providers.
- All isolates (100%) had single mutations in V10 and N51 of the DHFR gene (C7 (C7) or the isoleucine will not result in any amino acid substitutions) at codon 51 (GOT) accounting for the occurrence of a triple mutation

**Discussion & Conclusions**
- In general, 54% quinoline (three DHFR and double DHPS) mutations were observed.
- Children below 5 years and patients who came from a nonresidential area here a high prevalence (6.7% and 65.3% respectively) of quinoline mutated parasites.
- There was no statistically significant association between the occurrence of mutation and the age group, sex, or immigration and with previous malaria attack and use of SP.
- Chloroprophazine (CPQ) and quinoline (CPQ+DDS) is dependent on the presence of a point mutation at codon 104 of the DHFR gene. In this study, as previously reported in other African countries, there is no point mutation at

<table>
<thead>
<tr>
<th>Gene</th>
<th>Codon</th>
<th>Result (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DHFR</td>
<td>10-Subsite</td>
<td>124 (100)</td>
</tr>
<tr>
<td>N1-Threonine</td>
<td>124 (100)</td>
<td></td>
</tr>
<tr>
<td>51-Isoleucine</td>
<td>124 (100)</td>
<td></td>
</tr>
<tr>
<td>53-Leucine</td>
<td>57 (46)</td>
<td></td>
</tr>
<tr>
<td>59-Arginine</td>
<td>67 (54)</td>
<td></td>
</tr>
<tr>
<td>105-Asparagine</td>
<td>124 (100)</td>
<td></td>
</tr>
<tr>
<td>106-Threonine</td>
<td>124 (100)</td>
<td></td>
</tr>
<tr>
<td>108-Threonine</td>
<td>124 (100)</td>
<td></td>
</tr>
<tr>
<td>DHPS</td>
<td>10-Subsite</td>
<td>124 (100)</td>
</tr>
<tr>
<td>10-Glutamine</td>
<td>124 (100)</td>
<td></td>
</tr>
<tr>
<td>10-Glutamate</td>
<td>124 (100)</td>
<td></td>
</tr>
<tr>
<td>10-Asparagine</td>
<td>124 (100)</td>
<td></td>
</tr>
<tr>
<td>10-Threonine</td>
<td>124 (100)</td>
<td></td>
</tr>
<tr>
<td>10-Serine</td>
<td>124 (100)</td>
<td></td>
</tr>
</tbody>
</table>

Note: Anemia grade shown in bold (pp. 144-145)

**Future Perspectives**
- The current treatment recommendation, artesinin combination therapy, is too expensive to afford in Ethiopia.
- To replace SP, it is possible to use a cheaper and readily available drug like CPQ+DDS. However, since the safety issues of this antifolate drug is not settled, the use of the drug should be discussed further for its application in future as an alternative option for SP-resistant strains of P. falciparum.

---

Table 1. Polymorphism in DHFR and DHPS genes of P. falciparum isolates from Jimma, Ethiopia.

---

Figure 1. A bar graph indicating the distribution of DHFR/DHPS quinoline mutation of the isolates in different age groups of patients from Ethiopia.
**Pragsters**

**Tom Peto**
National Institute for Medical Research, Tanzania

### Establishment of two field stations for community-based clinical trials in rural Tanzania

- **Objectives**
  1. To implement a community-based placebo-controlled trial in two rural districts where previously no similar research had been conducted.
  2. To establish permanent field stations where other medical research can be conducted at hospital and/or community level.

- **Methods**
  - Inform all levels of political and medical authorities.
  - Establish study area profile.
  - Establish field station: renovate and build offices and set up study infrastructure.
  - Recruit research team and investigators and train them in Good Clinical Practice.
  - Identify and train village health workers as study recruiters.

### Results
- Kisa and Hamde districts are now mapped, profiled and established study areas capable of conducting GCP community-based trials.
- 32 village in Kisa and 73 villages in Hamde are operational for 5 years.
- Villagers actively participate and are now familiar with the idea of clinical trials and are willing to accept it in their property.
- 1200 village health workers have been trained as recruiters, and 20 clinical officers as study field supervisors.
- 3 Tanzanian doctors have been trained as co-principal investigators and as site managers.

### Discussion & Conclusions
- We needed to spend a lot of time in villages to establish good community relations and achieve a reliable field supervision model where every recruiter was visited every 2-3 days.
- Senior staff had to be ready to personally attend any reports of problems or requests for information from villagers.
- It was helpful to include staff from outside the district. It was important for us to interact daily with the hospital staff and to be seen as an asset, to keep them informed and assist them when required.
- Regular dissemination of progress and other information to the authorities and in villages helped people understand our work.

### Future perspectives
- The Tanzanian National Institute for Medical Research has now made these sites permanent field stations for community clinical trials and interventions and other medical research.
- We are proud that the first new clinical trial, looking at improved methods diagnosing anemia in rural dispensaries is beginning right now in one of the sites.
Thuli Mthiyane

Medical Research Council, South Africa

1. Objectives
   1. To compare hepatotoxicity grade 1-4 in all participants.
   2. To compare adverse events (AEs) and serious adverse events (SAEs) including immune reconstitution syndrome (IRS) in participants receiving TB treatment and HAART with different CD4 T cell counts.
   3. To estimate the improvement in HRQOL in infected patients receiving concurrent treatment.
   4. To determine the relationship between the N-acetyltransferase and cytochrome P450 enzymes and hepatotoxicity and elevated liver function levels.
   5. To determine the effect of early introduction of HAART in TB-HIV co-infected patients and in patients receiving antiretroviral therapy.

2. Background
   The title of the first study is: “Bebolizability of the fixed dose formulation Ritfoufour containing lisonidipine, efavirenz, pyrprofazide, ethambutol and the WHO recommended first line antiretroviral drugs zidovudine, lamivudine, efavirenz and tenofovir for TB patients at different levels of immunosuppression.”
   The second is a multicentre study entitled: “An evaluation of the impact of early initiation of HAART on TB treatment outcomes for TB patients coinfected with HIV.”

3. Aims
   Aim 1: The aim of the study is to prospectively monitor adverse events of HAART and TB concurrent therapy in HIV infected patients. The aim of the study is to monitor adverse events of HAART and TB concurrent therapy in HIV infected patients.
   Aim 2: To determine the health-related quality of life (HRQOL) of participants receiving concurrent TB and HAART treatment and HAART with those receiving TB treatment alone.
   Aim 3: To compare the health-related quality of life (HRQOL) of participants receiving concurrent TB and HAART treatment and HAART with those receiving TB treatment alone.
   Aim 4: To determine the health-related quality of life (HRQOL) of participants receiving concurrent TB and HAART treatment and HAART with those receiving TB treatment alone.

4. Study population
   - 100 Male and female adults ages 18-65 diagnosed with TB and HIV at different levels of CD4 counts will be studied for the objectives.
   - 200 patients will be studied for hepatotoxicity and adverse events associated with concomitant TB and HIV therapy.
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   - 200 patients will be studied for hepatotoxicity and adverse events associated with concomitant TB and HIV therapy.

5. Methods
   1. Data collection for adverse events will be done:
   - History taking from patients and their DOT supporters.
   - Physical examination and laboratory parameters at baseline and at each visit, all findings graded.
   - A questionnaire will be applied to gather information about participants’ quality of life and CD4 toxicity at baseline and at one month and six months.
   - Blood for N-acetyltransferase and cytochrome P450 enzymes taken at baseline. Blood for drug levels taken as part of a pharmacokinetic study at day 7, 14, 21, 28 and 56.
   - Blood for INF-γ assay taken at day 0, month 3, 6, 12 and 18.

6. Timelines
   - The study has been submitted to ethics.
   - Training of study staff has commenced.
   - Recruitment is anticipated to start within the next two months.

7. Input
   Thank you to:
   - Medical Research Council of South Africa for supporting my salary for the period of the study.
   - EDCTP for the grant
   - International AIDS Society for training support
Presentations: Abstracts and Pragsters

Pragsters

Videlis Nduba
Kenya Medical Research Institute, Kenya

**Objectives**
- **Primary objective:** Assess HIV transmission to HIV-negative partners
  - **Methodology:** HSV-2 suppression with HIV transmission by 50% in context of prevention services & lifelong (STI treatment)
- **Secondary Objectives:**
  - Effect of HSV-2 suppression on:
    - HIV levels in blood and genital tract
    - Incidence of asymptomatic & symptomatic genital herpes

**Methods**
- Multi-site trial being conducted in 14 African sites (4 Kenya) one of which is in Nairobi, Kenya
- Initially no infrastructure was in place — clinic, laboratory, OCP/POP-trained personnel
- Free HSV ICT slides existed and majority offered individual counseling, only 10% of clients were seen 26 couples
- From previous data the screen to enroll ratio was estimated at 20:1 couples
- Challenge was to create successful outreach strategies and referral linkages to generate adequate referrals for sustainable enrolment

**Discussion**
- breadcrumbs need new prevention strategies
- HSV-2 is highly prevalent in HIV-negative (50%) and HIV-positive (60%) partners
- HSV-2 appears to increase HIV acquisition & transmission
- Genital, low-cost, well-tolerated treatment (acyclovir)
- More research needed on long-term use of acyclovir
- HSV transmission in Africa occurs within HIV discordant couples in stable partnerships
- Per month couples in which one partner is HIV-positive, 30-35% change to discordant as HSV discordant
- Genital ulcers, may be caused by herpes, increase risk of HIV transmission
- Only couples are not aware of their HIV discordance
- "HIV discordant by HSV is low (< 25%)
- Men are reluctant to be tested for HSV
- Small proportion (~10%) test for HIV as couples
- "Bedsides, will not refuse same these couples

**Conclusions**
- Clinical trials require:
  - An important, clear & testable hypothesis
  - A safe, acceptable intervention to test
  - Well-written, feasible protocol
  - Focused teams, clear roles & communication
  - Strong stakeholder motivated study investigator
  - Proactive & collaborative trouble-shooting
- Clinical trials with multiple sites recruiting HIV discordant couples are the most challenging
- Need multiple strategies to bring in couples
- Sites must find their own formula

**Future perspectives**
- Recruitment & enrollment
  - Requires close monitoring & trouble-shooting
  - Retention
  - Pregnancy in index partner (75% of index partners are)
  - Increases time off study drug in ITT analysis
- Embedding trial
  - Embedding trial within wider context of prevention & linkage to care
  - Need to perform registries by comparing in case HIV acquired from partner outside study
  - Scale-up of strategy has efficacy in reducing HIV transmission
  - Acceptable cost, procurement, availability
  - Diagnostic testing issues
  - Provider education & motivation to address genital herpes
  - Need to begin assessing needs & planning demonstration projects now
  - Replicate recruitment strategies in future clinical trials
**Pragsters**

**Zakayo Mrango**

**NIMR, Kilosa, Tanzania**

<table>
<thead>
<tr>
<th>Experience from a large placebo-controlled trial in rural Tanzania: testing rectal artesunate for severe malaria</th>
</tr>
</thead>
<tbody>
<tr>
<td>- We would like to thank the study director, Dr. Matiza Gomes, the study monitor Dr. Isabella Rihim, and our sister studies in Ghana and Bangladesh. This study was a collaboration between NIMR and WHO/TDR with support from SAREC.</td>
</tr>
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<table>
<thead>
<tr>
<th>Objectives</th>
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<tbody>
<tr>
<td>To test a single dose of rectal artesunate as an emergency pre-referral treatment for Non-Parasitic children aged 6-40 months suffering from malaria on route to hospital from rural areas.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Methods: Study structure</th>
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<tbody>
<tr>
<td>- Community health workers recruited severely ill children with suspected malaria at village level.</td>
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<tr>
<td>- Clinical officers supervised recruiters every 2-3 days.</td>
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<tr>
<td>- Collecting forms and replenishing study materials.</td>
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<tr>
<td>- Following up children who had been recruited.</td>
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<tr>
<td>- Clinicians conducted verbal autopsies of all deaths and neurological investigations for all reported sequelae.</td>
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<tr>
<th>Methods: Implementation</th>
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<tr>
<td>- Inform all levels of political and medical authorities.</td>
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<tr>
<td>- Establish research infrastructure for the trial central to community level.</td>
</tr>
<tr>
<td>- Randomise and randomly assign participants to study SOP and SOP.</td>
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<tr>
<td>- Identify village health workers and train them in study SOP.</td>
</tr>
<tr>
<td>- Obtain community consent.</td>
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<tr>
<th>Results</th>
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<tr>
<td>- Over 5,000 children randomised between 2001-2006.</td>
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<td>- Follow up rate of over 99%.</td>
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<tr>
<td>- Blood films confirmed malaria in &gt;70% of cases.</td>
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<tr>
<td>- A very high rate of referral compliance was observed in both study sites.</td>
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<tr>
<th>DATA TO COME August 2006</th>
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<tbody>
<tr>
<td>- Main study endpoint: survival benefit of rectal artesunate versus placebo of “relevant deaths” pre-defined to exclude those where effective malaria treatment could not have helped at the time given (e.g. non-malaria cases or cases who immediately after recruitment).</td>
</tr>
<tr>
<td>- Other major endpoints: overall mortality impact, overall neurological event impact, fractional reduction in parasitaemia on arrival at health facility, referral compliance, time to return to par oximetry.</td>
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<thead>
<tr>
<th>Discussion &amp; Conclusions</th>
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<tbody>
<tr>
<td>- Placebo-controlled trials and high rate of recruitment and good performance indicators showed that the village health workers performed well.</td>
</tr>
<tr>
<td>- Testing occurred in close to real-life conditions and gave us additional and unexpected information which will help in the design of deployment studies.</td>
</tr>
<tr>
<td>- Rectal artesunate has now become part of WHO guidelines for initial and treatment for severe malarial in places where no facilities for injections are available.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Future perspectives</th>
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<tbody>
<tr>
<td>- We are looking at co-packaging an artesunate suppository with other drugs.</td>
</tr>
<tr>
<td>- WHO in collaboration with other groups is now working on wider deployment programs of artesunate rectal suppositories.</td>
</tr>
<tr>
<td>- Rapid Diagnostic Tests could be used for mass interventions to avoid the mismanagement of other febrile illnesses, e.g. pneumonia.</td>
</tr>
<tr>
<td>- The present indication of targeting suppositories only to those too sick to swallow may be relaxed to allow earlier treatment.</td>
</tr>
<tr>
<td>- The issues surrounding ensuring that there are appropriate incentives for distribution to create sustainability of programs.</td>
</tr>
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