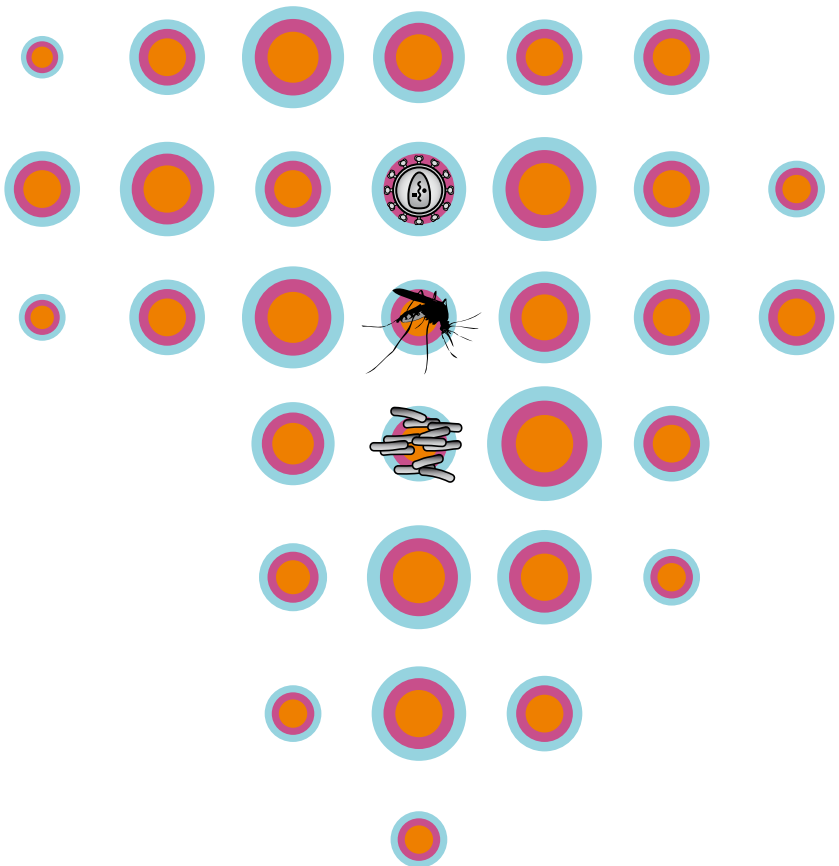




Fifth EDCTP Forum

Fighting HIV/AIDS, Tuberculosis and Malaria

One World, One Partnership



12–14 October 2009

Arusha, Tanzania



Fifth EDCTP Forum

Fighting HIV/AIDS, Tuberculosis and Malaria

One World, One Partnership



www.edctpforum2009.org
www.edctp.org/forumblog

For more information about the Forum and to order Forum publications please contact: forum@edctp.org

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FIGHTING



HIV/AIDS



TUBERCULOSIS



MALARIA

ONE WORLD
ONE PARTNERSHIP

Welcome



Dear Colleagues and Friends,

On behalf of the Fifth EDCTP Forum organising committee I extend my warmest welcome to you to this conference held in the pristine countryside of Arusha, Tanzania. The theme of the forum Fighting HIV/AIDS, Tuberculosis and Malaria: One World, One Partnership reflects the global call for all partners and stakeholders to work in synergy to control and possibly rid the world of these diseases of poverty.

The forum highlights the outcomes of projects supported by EDCTP and its partners. It presents a unique opportunity for a wide spectrum of stakeholders to review ongoing clinical research on poverty-related diseases, share the latest findings, technical expertise and experiences and also to network and plan for future research.

The programme includes thematic topics presented in plenary, parallel and poster sessions, roundtable discussions, and two satellite meetings. EDCTP and its partners will also have a marketplace where different project activities will be on display.

On-site registration starts on Sunday 11 October and continues on the first official Forum day on Monday 12 October. The first day engages political speakers reinforcing the political commitment from Africa, Europe and other partners towards the Partnership. Broader topics will be discussed in the afternoon, including regional Networks of Excellence, ethics, regulatory framework and clinical trials registration in Africa. The second and third days focus on scientific presentations of projects that have been supported by EDCTP and its partners and from other scientists from the North and South. During the Wednesday closing session, EDCTP awards to outstanding Junior and Senior African scientists will be granted. Additionally, there will be an award giving ceremony to future scientists during the closing dinner, courtesy of our hosts in Tanzania, NIMR and the Ministry of Health of Tanzania.

Social events are planned every evening that offer participants an opportunity to enjoy the hospitality and diverse cultural activities of Tanzania.

We hope you will enjoy this varied Forum programme and wish you a fruitful Forum in Arusha.

Dr Michael Makanga
Chair of Organising Committee

Introducing the Hosts

We extend our deepest thanks and appreciation to our local hosts the Ministry of Health and Social Welfare (MoHS&W) and the National Institute for Medical Research (NIMR) for providing invaluable support to the organisation and making the stay in Tanzania a truly memorable one.

National Institute for Medical Research (NIMR)

The National Institute for Medical Research (NIMR) is a parastatal service organisation under the Ministry of Health established by the Act of Parliament No. 23 of 1979 and became operational in 1980. NIMR was empowered to take over all health research institutions in the country, which until the demise of the East African Community (in 1977) were administered by the East African Medical Research Council. The establishment of this institute was in recognition by the government of the need to generate scientific data and information required in the development of better methods and techniques of enhancing disease management, prevention and control in the country.



Ministry of Health and Social Welfare (MoHS&W)

The Ministry of Health and Social Welfare ensures Tanzanians have access to good and affordable healthcare that is appropriate to needs. The Ministry's mission is to facilitate the provision of basic health services that are of good quality, equitable, accessible, affordable, sustainable and gender-sensitive. Its vision: a healthy community that contributes effectively to individual as well as the nation's development.

The roles of the Ministry of Health and Social Welfare are:

- Formulation of health-related policies
- Provision of hospital services, preventive services, chemical management services, forensic science services, food and drug quality services, reproductive health service, promotion of traditional medicine, inspection of health services, participating in international health and medical organizations, developing human resource under the ministry, overseeing extra ministerial development parastatal and projects under the ministry and supervising government agencies under the Ministry.



Belgium
Institute of Tropical Medicine
www.itg.be

France
Institut Pasteur
www.pasteur-international.org

Agence Nationale de Recherche sur le Sida et les
Hépatites Virales (ANRS)
www.anrs.fr

Germany
Federal Ministry of Education and Research
www.bmbf.de

Luxembourg
Fonds National de la Recherche Luxembourg (FNR)
www.fnr.lu

Netherlands
NACCAP
www.nwo.nl/naccap

Norway
The Norwegian Directorate of Health
www.helsedirektoratet.no

Spain
Institute of Health Carlos III (ISCIII)
<http://aes.isciii.es>

Sweden
Sida
www.sida.se

Switzerland
State Secretariat for Education and Research SER
www.sbf.admin.ch

United Kingdom
Medical Research Council
www.mrc.ac.uk

Aeras Global TB Vaccine Foundation
www.aeras.org

CONRAD
www.conrad.org

International Partnership for Microbicides (IPM)
www.ipm-microbicides.org

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www.novartis.com

The Sponsors

We gratefully acknowledge
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de Salud
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Sida



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AERAS
GLOBAL TB VACCINE FOUNDATION

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Leaders in Reproductive Health and HIV Prevention

INTERNATIONAL
PARTNERSHIP for
MICROBICIDES

NOVARTIS

The Organisers

Chairs

Michael Makanga (EDCTP)
Mwele Ntuli Malecela (NIMR)

Executive organising committee

Ilona van den Brink (Communications & sponsors)
Chris Bruinings (Finance)
Suzanne Hoogervorst (Travel & venue)
Thomas Nyirenda (Abstracts)
Daniela Pereira-Lengkeek (Communications & registration)
Marjolein Robijn (Abstracts)
Danielle Roordink (Sponsors & bursaries)
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Peter Kremsner (EDCTP-PB member, Germany)
Christine Manyando (EDCTP-DCCC member, Zambia)
Pascoal Mocumbi (EDCTP High Representative, South Africa)
Rosemary Musonda (EDCTP-PB member, Botswana)
Veronique Penlap (EDCTP-DCCC member, Cameroon)
Dirk van der Roost (EDCTP-ENNP member, Belgium)

Local organising committee –

National Institute for Medical Research (NIMR)

Raphael Hokororo (Communications)
Namdula Komba (Travel & venue)
Polycarp Mareba (Travel & venue)
Kisaka Mhando (Travel & venue)
Mary Mmbuji (Communications)
Gasper Mponda (Team leader)
Irene Mremi (Registrations)
Theckla Mutemi (Travel & venue)
Virdiana Mvungi (Communications & registrations)



The Venue

Ngurdoto Mountain Lodge

All Forum activities will take place at the Ngurdoto Mountain Lodge, located in Arusha, Tanzania. This conference hotel is located within a lush coffee plantation around 27 kms from Arusha town and Kilimanjaro International Airport, and only a short drive from Arusha National Park.

Amenities

Besides many amenities such as a swimming pool, a golf course, a simple fitness centre and tennis courts, the hotel has three restaurants and a coffee shop. There is also a small shop on the Lodge property which has basic supplies of toiletries, batteries, snacks and a wide variety of gifts.

Hotel rooms

Bedrooms are simple but comfortable, with tea/coffee making facilities, telephone, television (limited channels) and room service. Guest supplies (soaps, shampoos etc.) are limited.

Electricity and internet access

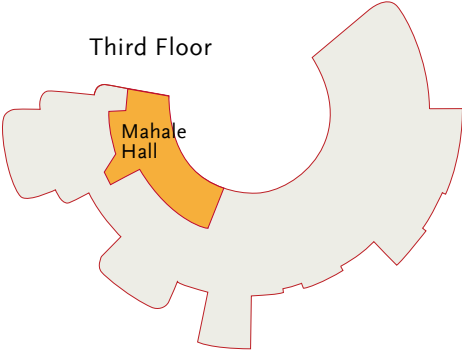
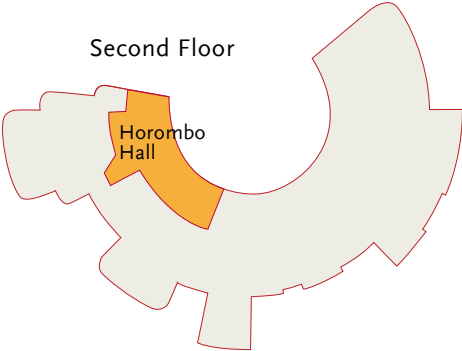
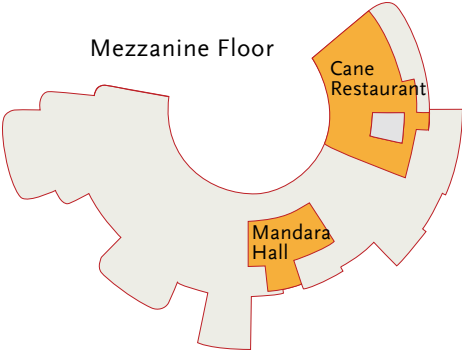
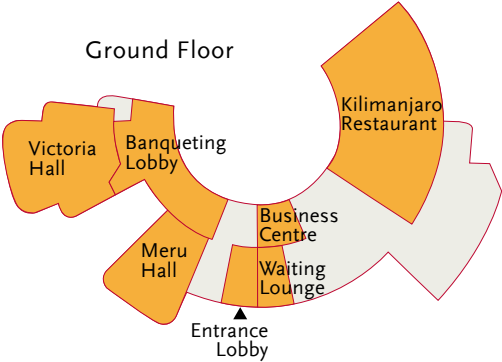
There is a business centre at the ground floor of the main building. Hotel staff will be able to inform about any fees for using the facilities in this centre. WIFI Internet access is available in the main building and hotel rooms, but expect slower speeds. For using electricity, 240 volts 3-pin square plugs are required. Please note that there may be intermittent power outages and surges, which will be very short as emergency generators will be immediately activated.

Local transport

For transport between Kilimanjaro International Airport and the Ngurdoto Mountain Lodge, delegates can use dedicated shuttle buses. For local transport, taxis are plentiful and cheap. It is best to agree a price before leaving for your destination. Car hire is possible though most companies prefer to provide their own drivers.

Ngurdoto Mountain Lodge
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PO Box 7302
Arusha
Tanzania
TEL: +255 (27)2555217
FAX: +255 (27)255 5227/28
ngurdoto@thengurdotomountainlodge.com

Conference Rooms



Social Events

Social events

All Fifth EDCTP Forum delegates are cordially invited to attend the social events on the evenings of Sunday 11 to Wednesday 14 October. During these events, food and drinks will be served, and our guests will have the opportunity to meet, catch up and enjoy the entertainment programmes. Please refer to the information below for the times and locations of this Forum's social events.

Sunday 11 October

Welcome reception

18:00–19:30

Kilimanjaro Restaurant

Entertainment programme: Maasai Cultural Dances

Monday 12 October

Official Forum dinner

19:00–20:30

Kilimanjaro Restaurant

Entertainment programme: Acrobatic
(courtesy of Ngurdoto Mountain Lodge)

Tuesday 13 October

Cultural dinner

(courtesy of NIMR)

19:00–20:30

Kilimanjaro Restaurant

Entertainment programme: Cultural dance, JKT/JWTZ Group

Wednesday 14 October

Closing dinner and Award ceremony for young future scientists

(courtesy of NIMR)

19:00–20:30

Kilimanjaro Restaurant

Entertainment: Msondo Ngoma band

Sunday 11 October 2009	Monday 12 October 2009
	08:00–09:00 Registration [ENTRANCE LOBBY]
	09:00–10:40 Official opening ceremony Brief statements from representatives of EDCTP, European Commission, WHO-AFRO, Government of the Republic of Tanzania [VICTORIA HALL]
	10:40–11:00 Coffee / Tea break
	11:00–12:00 Plenary session I The global picture Presentations by EDCTP, NEPAD [VICTORIA HALL]
	12:00–13:00 e-Poster presentations [CANE RESTAURANT]
	All day Poster presentations [BANQUETING LOBBY]
	12:00–14:00 Satellite meeting Universal standards for clinical trials in practice [MAHALE XL ROOM]
	13:00–14:00 Lunch [KILIMANJARO RESTAURANT]
	14:00–15:45 Plenary session I The global picture (cont.) Presentations by EAC, WAHO, OCEAC, SADC, EU Member States [VICTORIA HALL]
	15:45–16:15 Coffee / Tea break
16:30–19:30 Registration [ENTRANCE LOBBY]	16:15–17:30 Plenary session II Global development Presentations by EDCTP, CANTAM, WHO, COHRED, PACTR [VICTORIA HALL]
18:00–19:30 Welcome reception [KILIMANJARO RESTAURANT]	19:00–20:30 Official Forum dinner [KILIMANJARO RESTAURANT]

08:30–10:30 Plenary session III Recent advances in HIV/AIDS, Tuberculosis and Malaria (keynote addresses)	8:30–9:00 Plenary session V Capacity development in sub-Saharan Africa [VICTORIA HALL]
08:30–09:10 HIV/AIDS	
09:10–09:50 Malaria	
09:50–10:30 Tuberculosis [VICTORIA HALL]	9:00–10:20 Parallel sessions Presentations of research findings HIV/AIDS [MERU HALL] Malaria [VICTORIA HALL] Tuberculosis [MANDARA HALL]
10:30–11:00 Coffee / Tea break	10:20–10:50 Coffee / Tea break
11:00–12:05 Parallel sessions Clinical trials in sub-Saharan Africa HIV/AIDS [MERU HALL] Malaria [VICTORIA HALL] Tuberculosis [MANDARA HALL]	10:50–12:00 Parallel sessions Presentations of research findings (cont.) HIV/AIDS [MERU HALL] Malaria [VICTORIA HALL] Tuberculosis [MANDARA HALL]
12:05–13:05 e-Poster presentations [CANE RESTAURANT]	12:00–13:00 e-Poster presentations [CANE RESTAURANT]
All day Poster presentations [BANQUETING LOBBY]	All day Poster presentations [BANQUETING LOBBY]
12:30–14:00 Satellite meeting Ownership of research outcomes in sub-Saharan Africa [MAHALE XL ROOM]	
13:00–14:00 Lunch [KILIMANJARO RESTAURANT]	13:00–14:00 Lunch [KILIMANJARO RESTAURANT]
14:00–16:00 Parallel sessions Clinical trials in sub-Saharan Africa (cont.) HIV/AIDS [MERU HALL] Malaria [VICTORIA HALL] Tuberculosis [MANDARA HALL]	14:00–15:35 Plenary session VI EDCTP and global partnerships [VICTORIA HALL]
16:00–16:30 Coffee / Tea break	15:35–16:00 Coffee / Tea break
16:30–17:30 Plenary session IV Summaries and recommendations [VICTORIA HALL]	16:00–17:30 Closing session EDCTP future perspectives 16:45–17:00 Award ceremony [VICTORIA HALL]
19:00–20:30 Cultural dinner [KILIMANJARO RESTAURANT]	19:00–20:30 Closing dinner [KILIMANJARO RESTAURANT]

Monday 12 October 2009

08:00–09:00 Registration

[ENTRANCE LOBBY]

09:00–10:40 **Official opening ceremony**

Brief statements from representatives of
EDCTP, European Commission,
WHO-AFRO, Government of the Republic
of Tanzania

[VICTORIA HALL]

10:40–11:00 Coffee / Tea break

11:00–12:00 **Plenary session I**

The global picture
Presentations by EDCTP, NEPAD

[VICTORIA HALL]

12:00–13:00 **e-Poster presentations**

[CANE RESTAURANT]

All day **Poster presentations**

[BANQUETING LOBBY]

12:00–14:00 **Satellite meeting**

Universal standards for clinical trials in
practice

[MAHALE XL ROOM]

13:00–14:00 Lunch

[KILIMANJARO RESTAURANT]

14:00–15:45 **Plenary session I**

The global picture (cont.)
Presentations by EAC, WAHO, OCEAC,
SADC, EU Member States

[VICTORIA HALL]

15:45–16:15 Coffee / Tea break

16:15–17:30 **Plenary session II**

Global development
Presentations by EDCTP, CANTAM, WHO,
COHRED, PACTR

[VICTORIA HALL]

19:00–20:30 Official Forum dinner

[KILIMANJARO RESTAURANT]

OFFICIAL OPENING CEREMONY

Brief statements

09.00–10.40

Victoria Hall

Master of Ceremony from host country Tanzania: Mr Peter Mavunde

09:00–09:10

Prof. Charles Mgone • EDCTP Executive Director

09:10–09:20

Dr Pascoal Mocumbi • EDCTP High Representative

09:20–09:30

*Dr Diana Dunstan • EDCTP General Assembly
Chairperson*

09:30–09:45

*Prof. José Manuel Silva Rodríguez • EC Director
General Research*

09:45–09:55

Dr Janez Potočnik • EU Commissioner for Science and Research

09:55–10:10

*Dr Matshidiso Moeti • WHO Assistant Regional
Director for Africa*

10:10–10:40

*Minister of Health of Tanzania,
His Excellency the President of the Republic of Tanzania*



PLENARY SESSION I

The Global Picture

The need for clinical trials and EDCTP

11.00–12.00

Victoria Hall

CHAIRS

Dr Diana Dunstan

Dr Matshidiso Moeti

Dr Pascoal Mocumbi

11:00–11:20

Introduction of the theme: Fighting HIV/AIDS, Tuberculosis and Malaria: One World, One Partnership

Prof. Charles Mgone • EDCTP Executive Director

11:20–11:40

European and African programmes partnership: The role of European Member States and agencies

Dr Diana Dunstan • EDCTP General Assembly Chairperson

11:40–12:00

Clinical research agenda/strategies and capacity building initiatives in the African region

*Prof. Aggrey Ambali • Acting Director of Science and Technology
Unit of NEPAD*





HE 01

Episodic viremia during suppressive antiretroviral therapy: Impact on treatment outcomes in Nigerian patients

Olawale Salami • Clinical research Unit, Gede Foundation, Abuja, Nigeria

Introduction | The objective of the study was to investigate the impact of episodic viremia >500 copies/ml on treatment outcome in patients with previous VL of <50 copies/ml.

Methods | A retrospective cohort study was done. We included data from adult patients who had been on cART for 96 weeks and had at least one viral load measurement of <50 copies/ml. Episodic viremia was defined as VL >500 copies/ml. baseline VL, and baseline CD4 counts were recorded. VL assays at the 24th, 48th, 96th, and 120th week of therapy were included. Patients received a combination of 2 NRTIs+ 1 NNRTI or PI. Univariate analyses were performed.

Results | N=107 patients [58% female], Median age=34 years. Mean baseline Viremia was 99456 copies/ml and CD4 180 cells/uL. 62% of patients had VL <50 copies/ml at 24 weeks. Reported adherence was 96%. 49% of patients had at least 1 episodic viremia during follow-up. 59% of those who had virologic failure at 120 weeks had 2 or more episodes of viremia ($P=0.042$). High baseline viral load and detectable viral load at 24 weeks were independently associated with episodic viremia ($P=0.047$, $P<0.001$ respectively).

Discussion | Episodic viremia >500 copies/ml is common in patients on successful HAART and may negatively impact on long term virologic and immunologic treatment outcomes.

HE 02

Prophylaxis and treatment of malaria in HIV-infected populations

Moses Kanya • Makerere University College of Health Sciences, Kampala, Uganda

Introduction | HIV infection may impair the acquired immune response to malaria and increase incidence and severity of malaria and reduce the efficacy of anti-malarial treatment regimens.

Methods | We reviewed the current literature on prevention and treatment of malaria in HIV-infected populations.

Results | Daily trimethoprim-sulfamethoxazole (TMP-SMX) has led to significant reduction in malaria incidence in HIV-infected populations and presumptive therapy for malaria should be avoided in individuals on TMP-SMX prophylaxis. A synergistic preventative effect is seen with a combination of TMP-SMX, insecticide treated bed nets (ITNs) and antiretroviral therapy. Widespread TMP-SMX use may lead to selection and spread of anti-folate resistant malaria parasites. The impact of HIV induced immunosuppression on anti-malarial treatment outcomes progressively increases as anti-malarial drug efficacy decreases. ACTs are generally effective in management of malaria in HIV infected individuals. Concerns exist about the potential interactions between anti-malarial drugs and antiretroviral agents.

Discussion | TMP-SMX prophylaxis and ITNs are critical components for malaria prevention in the HIV-infected population. Treatment for malaria in the HIV-infected population should follow current guidelines for the non-HIV infected population. There is a need for further studies to monitor the resistance to both TMP-SMX and SP and the effect on protective efficacy. Ongoing surveillance and clinical studies are needed to evaluate for potential interactions and adverse events that result from co-administration of therapies used to manage malaria and HIV infection.



HE 03

Clinical pharmacology for global health – A North-South partnership

Mohammed Lamorde • Makerere University, Kampala, Uganda

Introduction | Africa's pharmacopoeia is changing. The roll-out of antiretroviral drugs coincides with the adoption of new drugs for malaria treatment and increased use for drugs for co-infections like tuberculosis. Although unfavourable drug interactions may occur during co-treatment with these drugs, few pharmacokinetic (PK) studies have been conducted in Africa. A public health-oriented pharmacology unit was proposed for Uganda, supported by a laboratory and treatment information centre.

Methods | A memorandum of understanding was signed between Trinity College Dublin (TCD), Ireland and Makerere University, Uganda in November 2006. A research team was set up comprising a pharmacologist, 2 African PhD students and support staff at the Infectious Diseases Institute (IDI), Makerere University. In June 2007, an EDCTP networking meeting for African and European pharmacologists working in Africa was held in Uganda. Training and research collaborations were established with the University of Liverpool, St Stephens PK Research, London; National Medicines Information Centre Ireland, University of Cape Town and University of Jos, Nigeria. Research questions were identified and prioritised. A HPLC machine was installed at IDI. The AIDS Treatment Information Centre, IDI, was established to provide free treatment information services and disseminate research findings.

Results | The clinical Phase of three PK studies is complete. Two papers have been published. Six studies are ongoing. The unit has received funding to conduct food, anti-malarial and antiretroviral PK studies.

Discussion | Capacity building for pharmacokinetic research is feasible in Africa.

HE 04

Efavirenz-based antiretroviral therapy induced hepatotoxicity among Ethiopian patients

Getnet Yimer Ali • Addis Ababa University, Ethiopia

Introduction | Hepatotoxicity is one of the most commonly encountered adverse drug reactions when managing patients with antiretroviral drugs. Objective of the study was to prospectively determine the prevalence and possible risk factors for antiretroviral drug induced hepatotoxicity among treatment naïve HIV patients in Ethiopia.

Methods | A total of 178 newly diagnosed HIV-infected patients ≥ 18 years of age with no past history of treatment for HIV and tuberculosis, baseline CD4 cell count $< 200/\text{mm}^3$ and no clinical evidence of liver damage were enrolled. Patients received efavirenz-based Highly Active Antiretroviral Therapy (HAART) and followed up prospectively for 3 months to assess clinical and biochemical liver function test.

Results | Elevation of liver enzymes greater than 3 times the upper limit of normal value was seen in 17.4% of patients, and the median time for development of hepatotoxicity was 2 weeks. There was no statistically significant association of sex, body mass index, age, CD4 count, as well as presence of hepatitis B surface antigen and anti-hepatitis C virus antibody (the incidence rate for a positive test result was 6.4% and 1.8% respectively) with efavirenz-based antiretroviral drug induced hepatotoxicity in our study.

Discussion | The observation of hepatotoxicity in a relatively larger number of patients from our cohort indicates that patients taking efavirenz-based Antiretroviral Treatment (ART) need close follow-up, early detection, and management for an elevated liver enzyme. This becomes highly useful especially during the first 2 weeks after initiation of treatment.



HE 05

Paradoxical tuberculosis immune reconstitution inflammatory syndrome and its management in HIV/TB co-infected patients commencing antiretroviral therapy in Kampala, Uganda

William Worodria • Infectious Diseases Network for Treatment and Research in Africa, Kampala, Uganda

Introduction | Tuberculosis Immune Reconstitution Inflammatory Syndrome (TB-IRIS) is a common complication of TB/HIV co-infected patients commencing Highly Active Antiretroviral Therapy (HAART). The frequency, predictors and outcomes of this disorder in resource limited settings are not well known.

Methods | A prospective cohort of ART-naïve TB/HIV-infected patients eligible for HAART in Mulago Hospital, Kampala, Uganda was enrolled to study the occurrence of TB-IRIS. A consensus definition of TB-IRIS was used to identify cases.

Results | Of 256 patients enrolled with a median age of 35 years (IQR 28–39), and CD4 count of 55 cells/μL (IQR 21–138); 114 (45%) were females and 65 (25%) were in WHO clinical stage IV. Forty-five (23.8%, (CI 18.2%–30.7%)) patients developed TB-IRIS within 17.9 days (IQR 13.5–28) of HAART and 68 days (IQR 42–104) of TB treatment initiation. Thirty-seven (82%) patients with TB-IRIS recovered fully on treatment while 4 (9%) worsened and 4 (9%) died.

Discussion | TB-IRIS is an important complication of advanced HIV/TB disease and clear guidelines for its management in resource limited settings are urgently needed.

HE 06

Molecular epidemiology of HIV-1 dual infection in monogamous and polygamous sexual partners in Uganda

Nicaise Ndembu • MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda

Introduction | Both inter-subtype and intra-subtype dual infections have the capacity to facilitate more rapid diversification of the HIV-1 population through the generation of recombinant viruses, and this has the potential to make the development of effective vaccines against HIV-1 even more difficult. This study aimed to (1) determine the frequency of co-infection and incidence of superinfection in this large well-characterised rural clinical cohort (RCC) in South Western Uganda, and (2) determine the frequency of recombination between divergent HIV-1 subtypes.

Methods | In this preliminary study, we report on an analysis of 35 HIV-1 infected individuals from 7 monogamous and 6 polygamous partnerships within the RCC. 10–20 clones were selected for each sample to detect dual infections in env-C2V3 and gag-p24 sequences. Polygamous partners that had subtype discordant and recombinant viruses were analysed further in the pol-integrase gene. We used single genome amplified env-V1-V4 genes to map recombination breakpoints.

Results | Out of the 29 HIV-1 strains with positive polymerase chain reaction (PCR) for both gag-p24 and env-C2V3, 31.0% had discordant subtype A/D (n=9), 37.9% had concordant subtype: D/D (n=11), 24.1% were A/A (n=7) and 6.9% were C/C (n=2). We identified 5 cases of dual infections among 8/9 individuals with discordant subtype in 13 partnerships studied. The bootscanning and phylogenetic trees of V1-V4 (4000bp) confirmed the existence of A/D recombinant in four dually infected individuals.

Discussion | In this retrospective study of a limited number of HIV-infected multiple sexual partners, dual infections appear to be a frequent event.



HE 07

InfCare HIV – A health-informatic tool for improvement of HIV clinical care and research in Africa

*Anders Sönnernborg • Karolinska Institutet,
Stockholm, Sweden*

Introduction | A major problem in HIV clinical care and research is to handle the vast amount of data produced for each patient. Antiretroviral Treatment (ART) may fail due to inability to gather all the data in the clinical decisions and the research quality may decline. Karolinska Institutet has developed a computer based treatment support system, InfCare HIV, to manage this which is applied at all Swedish clinics. It is either integrated into electronic record system or used via the web.

Methods | InfCare contains 4 main elements; decision support tool, a quality assurance registry, a long-distance expert support system, a research database, in the same service. The core module is the decision support which graphically and pedagogically summarises clinical data from many sources.

Results | We have adapted and contextualised InfCare for low-income countries which improve the quality of the care and research substantially. Assessments of the IT-infrastructures at Muhumbili National Hospital (a national tertiary referral and teaching hospital for MUHAS) revealed the feasibility to use InfCare. A query tool enables the creation of questions for the database. Patient cohorts for research are produced and external enquires are answered quickly.

Discussion | Transferring important parameters from routine medical treatment into an R&D context in a structured and simple way creates new opportunities for doctors to contribute to clinical HIV research. Developing cross-border systems such as InfCare HIV means that we can achieve synergistic effects in trials performed in Africa.



ME 01

A pilot study of intermittent preventive treatment and home-based management of malaria in a rural area of the Gambia

Sanie Sesay • Medical Research Council (UK),
Banjul, The Gambia

Introduction | Malaria remains an important cause of mortality and morbidity among young children. The global malaria control strategies include prompt treatment with an effective antimalarial drug, vector control using ITNs or curtains or indoor residual spraying (IRS) and intermittent preventive treatment (IPT). However, individually these interventions provide only imperfect protection. Thus, there is a need to investigate whether additional control measures provide added benefit in reducing mortality and morbidity.

Methods | Thus, during the 2008 malaria transmission season, 1,277 children under 5 years of age were randomly allocated to receive IPT or placebo from village health workers (VHWs) based in primary health care villages. Treatment with a single dose of sulfadoxine / pyrimethamine plus three doses of amodiaquine or placebo were given to all study subjects at monthly intervals on three occasions during the peak malaria transmission season (September, October, and November). In addition, VHWs were trained to administer treatment with Coartem to children if they develop symptoms compatible with malaria during the malaria transmission season. The primary endpoint was incidence of clinical attacks of malaria detected by passive case detection during the study.

Results | Results of the trial will be presented.

Discussion | Results will follow.

ME 02

The best approach to retreating patients with recurrent malaria in the era of artemisinin based combination therapy

Adoke Yeka • Uganda Malaria Surveillance
Project, Kampala, Uganda

Introduction | Several African countries having adopted artemisinin combination therapy (ACT) as first-line treatment for uncomplicated *falciparum* malaria use also quinine monotherapy as second line. This policy goes against the World Health Organization (WHO) recommendations for combination therapy. The adherence to a seven-day quinine treatment schedule is probably poor. The study aims at assessing the best approach for retreating patients with recurrent malaria within 28 days of initial therapy with ACTs.

Methods | The study was conducted in Tororo, Uganda, and is a nested, randomised, single blinded, multi-arm clinical trial of rescue therapy. Children aged 6–59 months with recurrent uncomplicated *Plasmodium falciparum* malaria after an ACT treatment were recruited and randomised to either the standard 7-day quinine or to a 3-day ACT (artemether – lumefantrine (AL) to quinine or dihydroartemisinin-piperaquine (DP), DP to quinine or AL). All doses were directly observed. The main outcome measure was the risks of recurrent parasitemia at 28 days, unadjusted and adjusted by PCR genotyping.

Results | Recruitment is ongoing with a planned sample size of 260 patients. 221 of 222 (99.5%) participants enrolled completed follow-up. The risk of recurrent *P. falciparum* parasitemia unadjusted by genotyping for all study participants is 57.2% after 28 days of follow up. Full corrected results shall be presented.

Discussion | We shall discuss whether quinine monotherapy or an alternative ACT is the most appropriate treatment for recurrent malaria.



ME 03

Comparative efficacy and safety of artemether-lumefantrine, artesunate plus amodiaquine and artesunate plus amodiaquine plus chlorpheniramine (artemoclo)

Catherine Falade • University of Ibadan, Nigeria

Introduction | Artemisinin-based combination therapy (ACT) is the current the golden standard for the treatment of acute uncomplicated malaria. Amodiaquine (AQ) plus artesunate (AS) is one of the preferred ACTs. Chlorpheniramine (CP) has been shown to enhance the efficacy of amodiaquine.

Methods | In an open-labeled randomised trial, the comparative efficacy and safety of artemether-lumefantrine (AL), artesunate-amodiaquine (ASAQ) and artesunate-amodiaquine-chlorpheniramine (AQC) was evaluated in 159 Nigerian children aged 6 months to 10 years with acute uncomplicated malaria. Enrollees were randomised to receive AL, ASAQ or AQC at standard doses over 3 days. (AQC: 100mg AS + 300AQ + 4mg CP/tablet using AQ 10 mg/kg/day for dosing). Assessment was by 28 days WHO 2003 efficacy test (PCR unadjusted cure rates only).

Results | 144/159 (90.6%) completed the study. Mean fever and parasite clearance times for AL, ASAQ and AQC were similar ($P=0.94$ and 0.12 respectively). Day 14 ACPR was 100% for AL and AQC while that for ASAQ was 98% ($P=0.39$). Day 28 ACPR were 91.1%, 92% and 95.9% for AL, ASAQ and AQC respectively ($P=0.62$). ACPR at day 42 for 115/144 (79.9%) evaluable children were similar ($P=0.48$). AQC gave the best parasitemia clearance and haematological recovery on day 2 ($P=0.022$ and 0.018 respectively). The three ACTs were well tolerated.

Discussion | The three drugs were efficacious and safe. AQC gave non-significant higher ACPR than the other two on days 28 and 42. The better haematological recovery and parasite clearance with AQC on day 2 may be a fine indication of the enhancement ASAQ effect.

ME 04

Intermittent preventive treatment with sulfadoxine-pyrimethamine versus intermittent screening and treatment of malaria in pregnancy

Harry Tagbor • Kwame Nkrumah University of Science & Technology, Kumasi, Ghana

Introduction | The incidence of malaria, including the incidence in pregnant women is declining in many African countries. Thus, there is a need to re-examine the efficacy and cost effectiveness of giving intermittent preventive treatment in pregnancy (IPTp) on several occasions during pregnancy.

Methods | A randomised, multi-centre controlled trial in 5000 pregnant women who sleep under an insecticide treated bed net to compare the standard SP-IPTp regimen (3 doses of SP in second and third trimester) and intermittent screening using a rapid diagnostic test and treatment of parasitaemia at scheduled antenatal clinic visits in the second and third trimester undertaken in four west African countries. The primary end points of the trial will be birth weight and anaemia at 36–38 weeks of gestation and at the time of delivery or shortly afterwards. Mothers and infants will be seen again six weeks after delivery. The study is powered to show that intermittent screening and treatment of parasitaemia is not inferior to standard SP-IPTp regimen. The costs and cost effectiveness of each intervention will be evaluated.

Results | This presentation will focus on study design. Results will be ready for presentation in two years.

Discussion | The study will provide information to national malaria control programmes in countries with seasonal malaria transmission on whether there are alternative, safe and effective methods to the WHO recommended SP-IPTp regimen for managing malaria in pregnancy.



ME 05

Risk of hemolysis after chlorproguanil-dapsone + artesunate treatment in G6pd deficient infants

Jean-Pierre Van Geertruyden • Institute of Tropical Medicine, Antwerp, Belgium

Introduction | Malaria is a leading cause of mortality, particularly in sub-Saharan Africa and among children. Prompt and efficacious treatment is important. If ineffective drugs are given or treatment is delayed, a patient may progress within a few hours to severe disease, which if untreated is almost always fatal. Chlorproguanil-dapsone plus artesunate (CD+A) is an artemisinin-based combination treatment (ACT), with the potential risk of triggering a haemolytic anaemia in glucose-6-phosphate (G6PD) deficient patients because of the oxidative properties of dapsone. We assessed the haemolytic risk related to G6PD deficiency and to CDA intake in African children with uncomplicated malaria.

Methods | This is a nested study of a Phase IV multicentre study comparing safety and efficacy of several ACTs in children. In a matched case-control design we compared children with a haemoglobin drop ≥ 2 g/dl in the three days after the first treatment dose with those with a drop < 2 g/dl. Cases and controls were matched for study site, gender, age and haemoglobin at baseline. Data were analysed with a conditional logistic regression model.

Results | G6PD deficiency, homo- and heterozygote, was present in 8.5% (10/117) of cases and 6.8% (16/234) of controls. After adjusting, neither G6PD deficiency (OR: 0.36; $P=0.25$) nor CDA (OR: 1.20; $P=0.50$) were independent risk factors for a haemoglobin drop. However, CDA and G6PD deficiency interacted ($P=0.02$) leading to a higher risk estimate (OR 5.71; 95% CI 0.15 to 225.79).

Discussion | Administering CDA to patients with uncomplicated malaria and with a G6PD deficiency could result in a higher risk of haemolytic anaemia.

ME 06

Malaria vaccines for Africa - Experience of AMANET R&D

Ramadhani Noor • African Malaria Network Trust, Dar es Salaam, Tanzania

Introduction | As a not-for-profit NGO, one of AMANET's key objectives is clinical development of candidate malaria vaccines through sponsorship of clinical trials in Africa. AMANET fundraises by competing for publicly available grants to provide sub-grants to research sites to conduct candidate malaria vaccine trials. The objective of the current presentations is to provide an overview of ongoing activities within the AMANET malaria vaccine portfolio and share experiences of sponsorship of clinical trials by an African Organisation.

Methods | Through an established relationship with the European partners, AMANET has so far been evaluating candidate malaria vaccines that are ready for clinical testing in endemic countries. AMANET ensure standards are maintained and research participants and investigator welfare are protected.

Results | Three malaria vaccine candidates have been attracted to the portfolio and are at various stages of clinical evaluation:

- (1) The AMA1 malaria vaccine is currently undergoing clinical trials at Bandiagara in Mali
- (2) The MSP3 LSP malaria vaccine undergoing paediatric development through two Phase Ib trials, in Balonghin Burkina Faso and Korogwe Tanzania, and a Phase IIb trial in Soutuba, Mali
- (3) The GLURP-MSP3 recombinant hybrid vaccine (GMZ2) is currently undergoing clinical trials at Lambaréné, Gabon.

Potentially, there are at least ten separate clinical trials envisioned within the next four years.

Discussion | An African organisation is able to take the role of sponsorship to trials at GCP standards trials and effectively accelerate development of malaria vaccines.



ME 07

Baseline information at Iganga-Mayuge demographic surveillance site: A new malaria field study site in Eastern Uganda

Fred Kironde • Makerere University, Uganda

Introduction | Control of malaria requires reliable information on the profiles of malaria-associated factors in endemic areas. Makerere University Iganga/ Mayuge DSS rural site established 3 years ago with international partners is 120 km east of Kampala city. The population is 100,000 with 15,000 children under five. It has an equatorial climate, and transmission throughout the year, with two peaks after rains. *Plasmodium falciparum* is the predominant species.

Methods | In capacity development for malaria vaccine trials at the site, a cohort of children is followed up to determine malaria related indicators.

Results | Our preliminary findings show the frequency of *P. falciparum* is 65% among under-fives, and 40% in all children below 10 years. The following will be further described: vector distribution, human blood group profiles, gametocyte carriage, hematologic indices, relationships between RANTES promoter polymorphism, parasite density versus G6PD deficiency, and factors affecting time to first new infection after treatment.

Discussion | This project best illustrates potential for multi-disciplinary competency collaboration in major scientific undertaking and planning.

ME 08

Spatial distribution and temporal dynamics of clinical malaria cases in a western Kenya highland site

Yaw Afrane • Centre for Global Health Research, Kenya Medical Research Institute, Kisumu, Kenya

Introduction | One important issue for evaluating the efficiency of new malaria control measures on febrile malaria is the accuracy of hospital-based malaria case data. Further, the distribution pattern of febrile malaria may be used to infer environmental risk factors. This study investigated the spatio-temporary distribution of clinical malaria cases through active and passive case surveillance in a western Kenya highland site.

Methods | Active case surveillance was done with a cohort of 1800 participants selected randomly from 350 households in 10 villages. Participants were visited fortnightly and screened for clinical malaria whilst passive case surveillance was done from the local clinic in the study area. A clinical malaria case was defined as an individual with malaria-related symptoms (fever [axillary temperature $\geq 37.5^{\circ}\text{C}$], chills, severe malaise, headache or vomiting) at the time of examination or 1–2 days prior to the examination in the presence of a *Plasmodium falciparum* positive blood smear.

Results | Topography was associated with increased malaria risk. Clinical malaria cases from active case surveillance were clustered along valley bottoms with a 2 to 2.5-fold increase during the rainy season. Children between 6–10 years and those under 5 years had more clinical cases than the rest of the population. Bednet coverage was over 60% among households. However, households with bednets still had clinical malaria cases. There was no relationship between active clinical cases and passive hospital case surveillance. Hospital cases seem to be the same throughout the year with no pattern of seasonality compared to the active clinical cases.

Discussion | We suspect misdiagnosis and over treatment from the hospitals account for the ambiguity in the passive cases. This is being investigated.



TE 01

Pulmonary tuberculosis among health care workers in Ibadan, Nigeria

Aderemi Kehinde • University College Hospital, University of Ibadan, Ibadan, Nigeria

Introduction | Tuberculosis (TB) infection control programmes are not routinely implemented in many TB endemic countries. The study was carried out to determine the prevalence of hospital acquired TB among health care workers (HCWs) in Ibadan, Nigeria.

Methods | This is a six-month cross-sectional study (January to June 2008) involving all consenting HCWs working at DOTS centres at the University College Hospital (UCH) and Jericho Chest Hospital in Ibadan, Nigeria. Socio-demographic data was obtained by administering standardised questionnaire. Three early morning sputa were collected from each subject. The sputa were processed at the TB laboratory of the Department of Medical Microbiology, UCH, Ibadan, Nigeria. Each sputum was stained for acid fast- bacilli (AFB) with Zeihl-Neelsen reagents. The sputum was then inoculated onto prepared acid buffered Ogawa medium and incubated at 37°C for six weeks.

Results | A total of 271 subjects were studied. Five (1.8%) were physicians, 36 (13.3%) were nurses while laboratory scientists, laboratory assistants and hospital maids accounted for 12 (4.4%), four (1.5%) and three (1.1%) respectively. The majority 211 (77.9%) were students. Nine (3.3%) out of the total sputa processed were positive for AFB while five (1.8%) were culture positive. Of the positive AFB, seven were from students (77.8%), one (1.2%) each from hospital maid and laboratory assistant cadres.

Discussion | The high infection rates among the hospital maids and laboratory assistants may be attributed to their low educational status. Implementation of TB infection control strategies is advocated to prevent TB transmission.

TE 02

Widespread fluoroquinolone sale in northern Tanzania: A potential threat for fluoroquinolone use in tuberculosis treatment

Josy van den Boogaard • Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands

Introduction | The fluoroquinolones moxifloxacin and gatifloxacin are being evaluated for their potential to shorten tuberculosis (TB) treatment. The widespread use of the fluoroquinolones to treat other infections raises concerns about mycobacterial resistance development to the fluoroquinolones. Data that quantify the use of fluoroquinolones in countries with a high burden of TB, such as Tanzania, are not readily available.

Methods | Fluoroquinolone sale in northern Tanzania was quantified in a two-month, prospective study. Antibiotic agents sold in February and March 2009 were registered by all retail pharmacies in Moshi town. Defined Daily Doses (DDD) per 1000 inhabitant-days were calculated. Private drug-outlets were visited to evaluate the availability of fluoroquinolones through unauthorized sale. Ciprofloxacin tablets obtained from four pharmacies and six private drug-outlets were analysed for the presence of active ingredient.

Results | Preliminary results (final results, including DDDs and analysis of ciprofloxacin tablets, will be available in April 2009) indicate that the dominant classes of antibiotics distributed by pharmacies in northern Tanzania are penicillins (34%), macrolides (12%) and fluoroquinolones (11%). Ciprofloxacin was available in 8 of 8 unauthorised drug-outlets visited.

Discussion | The considerable sale of fluoroquinolones in northern Tanzania through authorised and unauthorised channels warns of the challenges ahead of incorporating fluoroquinolones in (first-line) TB treatment. If the use of fluoroquinolones is not controlled, their use in TB treatment might be hindered by the emergence of mycobacterial resistance.



TE 03

Modulatory activities of antioxidants against the toxicity of rifampicin

Olufunsho Awodele • University of Lagos, Nigeria

Introduction | WHO has shown great concern about the burden of Tuberculosis in the developing countries and most of the drugs used in Tuberculosis management have been relatively known to be toxic. This study intends to investigate the modulatory effects of vitamin C and E on the hepatotoxic, lipid peroxidation, sperm quality damage and brain toxicity of rifampicin which is a first-line drug in tuberculosis therapy.

Methods | 40 Wister albino rats of 10 animals per group were used. Group 1 animals were administered 0.3 mls of distilled water, Group 2 received therapeutic dose of rifampicin, Group 3 animals were given therapeutic doses of rifampicin plus vitamin E, while Group 4 received therapeutic doses of rifampicin and vitamin C. The blood of the animals were collected and analysed for liver function and lipid profile using fully automated clinical chemistry analyse. The sperm analysis was done using Morakinyo et al, 2008 and histopathological examination of the organs were carried out.

Results | Rifampicin increased the liver function enzymes ($P < 0.05$). However, the vitamin E treated group showed remarkable protection. The results showed vitamin E and C treated group to significantly ($P < 0.05$) increase sperm count as compared with rifampicin alone. The decrease in sperm quality caused by rifampicin was also reversed in the vitamin E and C treated groups.

Discussion | It can be concluded that vitamin E demonstrates hepatoprotective, improved sperm count and protection against brain damage caused by rifampicin. While vitamin C demonstrated lesser improvement.

TE 04

Improving diagnosis of pulmonary tuberculosis in resource-limited settings

Werner Maokola • Ifakara Health Institute, Dar es Salaam, Tanzania

Introduction | Ziehl-Neelsen microscopy which is the main diagnostic tool for Tuberculosis in endemic countries has low sensitivity especially in paucibacillary tuberculosis as one of its main shortcoming. There is an increasing need to improve sputum smear microscopy and develop new diagnostic methods for Tuberculosis.

Methods | To evaluate different ways to improve tuberculosis diagnosis in developing countries, a cross-sectional study in Wuse General Hospital and Zankli Medical Centre in Abuja Nigeria was conducted between April and May 2008. Individuals >18 years with clinical suspicion of tuberculosis were recruited.

Results | Examining of the first 2 specimens identified 45 (92%) smears out of 49 in Ziehl-Neelsen 'spot-spot-morning' scheme and identified 27 (96%) out of 28 in the 'spot-morning-spot' scheme ($P = 0.07$). In Light Emitted Diodes Fluorescent Microscopy the yield was 21 (78%) out of 27 in frontloaded and 11 (92%) out of 12 in the standard scheme ($P = 0.05$). Light Emitted Diode-Fluorescent Microscopy had the highest proportion of tuberculosis positive individuals: 45 (45%) than Ziehl Neelsen: 17 (20%) and in Lipoarabinomann assay: 12 (14%) with poor correlation with smear microscopy. Light Emitted Diodes-Fluorescent Microscopy used less time, required less numbers of examination fields than Ziehl-Neelsen and was highly accepted by the laboratory staff.

Discussion | Deployment of Light Emitted Diode-Fluorescent Microscopy and adoption of frontloaded scheme using the first 2 specimens may greatly improve TB diagnosis in resource-poor settings.



CE 01

Capacity building on HIV/AIDS care in the eastern regions of Uganda

Peter Olupot-Olupot • Mbale Hospital, Uganda

Introduction | HIV/AIDS continues to ravage sub-Saharan Africa with evident lack of leadership training for frontline senior clinicians in countries most affected. Uganda, an east-African country with a remarkable history of first demonstrable decline in incidence of HIV infections, finds itself in a position of lack of leadership in HIV/AIDS care for the huge accumulated cases and additional new infections.

In the eastern regions of the country, MforM Africa (a UK charity) and the Mbale Regional Referral Hospital of Uganda have championed leadership training conferences, mid-year short workshops and local mentorship activities. In the last three years the training conferences and other activities have been well received with participants drawn from 7 districts in the regions annually.

Methods | Senior clinicians in leadership on care and management of HIV/AIDS who have limited access to update HIV/AIDS courses and conferences were identified and invited for annual HIV/AIDS update courses and mid-year workshops.

Results | 30 senior clinicians were trained during 3 annual conferences and courses and two mid-year workshops. Two treatment guidelines were developed and disseminated. Mentorship programmes were initiated by the trained senior clinicians and a total of over 70 health workers have been mentored under the supervision of the trained senior clinicians. Two research projects were initiated with the aim of feeding into the treatment guideline making process in the country.

Discussion | Capacity building in the care of HIV/AIDS patients is possible through collaborations, well-tailored courses and empowerment of the local health community.

CE 02

Creating web-based platforms for teaching research ethics and GCP to Africa

Roma Chilengi • Oxford University/KEMRI Wellcome Trust Research Programme, Kilifi, Kenya, and African Malaria Network Trust (AMANET), Dar es Salaam, Tanzania

Introduction | There is a dearth of appropriate non-academic training opportunities for Africans in the fields of research ethics and Good Clinical Practice (GCP) that are both relevant and accessible. Available courses are often prohibitive due to cost, time and affiliation requirements.

Methods | With EDCTP support, we developed web-based training capacity at AMANET in a phased manner. Based on the success of the pilot course, web-based learning has been continued for the basic Human Research Ethics (HRE), has been translated into French, has created a GCP course, and has created an advanced HRE course.

Results | Training faculties of experts in research ethics and GCP were constituted to create the courses. The first course was validated through a practical face-to-face workshop. By October 2008, a robust platform had been established running four courses with over 500 enrolments and at least 135 successfully completed. Each course has several modules with specific tests to be passed before a certificate can be awarded.

Discussion | The utilisation of the courses confirms that internet is a cost-effective training tool overcoming traditional barriers to capacity building.

CE 03

Understanding the consent of research participants in an enterotoxigenic vaccines trial (in HIV seropositive people) in Misisi, Lusaka

Bornwell Sikateyo • Ministry of Health, Directorate of Public Health & Research, Lusaka, Zambia

Introduction | The ethnographic focus of this research project is a 2-year immunological vaccines trial managed as part of a multi-site trial. The investigative focus of the trial is on the prevalent opportunistic infections, and how they are affected by the absorption of vaccines.

Methods | The general aim of this study was to identify and explore factors that affect participants' ongoing consent to participate in medical research. Rather than considering the principles upon which informed consent is based, this study aimed to understand how ethical and moral behaviours emerge in the specific context of a complex and challenging trial in a resource-constrained setting. Data collection consisted of library research, ethnographic and qualitative research methods. Research techniques included literature review, extensive observations and contextualisation, in-depth interviews and group discussions. Formal interview and narrative data were audio-recorded, transcribed verbatim, and translated into English. QSR Nvivo 2 were used to highlight common themes and to select quotes that either supported or refuted these themes.

Results | The study found availability of free medical attention for all the illnesses for the whole family as the major motivation to enrolment. Participants did not perceive the endoscopy procedures to be potentially harmful. Participants were of the view that the study was about routine care.

Discussion | Although it is evident that the informed consent process was followed, researchers could benefit from acknowledging the highly social nature by considering it as an ongoing and continuous engagement throughout the process.

CE 04

Data management and archiving systems of a cohort of African Ethics Review Committees: From paper-based to electronic systems

Aceme Nyika • African Malaria Network Trust (AMANET), Tanzania

Introduction | A baseline survey conducted by the African Malaria Network Trust (AMANET) in 2007 revealed that African Ethics Review Committees (ERCs) relied entirely on conventional paper-based data management systems, which compromised competence of the committees that are overwhelmed by workload in resource-constrained settings.

Methods | As part of a longitudinal capacity strengthening programme funded by the Bill & Melinda Gates Foundation, AMANET is making efforts to upgrade data management and archiving systems of a cohort of 20 African ERCs. Training of ERC administrators is being done through training workshops, face-to-face interactions on site and through a web-based discussion forum. The provider of the software, ProIRB Plus Inc, also gives technical support directly and via AMANET online discussion forum.

Results | ERCs in the AMANET capacity strengthening project are in the process of upgrading their data management and archiving systems. Office refurbishments have been done, office furniture including ERC data management software have been procured, trainings provided and routine management and storage of data is being improved.

Discussion | In developing countries, ethics committees currently rely on external support to match up with the advances in technology. Improved efficiency and effective review and oversight of health research protocols would go a long way in enhancing the protection of the welfare of research participants while promoting ethical conduction of the much needed health research. This paper reports progress in strengthening ERCs capacity to manage and store data, and flags practical challenges to be tackled.

CE 05

Uganda Virus Research Institute (UVRI), EDCTP, IANPHI and MRC (UK): A successful example of capacity development through an international partnership

Jonathan Kayondo • Uganda Virus Research Institute (UVRI), Entebbe, Uganda

Introduction | The Uganda Virus Research Institute (UVRI) is a major research institution in the region. From late 1970s to mid 1980s research and infrastructure deteriorated due to civil strife and interruption of international collaboration. This trend has been reversed in the recent past, due to partnerships such as the capacity building support by the EDCTP, IANPHI and MRC UK.

Methods | Support to UVRI through various EDCTP funding, MRC UK and IANPHI have been used to strengthen human resource and infrastructural capacity.

Results | The following have been achieved: (1) The capacity of a Science and Ethics Committee (SEC) enhanced with provision of a Regulatory Office, Secretary, SEC member trainings in bioethics, SEC facilitation, and development of Operating procedures for protocols review; (2) Administration and Finance management have been strengthened with recruitment of an administrative officer and a senior grants officer; (3) A scientific officer has been recruited to strengthen capacity for networking and research; (4) Training courses on grants writing & management, statistics, preparation of publications etc have been organised; (5) UVRI and partners have been successful in the joint acquisition of several grants including an EDCTP one to create a Network of Excellence in East Africa; (6) ICT enhancement with Local Area Network creation to facilitate information access, creation of a centralised data management and storage center; (7) Equipment for information retrieval, dissemination and laboratory upgrades.

Discussion | Collaborations have been established and funding secured. This model of capacity building works well as evident above.

CE 06

Governance of health research in Africa: The Senegalese example

Samba Cor Sarr • Ministry of Health & Medical Prevention, Dakar, Senegal

Introduction | The development of health research in Africa creates several problems in management. In fact, medical science produces new challenges for policy makers in protecting the interest and security of the population. For this our countries need strengthening of the health research regulation system and establishment of standard operating procedures.

Methods | To study the potential role of health research actors (researchers, national regulatory authority, national ethics committee for health research, population, sponsors) we conducted group discussions and individual interviews. We also analysed documents about procedures and regulations in country members of the Economic Community of West African States (ECOWAS).

Results | In several African countries regulatory authorities and ethical committees exist, but there is no real coordination between them. Regulation of health research in African countries is weak, and in a few national ethics committees procedures were not in place. There is progress in the implementation of legal provisions in governance of health research. For example in Senegal we have a new ethical code for health research from 2009, and in Gabon a National Ethics Committee for health research was established in 2009.

Discussion | Despite our effort to control health research in our countries, we mark the persistence of non-ethical studies and new challenges. What position do we adopt when we have a proposal for research on cell-strain, organ transplants etc? There is a need to strengthen the members of national ethics committees and to make room for discussions about bioethics. Elaborate guidelines and legal provisions need to be developed to improve the governance of health research in ECOWAS countries.

CE 07

Training and resources in research ethics evaluation for Africa (TRREE for Africa)

Dominique Sprumont • University of Neuchâtel, Switzerland

Introduction | TRREE for Africa is a unique programme of African, European and North American partners who have come together to develop and distribute training materials in research ethics and regulation. The goal of this presentation is to describe how the initial purposes of TRREE have been achieved and to indicate how the lessons learned to date will be applied in the next phases of the programme.

Methods | TRREE began in 2006 with the establishment of a website of resources (www.trree.org) and a needs assessment study of research ethics committee members in three African countries: Tanzania, Mali and Cameroon. On the basis of the needs assessment, it was decided to develop three training modules: a primer on research ethics; roles and responsibilities of research ethics committees; and country-specific compendiums of relevant legislation and regulations for the three African countries and one European country (Switzerland).

Results | The modules were ready by May 2009 and are being distributed via the Internet and CD-ROM. The first two modules will be available in English, French and German. The language (s) of the third module will depend on the requirements of each country.

Discussion | The next Phase of TRREE will include expansion to three additional African countries (Nigeria, Senegal and Mozambique) with modules in Spanish and Portuguese. This will likely require a change in TRREE's governance structure, including the location of a coordinating office in one of the African partner countries, and the production of standard operating procedures for the development of new modules. The existing modules will undergo continuing evaluation and updating.

CE 08

Capacity development in health research ethics: A unique and practical experience in a developing country

Adeyinka Falusi • University of Ibadan, Nigeria

Introduction | It is important to understand the economic standpoint of African countries to actualise meaningful research output in Africa. From November 2006 - December 2008, a project on strengthening the capacity of Research Ethics Committees in Africa was conducted in Nigeria. The project was to develop human capacity and provide facilities for functional ethics research in developing country setting such as Nigeria.

Methods | Important steps taken to achieve the goal of the project are as enumerated. Health Research Institutions were selected based on Needs Assessment criteria. Focus Group Discussions (FGDs) were conducted, followed by a Training of Trainers (TOTs) workshop at the University of Ibadan. Facilities were delivered to each site. Monitoring was done for a period of one year, followed by a step down mini-TOT workshop by each collaborating site.

Results | As a project outcome, it is observed that the FGD adequately assessed the needs, and 'Seed grant' facility served as an empowerment tool for the implementation of the new knowledge and skills gained. The monitoring encouraged active pursuit of goals and influenced ethics research collaboration. The step-down TOT seminar demonstrated the effectiveness of the training.

Discussion | The current project is unique as it effectively actualised and practicalised the TOT process. The project appraisal was followed by wide dissemination to research institutions, professional associations, NGOs and government parastatals throughout the country. The project contributes to research ethics by strengthening the manpower capacity, providing essential facilities and serving as a TOT-model for other funding agencies and ethics committees in Africa.



HP 01

Monitoring the incidence and severity of adverse drug reactions in patients with tuberculosis, and tuberculosis-HIV co-infection: A digital database approach

Michael Obaro • University College Hospital, Ibadan, Nigeria

Introduction | HIV complicates the treatment of tuberculosis. There is increased morbidity, risk of adverse drug reactions (ADRs), increased case fatality, and an increased recurrence of TB after treatment completion. While treatment guidelines are being refined, there is a need for structured and controlled data acquisition systems for recording and monitoring adverse drug reactions in these groups of patients.

Databases are good platforms for development of guidelines on the rational management and monitoring of patients with chronic illnesses.

Methods | A digital database was designed using EPI-INFO v. 6.0b and installed in a study laptop located at the chest clinic of the Medical outpatient department. The database was prospectively used to record clinical and treatment details of all newly diagnosed TB and TB-HIV patients from February 2007.

Results | Analysis of the database clearly showed the effects of HIV on TB and the evolution of ADRs with treatment. 53.4% of all the patients enrolled experienced ADRs. The majority (70.5%) of ADRs occurred in the first week of treatment. In both treatment groups (TB, TB-HIV), urine discoloration, peripheral neuropathy, and skin rash were the commonest reported ADRs. All cases of serious reactions occurred in the TB-HIV group with a poorer treatment outcome.

Discussion | The use of a prospective digital database made it easy to monitor therapy, the pattern and severity of ADRs, and clinical outcome in patients with TB and TB-HIV. The database was versatile, easy to deploy and use, adaptable, and promises to be a very useful source of data for monitoring therapy in these groups of patients.

HP 02

Treatment limitations imposed by antiretroviral drug resistance mutations: A comparison of initial regimens containing boosted PIS with those containing NNRTIS

Andy Mtambo • Simon Fraser University, Burnaby, Canada

Introduction | NNRTI-based combination antiretroviral therapy (ART) is mainly used as first-line treatment for HIV in resource-limited settings. However, failing NNRTI-based regimens may have greater potential to develop resistance, which may limit the effectiveness of second-line therapy, than boosted-PI based regimens.

Methods | We conducted a study of ART-naïve individuals aged ≥ 18 years who initiated ART consisting of 2 NRTIs and either an NNRTI or a boosted PI in BC, Canada. Development of resistance mutations between boosted-PIs and NNRTIs regimens was compared. Genotypic sensitivity scores (GSS) were calculated to determine the effects of these mutations on remaining active drugs typically available in resource-limited settings. We also examined the virologic outcomes after switching second line therapy.

Results | 1666 participants initiated ART; 818 (49.1%) with NNRTI-based regimens and 848 (51.9%) with PI-based regimens. Among those with resistance mutation after 36 months median follow up, 40.3% started with NNRTI and 27.3% with boosted-PI ($P < 0.001$). Participants on NNRTI-based regimens had lower median GSS (9.8 vs. 11.0; $P < 0.001$) than those in the PI group. The odds of achieving two consecutive suppressed viral loads after switching to second line was inversely associated with NNRTI use in initial ART regimen (OR: 0.32; 95% CI: 0.11–0.97) after adjusting for other factors.

Discussion | The use of NNRTI-based first-line regimens was associated with ART drug resistance patterns which limit the number of available second-line drug choices. These findings are consistent with some results from clinical trials, and may have policy implications.

HP 03

Antiretroviral drug resistance following the prevention of mother-to-child transmission of HIV in a group of Cameroonian women

Boghuma Titanji • University of Yaoundé, Yaoundé, Cameroon

Introduction | The prevalence of mutations associated with resistance to antiretroviral (ARVs) following prevention of mother-to-child transmission of HIV (PMTCT) in Cameroon remains unknown.

Methods | Forty consenting women who received nevirapine, zidovudine and/or lamivudine in different prophylactic regimens were enrolled in this cross-sectional study. HIV-genotyping was performed using an in-house assay at the International Laboratory Branch, CDC, Atlanta, GA, USA. Drug resistance mutations (DRM) were interpreted with the Stanford genotypic resistance algorithm and the IAS mutations database.

Results | Genotyping in the pol region was successful in 36 of the 40 plasma samples. Four (11.11%) had DRMs to two classes of ARVs: NRTIs (V118I and T215A) and NNRTIs (K103N and V106A). Phylogenetic analyses revealed that the predominant strain is CRF02_AG (66.7%), followed by subtypes A1 (11.1%), and F2 and G (each 5.6%) as well as 11.1% unclassifiable.

Discussion | ARV DR mutations are present in women who received PMTCT prophylaxis in Cameroon. This may have implications on the subsequent choice of ARV treatment in these women if these DR mutations are confirmed to be persistent and prevalent in large studies.

HP 04

Prevention of mother-to-child transmission of HIV-1: The effect of single dose carbamazepine on the pharmacokinetics of single-dose nevirapine

Eva P Muro • Tumaini University, Moshi, Tanzania

Introduction | A pilot study in HIV-negative healthy women showed that the nevirapine (NVP) elimination half-life was decreased with approximately 35% by the addition of a single dose (sd) of the hepatic enzyme inducer carbamazepine (CBZ). This intervention meant to reduce the development of resistance to NVP. We aimed to confirm whether the use of sdNVP-CBZ also decreases NVP half-life in pregnant HIV-infected women and their newborns.

Methods | HIV-positive, pregnant and antiretroviral treatment-naïve women were included. Women were randomised to receive either 200mg sdNVP alone or sdNVP (same dose) plus 400mg sdCBZ. Infants received 2mg/kg oral dose of NVP within 72 hours of birth.

Results | 52 women were evaluable for analysis. Mean (+range) NVP elimination half-life ($t_{1/2}$) in the women was 66 (36–117) hours in the sd-NVP arm and 57 (29–100) hours in the sdNVP-CBZ arm. Mean NVP concentrations at delivery (C_{del}) in the mothers was 1.36 (0.03–2.76) mg/l in the sdNVP arm and 1.44 (0.03–2.68) mg/l in the sdNVP-CBZ arm. Mean C_{del} in the newborns was 1.44 (0.05–4.54) mg/l in the sdNVP arm and 1.35 (0.05–6.89) mg/l in the sdNVP-CBZ arm.

Discussion | The study observed that addition of sdCBZ to sdNVP at onset of labor in HIV-infected pregnant women reduced the mean ($t_{1/2}$) of NVP by 14 %, which is less than what we have observed in healthy volunteers. These data should be confirmed in a larger data set and will be correlated to potential differences in the development of NVP resistance in the mothers.



HP 05

The auto induction of efavirenz metabolism and the resulting effect on the efavirenz steady state levels

Eliford Ngaimisi • Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania

Introduction | Despite good initial clinical recovery, some HIV-infected patients suffer from treatment failure following long-term ART. Efavirenz induces its own metabolism, thus reducing its plasma level by 20–40% after 10 days. Patients with efavirenz levels below 1µg/ml and above 4µg/ml are prone to treatment failure and CNS toxicity, respectively. We hereby report the long term efavirenz auto induction effect on the proportion of patients in the sub-optimal, normal and toxic concentration ranges.

Methods | A cohort of HAART naïve patients with CD4<200 cell/ml and normal liver and renal functional tests was recruited (n=63). The patients were initiated on the efavirenz-based HAART and 16hr post dose plasma efavirenz concentration and its metabolic ratio ([EFV]/[8-OH-EFV]) were determined at the 4th and 16th week.

Results | Most patients (62%) had lower plasma efavirenz concentration and metabolic ratio (73%) at 16th compared to their respective value at the 4th week ($P=0.001$). The proportion of patients with efavirenz concentration <1 µg/ml, between 1–4 µg/ml, and >4 µg/ml at 4th and 16th week were 8% vs 17%, 57% vs 67% and 35% vs 16% respectively.

Discussion | The proportion of patients with sub-therapeutic efavirenz plasma concentration at week 4 increased by more than 2 fold at week 16. While the proportion of subjects with above the normal plasma concentration range reduced by half after 16 weeks of efavirenz initiation. The results indicate that efavirenz auto-induction continues beyond the reported 10 days. This cumulative auto-induction may influence the long term HAART treatment outcome.

HP 06

Success of efavirenz-based HAART among HIV-positive Ethiopians with CD4 counts less than 200 initiating antiretroviral therapy

Wondwossen Amogne Degu • Addis Ababa University, Ethiopia

Introduction | The use of efavirenz (EFV) plus two NRTIs is recommended for initial therapy of patients with HIV-1 infection. The virological success rate of such regimen was not evaluated before among Ethiopian patients.

Methods | Evaluation was made on 129 treatment-naïve HIV-infected adult patients out of a cohort of 250 patients initiated with EFV-based HAART at baseline CD4 count of <200 cells/mm³. Viral load determinations were made in these patients at baseline and subsequently at weeks 12, 24 and 48. The proportion of patients who attained undetectable viral load at weeks 24 and 48 were analysed.

Results | Ninety-six patients (74%) had VL determinations until week 24. The median viral load level at baseline was 5.4 logs/ml. Three patients (3%) had VL below 500 copies/ml at baseline. Ninety-two patients (95%) had undetectable viral load at week 24. Out of 34 patients who had viral load data available at week 48, 33(97%) had undetectable viral load.

Discussion | The virologic efficacy of efavirenz based regimen in this selected group of patients is over 90%. This study verifies the success of efavirenz-based HAART as first-line regimen in Ethiopian patients.

HP 07

Challenges in PMCTC antiretroviral adherence in Northern KwaZulu-Natal, South Africa

Stephen Mephem • University of KwaZulu-Natal, Mtubatuba, South Africa

Introduction | Close adherence to antiretroviral regimens is crucial to maximise viral suppression and minimise the risk of resistance. However this may be difficult to achieve in areas of deprivation due to many reasons including poor social support, stigma, and alternative beliefs. This study examines the adherence challenges faced by HIV-infected pregnant women, many of whom are recently diagnosed, enrolled in a single site of the “Kesho Bora” PMTCT trial, a multicentre trial comparing triple therapy (ZDV/3TC/LPV/r) from 28 weeks until 6 months postpartum with short course therapy (ZDV/sdNVP) from 28 weeks until delivery, in women with a CD4 count of between 200 and 500.

Methods | Structured pill counting, adherence counselling, and clinic attendance data was recorded for all 100 randomised participants. Unstructured interviews were conducted by trained interviewers with 43 randomly selected women.

Results | Of 100 participants, the adherence of 32 was excellent (<2 pill discrepancy), 43 was average (<10 pill discrepancy), 19 was poor, and 6 did not bring their pills to be counted. HIV status disclosure to anyone was higher in those with excellent/average adherence than those with poor adherence (85% vs 42%); none of the women who did not return any pills for counting had disclosed to their partners. Excellent clinic attendance was similar between excellent/average and poor adherence groups (71% vs 68%). A qualitative assessment explored the issues underlying disclosure and adherence.

Discussion | This descriptive study provides an insight into the challenges faced by antenatal/postpartum women relating to disclosure, stigma, health beliefs, and domestic/social issues that impact on antiretroviral adherence.

HP 08

Pharmacokinetics of nevirapine in HIV-infected infants with body weight 3–6 kg taking pediatric fixed-dose combination tablets

Desiré Kabamba • University Teaching Hospital, Lusaka, Zambia

Introduction | We previously reported 12h pharmacokinetic (PK) profiles of nevirapine (NVP), stavudine and lamivudine in HIV-infected African children after taking fixed dose combination (FDC) antiretroviral tablets. However, this study included only 2 children weighing 3–6 kg. We therefore undertook PK evaluations in 13 additional children.

Methods | 15 HIV-infected children aged 1 month or older, eligible for antiretroviral therapy were enrolled and underwent a 12h-four point PK sampling session at least 4 weeks after starting treatment. NVP plasma concentrations and PK parameters were analysed.

Results | The mean NVP AUC_{0–12h}, C_{max} and C_{min} were 78.7 (30.2) mg/l, 8.1 (2.4) mg/l, and 4.9 (2.6) mg/l, respectively. These values are higher than reported in adults, but are 15–20% lower than observed previously in Zambian children weighing >6 kg. 27% of children had a subtherapeutic NVP C_{min} compared to only 5% of children weighing >6 kg (P=0.02). Whilst children aged <5 months appeared to have a higher risk for a subtherapeutic NVP C_{min}, numbers were too small to reach statistical significance (3/6 (50%) vs. 1/9 (11%); P=0.24).

Discussion | Exposure to NVP in African HIV-infected children with low weight taking FDC tablets appears on average adequate, but due to large inter-subject variability a relatively high proportion of children had subtherapeutic NVP C_{min} levels, particularly those aged <5 months. As these infants may be at risk for low NVP exposure for only a short time after initiating treatment, the clinical consequences of such low C_{min} may be minor, but require further evaluation.



HP 09

Microbial infections in HIV/AIDS women with abnormal vaginal discharge in Nigeria

Ngozi Otuonye • Nigerian Institute of Medical Research, Lagos, Nigeria

Introduction | This study focused on investigating HIV/AIDS women with symptoms of abnormal vaginal discharge in HIV Clinic of the Nigerian Institute Medical Research.

Methods | All clients who presented to the HIV clinic with symptoms of lower abdominal pain, itching and abnormal vaginal discharge were selected after obtaining written informed consent from them.

A total of 182 clients participated in the study. High vaginal/cervical swabs were collected, cultured and processed using standard microbiological methods. Sensitivity patterns of the isolates were determined. The characteristics of discharge, pH and Amine test with 10% KOH were used for bacterial vaginosis investigations.

Results | The age range of study population was between 20–45 years. Forty-nine had lower abdominal pain, eighty-seven had itching/irritation, forty-nine had sore/ blisters on the genitals. Microbial agents isolated were: *Candida* species 84, bacterial vaginosis 34, bacterial pathogens 57 and *T. vaginalis* 5. Twenty-nine bacterial isolates co-infected with *C. albicans*. About 3 patients had triple infection of bacterial vaginosis, yeast and bacterial pathogen. Most of the bacterial isolates were sensitive to ciprofloxacin and cefotriaxone antibiotics.

Discussion | Microbial infections in HIV/AIDS women was significant ($P < 0.05$). Vulvovaginal candidiasis accounted for the highest number of cases (46.1%). Other conditions that caused vaginal discharge included bacterial pathogens (30.9 percent), BV (18.7%) and *T. vaginalis* (0.5%).

HP 010

Development of vaginal probiotics to improve the vaginal microflora and reduce mother-to-child transmission of HIV

Rita Verhelst • Laboratory of Bacteriology Research, Ghent, Belgium

Introduction | The vaginal microflora is of utmost importance for the defence against a wide variety of infectious diseases. Currently, Ghent University, Belgium is developing a vaginal probiotic with an effective delivery system to restore and maintain the vaginal microflora with the aim to prevent and treat vaginal infections, and to lower HIV transmission.

Methods | Various clinical studies at Ghent University have been conducted in the development of new generation probiotics.

Results | So far, four clinical studies have been carried out showing that starch-based pellets are promising as vaginal delivery system for probiotics considering their efficient distribution in the vagina and their long retention time. A subsequent prospective clinical study with 18 female volunteers showed the delivery method was safe with regard to maintenance of vaginal pH and microflora. A recent study evaluated four potential probiotic strains among 16 volunteers. Two *Lactobacillus* strains, *L. jensenii* PB204 and *L. crispatus* PB128, showed to be most promising regarding safety, *in vivo* survival, and colonisation potential. Currently, a randomised placebo-controlled study to evaluate safety and efficacy of a combination of metronidazole with probiotics in women with bacterial vaginosis is ongoing.

Discussion | An effective probiotic and appropriate delivery system could play a role in the treatment of bacterial vaginosis and in restoring healthy vaginal microflora. If shown acceptable and effective, such interventions could be particularly relevant in sub-Saharan Africa, where the prevalence of BV is high. Lowering BV may have an impact on HIV as BV is a risk factor for sexual HIV transmission but more work is needed to elaborate this hypothesis.



MP 01

The efficacy of malartin / sulphadoxine-pyrimethamine (fansidar) combination in the treatment of uncomplicated *falciparum* malaria in a rural setting of Dibanda in Cameroon

Helen Kimbi • University of Buea, Cameroon

Introduction | The WHO now recommends the use of artemisinin-based combination therapy in the treatment of malaria in order to slow down the development of drug resistance against the parasite. The aim of this study was to assess the *in vivo* efficacy and tolerability of a combination of Malartin (artesunate) and Fansidar in the treatment of uncomplicated *falciparum* malaria in Dibanda, a rural setting in southwest Cameroon.

Methods | 197 subjects were recruited into the study, after meeting the inclusion criteria. They were then administered the appropriate doses of the drugs for 3 days and followed up on days 3, 7 and 14. A total of 174 subjects were successfully followed up.

Results | The drug combination was effective in clearing parasitaemia, fever and improving on the anaemia status of the patients. The overall success rate (ACPR) was 92.5% (161/174), and therapeutic failure was experienced in 7.5% (13/174) of the subjects. Parasite density decreased during the follow-up period in the different age groups and sexes. The prevalence of anaemia was 23.0 % at enrolment and decreased to 10.0 % on day 14. The drug combination was well tolerated as most of the side effects were self-limiting and disappeared by day 14.

Discussion | This study demonstrated that a combination of malartin and fansidar is effective and well tolerated in the treatment of uncomplicated *falciparum* malaria in this part of Cameroon. This confirms that artemisinin derivatives remain very potent and rapidly acting antimalarials to which the malaria parasite has not yet developed resistance.

MP 02

Clinical trial of Pr259CT1 versus artesunate-amodiaquine (AS-AQ) in patients with uncomplicated malaria in the Democratic Republic of Congo (DRC)

Tona Lutete Gaston • University of Kinshasa, Democratic Republic of Congo

Introduction | Besides *Artemisia annua* extract, other plant extracts used for the treatment of malaria in traditional medicine are still candidate for the development of active medicines from plants for the treatment of uncomplicated malaria. The objective of this study is to assess the efficacy of the herbal medicinal product PR259CT1, a standardised extract from a medicinal plant formulated in capsules, in humans with uncomplicated malaria.

Methods | All patients were selected according to the criteria defined by WHO guidelines (2003). Malaria was detected by medical examination using a thick blood film stained with Giemsa. Only patients with asexual parasites/ μl >500 of parasitaemia were selected. A total of 32 patients/group were treated with a drug regimen of two 500 mg capsules (3x/day, each 8 h) for three days, followed by one 500 mg capsule (3x/day) the four next days during meals under the supervision of a medical team. Patients were followed up until the 14th day (WHO, 2003).

Results | Results from the clinical examinations did not show a significant change in values of vital signs, ECG, biochemical and haematological parameters. All values obtained were in the normal range. The study showed a clear significant decrease of parasitaemia in patients treated with PR259CT1 (90.3% efficacy) versus As-Aq (96.9% efficacy). PR259CT1 was better tolerated than the AS-AQ mixture since more side effects were observed for the latter.

Discussion | The results pointed out that the herbal medicinal plant PR259CT1 can be considered a promising candidate for the development of a medicine for the treatment of uncomplicated malaria.



MP 03

Safety and tolerability evaluation of PR259CT1 in healthy volunteers: A Phase I clinical trial.

Mesia Kahunu Gauthier • University of Antwerp, Belgium

Introduction | PR259CT1 is a standardised 80% ethanolic extract from a medicinal plant widely used in traditional medicine in the Democratic Republic of Congo for the treatment of symptoms of uncomplicated malaria. Results from the *in vitro* and *in vivo* antiparasmodial activity studies were promising whereas toxicity studies in mice showed a positive risk-benefit effect. Before its use in Phase II clinical trial, the extract was submitted to Phase I to evaluate its safety and tolerability in healthy volunteers.

Methods | Capsules containing 500 mg of a standardised extract were formulated. In order to study the potential safety and tolerability of PR259 CT1, fifteen healthy male volunteers of 18–40 years having a bodyweight of 50–70 kg were enrolled in the study. They were treated with a drug regimen of two 500 mg extract containing capsules three times daily (each eight hours) for 7 days in the Centre de Santé de l'Université de Kinshasa. The volunteers were followed by a clinical team composed of doctors, pharmacists and nurses.

Results | After 7 days, all volunteers were submitted to different clinical examinations. Results indicated that values of vital signs, ECG, biochemical and haematological parameters were found in their respective normal ranges. No significant changes were observed. The most common adverse events observed were increase of appetite (33%), headache (20%) and nausea (20%). Other side effects included insomnia, somnolence and asthenia (7%).

Discussion | These results indicate that PR259CT1 presents a significant safety pattern and tolerability in healthy volunteers. Consequently, a Phase II clinical study would be envisaged.

MP 04

A prospective, open-label safety and pharmacokinetics Phase I study of methotrexate as an antimalaria drug in healthy Kenyan adults

Ahmed Abdallah • KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya

Introduction | Methotrexate is an analog of folic acid commonly used in high doses of 5,000 to 12,000 mg a week in the treatment of diverse malignancies. Preclinical studies have shown that methotrexate is potent against *Plasmodium falciparum* malaria, including multidrug resistant isolates. Two small clinical trials carried out in the 1970s indicated that a dose as low as 2.5 mg per day for 3 to 5 days could treat malaria, however this information was not exploited further because of concerns over toxicity. However since this time methotrexate has been used very widely at doses of less than 30 mg a week for several years in adults and children in the treatment of rheumatoid arthritis. There is now considerable new data supporting the safety and tolerability in this lower dose.

Methods | We are conducting a Phase I trial in Nairobi to assess the pharmacokinetics and safety of the low dose of 5 mg methotrexate a day for 5 days in 25 healthy adult Kenya volunteers.

Results | The trial was ongoing at abstract submission; results to be presented.

Discussion | We need a constant pipeline of new antimalarial treatments to keep ahead of possible development of resistance to existing therapies. There is a need for cheap and easily administered drugs. We suggest that methotrexate should now be re-evaluated as a potential new treatment for malaria. As a starting point in the drug development process we present this Phase I trial with a view to assessing a 3-day treatment in Phase II clinical trials in Kenyan children next.



MP 05

Clinical efficacy of amodiaquine + artesunate (AQAS) and artemether-lumefantrine (AL) in children treated for uncomplicated malaria in the northern region of Cameroon

Innocent Mbulli Ali • University of Yaounde, Cameroon

Introduction | Attributable drug resistant malaria is still a challenge in Cameroon and the knowledge of mechanisms of drug failure underpins the design of appropriate strategies for malaria control. This study was designed to assess the efficacy and safety of amodiaquine/artesunate (AQAS) and artemether-lumefantrine (AL), currently first-line drugs in Cameroon, in children with uncomplicated malaria in northern Cameroon.

Methods | The WHO 2004 criteria for classifying treatment outcomes was used to assess clinical response to treatment with AQAS and AL after 28 days of follow up in children (6–120 months) fulfilling eligibility criteria. Recrudescence was distinguished from re-infection by polymerase chain reaction. Microsoft Excel and Stata version 8 was used to evaluate data and look for significance between outcome measures.

Results | PCR corrected cure rates stood at 98.6% for AQAS and 97.3% for AL. These results show a non-significant superiority of AQAS over AL. One death that occurred during the study was not drug-related.

Discussion | Artemisinin-based combinations are efficacious and well tolerated in northern Cameroon.

MP 06

Larvicidal properties of Simalikalactone D from *Quassia africana*

Woqvan Sama • University of Ibadan, Ibadan, Nigeria

Introduction | Botanical and microbial insecticides have been increasingly used for mosquito control because of their efficacy and documented non-toxic effects on non-target organisms. The discovery of new insecticides is imperative because of the development of resistance by the mosquitoes to the readily available insecticides. The aim of this study was to isolate and characterise compounds from *Quassia africana* that are toxic to *Anopheles gambiae*.

Methods | The methanol extracts of the leaf, stem and roots of *Quassia africana* were tested against forth instar larvae of *Anopheles gambiae*. The root extract was partitioned into hexane, chloroform and ethylacetate and resulting extracts screened for larvicidal properties. The most active extract was subjected to column chromatography and fractions obtained screened for larvicidal properties. The fraction with the highest bioactivity was subjected to repeated column chromatography and isolated compounds evaluated for potential toxicity to *Anopheles gambiae* larvae. Experiments were accompanied by controls. The active compound structure was elucidated using spectroscopic techniques.

Results | The root extract showed strongest activity ($LD_{50}=75 \mu\text{g/ml}$). The chloroform soluble fraction obtained after partitioning the crude extract into solvents based on polarities was the most toxic. Further bioactivity-guided chromatographic separation of the chloroform fraction of the root extract led to the identification and isolation of a simalikalactone D as the larvicidal compound in *Q. africana* ($LD_{50}=2 \mu\text{g/ml}$).

Discussion | *Quassia africana* may serve as a source for development of malaria vector control compounds.



MP 07

Epidemiological impact of insecticide resistance on malaria control in Nigeria

Isaac Oyewole • Babcock University Ilisan Remo, Nigeria

Introduction | Malaria still kills more people than HIV/AIDS or any other killer disease. Yet, this is a disease that can be controlled by eradicating mosquitoes. The use of insecticide treated mosquito nets (ITNs) or indoor residual spraying (IRS) is an important component of this strategy.

Methods | In order to evaluate the pyrethroid resistance status of the local anopheline species, larvae collected from five ecological zones in Nigeria were reared to adulthood in a standard insectary. Susceptibility tests were conducted using standard WHO procedures, diagnostic kits and test papers (WHO, 1998). PCR assays were used for the identification of the species and for characterisation of the *kdr* allele.

Results | Samples from all the zones were susceptible to the diagnostic doses of insecticides tested. However, pyrethroid resistance mosquitoes were recorded in the forest-mosaic and Guinea savanna zones. The *kdr* frequency and mortality rates were lower in permethrin, indicating a level of resistance to this insecticide. Overall, *kdr* frequency was low in all the zones ranging between 37 and 53%.

Discussion | This study established the emergence of pyrethroid resistance anopheline species in Nigeria and the need for continuous monitoring in order to guarantee the success of ITNs and IRS as malaria control measures.

MP 08

Pregnancy outcomes in various malaria endemicities over a six-year period (2002–2007): A Rwandan case

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Introduction | Malaria has a negative effect on the outcome of pregnancy. It causes low birth weight, premature birth and still births. In Rwanda however, malaria has been decreasing for the last 6 years (2002–2007) depending on the area, from high to low transmission.

Methods | In this study we analysed if any association between the obstetric indicators (birth weight and outcome of pregnancy) and indicators of malaria endemicity (prevalence and incidence) can be detected in the national data of Rwanda, using associations over time (2002–2007) and space. Birth outcome data from 12053 patients was collected from maternity registers of 11 different health centres that were located in different malaria endemic areas. In addition malaria data for the same regions was collected from the national malaria control programme and both data sets were compared for association.

Results | A significant increase of birth weight over the years was found ($P < 0.001$) and birth weight was found to be different at different seasons of the year. An increase of 27.6 g every year was noted, however pregnancy outcomes and especially birth weight seems not to be associated with malaria. Overall, a statistically significant decline of the risk of still birth was found with increasing age of mothers ($P = 0.041$) and a decline over the years of premature delivery ($P = 0.010$) and still birth ($P = 0.036$) was observed.

Discussion | In contrast to many other studied areas, in Rwanda pregnancy outcome and especially birth weight seems not to be directly influenced by malaria, although malaria incidence overall has declined and birth weight has on average.



TP 01

Evaluation *in vitro* of some Nigerian medicinal plants for anti-*Mycobacterium* activities

Dorcas A Fadare • University of Ibadan, Nigeria

Introduction | Among communicable diseases tuberculosis is the second leading cause of mortality with the figure rising to 2 million people each year. The majority of the cases and death occurred in Asia and Africa. The emergence of drug-resistant strains of *Mycobacterium tuberculosis* and the demerits of the available anti-tuberculosis chemotherapies have prompted the search for active molecules and/or structural prototypes for the development of new anti-tuberculosis agents from natural sources.

Methods | Eight plants were selected from an ethnobotanical survey of indigenous flora for the treatment of tuberculosis and other respiratory diseases in South Western Nigerian. Plant parts were obtained from Ibadan, Nigeria. Air-dried plants were extracted by maceration with methanol (70%) for 72 h. Extracts were filtered and concentrated to dryness under reduced pressure. Antimycobacterial activities of the plants were determined using the broth micro-dilution method after incubation for six weeks.

Results | At the lowest concentration of 0.19 mg/ml, the growth of *M. tuberculosis* was inhibited completely by four out of the eight plants screened in the study, while the other four plants did not show any inhibition towards the organism.

Discussion | The overall results of the antimycobacterial activity of the plants revealed that some of them might be of value. They could be used as a guide in the continuing search for new natural products as therapeutic agents to control TB. The study justifies the traditional use of some of the plants

TP 02

Towards understanding the mechanism and safety of nano drug delivery system for tuberculosis treatment

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Introduction | The field of drug development experiences very low success rates with regards to drugs that enter the market. These shortfalls are due to factors such as toxicity of the therapeutic compounds, low solubility leading to lowered bioavailability and thus reduced efficacy. These challenges are even more pronounced in poverty-related diseases, such as tuberculosis and malaria. This has led to the development of novel and more effective drug delivery technologies, such as nanoparticulate systems. However since this technology is new, further understanding of the delivery systems is still required prior to entry into the market.

Methods | PLGA nanoparticles which are currently extensively used in drug delivery, particularly for TB, were prepared and characterised based on size, zeta potential and morphology. PLGA nanoparticle uptake was analysed in CaCo-2 cells via confocal microscopy where particle uptake was illustrated. Subsequent to oral administration of fluorescently labelled PLGA nanoparticles to Balb/C mice, fluorescence detection of the particles was performed.

Results | These particles were detected via FACS in the macrophages of the peritoneum cell exudates. The particles were further detected in all tissues analysed. When histopathology assays were conducted on all tissues, i.e. spleen, lungs, kidney, liver spleen, heart and the brain no lesions were observed.

Discussion | The *in vivo* uptake of the particles by cells as well as good biodistribution will enable improved bioavailability of the encapsulated drugs, reduce side effects and improve the efficacy of the drugs. Furthermore, this study has illustrated that PLGA nanoparticles are safe for use in drug delivery applications.



CP 01

Assessment of GCP compliance of clinical research sites in developing countries to determine target areas for capacity building

Sylvie Kwedi • Aeras Global TB Vaccine Foundation, USA

Introduction | Timely and targeted quality assessments help guide decision-making for more effective and efficient resource allocation for capacity building efforts in resource-limited environments. For clinical research sites in developing countries, it is critical to build infrastructures that ensure the protection of research volunteers and the soundness of the data. Quality assessments can be used as a tool to focus capacity building efforts in these settings.

Methods | In 2007–2008, independent quality assessments were conducted at 3 sites conducting large epidemiology cohort studies in Africa and India. The assessments aimed to determine compliance in accordance with ICH GCP guidelines and other regulations. Findings from each report were compiled and grouped into 8 categories. 3 main areas of noncompliance were identified and then linked to project planning, resource allocation, and timeline development for each site. Root cause analysis was conducted to determine the basis for noncompliance.

Results | The majority of the findings related to documentation (32%), informed consent (21%), data management (21%) and others (26%). The root cause analysis results showed that training and other capacity strengthening means (i.e. data management infrastructure, information technology capabilities, etc) are direly needed to improve compliance.

Discussion | To better direct resources for capacity building at clinical research sites in developing countries, it is recommended that quality assessments are conducted at these sites. Results can be used to drive programmatic planning for better outcomes and enhanced capacity for clinical research.

CP 02

Ethical review of clinical trials run by northern sponsors in Africa

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Introduction | Many international guidelines recommend that clinical trials conducted in developing countries by a Northern sponsor be submitted to ethical committees (EC) both in the countries where the trial is conducted and in the country of the sponsor. However, no laws and regulations currently enforce such a double ethical review. The objective was to assess the impact of double ethical review.

Methods | We carried out an EDCTP-funded trial, evaluating 4 artemisinin-based combinations for treating uncomplicated malaria in children. The trial, sponsored by the Institute of Tropical Medicine, is conducted in seven African countries. The protocol and amendments were submitted to the EC of Antwerp University Hospital and to the ECs in the study countries. All ECs received information on Serious Adverse Events (SAEs) on an ongoing basis.

Results | The double ethical review resulted in complementarities of comments, with Northern ECs stressing such aspects as study insurance and alternatives to participation, while Southern EC often asked clarifications on treatments, reimbursement to patient etc. The ethical review was done in a serial manner, first the EC of the sponsor followed by the ECs of sites, so delaying the overall approval timelines. No ECs ensured timely follow-up of SAEs.

Discussion | The double ethical review appeared beneficial and complementary, increasing protection of subjects and helping to prevent double-standard practices. However, the process could be more efficient and participatory if ethical review was done simultaneously (in parallel), by promoting interaction among the concerned ECs, and if a better follow-up was ensured after initial approval.

CP 03

Convergent ethical issues in HIV, tuberculosis and malaria vaccine trials in Africa

Nicole Mamotte • WHO/UNAIDS African AIDS Vaccine Programme's Ethics, Law and Human Rights Collaborating Centre, South Africa

Background | Globally HIV, tuberculosis (TB), and malaria account for 5.6 million deaths annually (Hotez *et al.*, 2006). Malaria and TB complicate the effective control of HIV, due to their shared risk factors, geographic overlap and co-infection, particularly in sub-Saharan Africa. Despite the variety of prevention, treatment and care initiatives in existence, significant challenges in curbing these diseases remain. The development and distribution of vaccines that are safe, effective and affordable is critical to reduce morbidity and mortality. However conducting malaria, TB and HIV vaccine trials in developing countries is ethically complex. These ethical complexities are likely to increase when malaria, TB and HIV vaccine trials are conducted simultaneously in developing countries, or in populations affected by all three diseases.

Methods | A consultation was hosted by the African AIDS Vaccine Programme (AAVP) Ethics, Law and Human Rights Working Group (ELH) to bring together key stakeholders from HIV, TB, and malaria vaccine initiatives to explore the convergent ethical issues in the three fields and promote and impact cooperation, networking and resource sharing in Africa.

Results | The consultation revealed that there is much common ground and scope for convergent work between stakeholders in the three fields. The convergent ethical issues identified during the consultation have been classified into a popular ethical framework (*cf* Emanuel, Wedler, Killen and Grady, 2004) and several recommendations on the way forward have been made.

CP 04

The challenges of developing viable frameworks for health research in Nigeria: The successes so far

John-Moses Maduabuchi • Association for Good Clinical Practice in Nigeria (AGCPN)

Nigeria is the most populous nation in Africa and certainly the most credible gateway to West Africa. With a population reaching 150 million, it is ranked the eighth most populated country on earth. Building sustainable health research capacity in Nigeria had major challenges: inadequate individual capacity, insufficiency of funding, lack of awareness and political will among policy makers/regulatory bodies etc. These problems have been the focus of several stakeholders, especially those galvanised under the auspices of the Association for Good Clinical Practice in Nigeria (AGCPN).

Considerable progress has been recorded in aspects of advocacy, public enlightenment and training especially in Bioethics, Human Subject Protection, Responsible Conduct of Research, GCP, Quality Management and other GXPs (Good Practice quality guidelines and regulations). AGCPN has successfully executed online trainings powered by the Collaborative Institutional Training Initiative (CITI) in addition to continuous onsite trainings. More landmark achievements include the setting up of a clinical trial facility at Lagos by Glaxo Smith Kline (GSK), and construction of a research laboratory at NIPRD with funding from National Institutes of Health (NIH). The training of over 350 Clinical Research Personnel over the years and a 30-member faculty on GCP are part of the achievements of AGCPN. This pool of GCP faculty will also help in promoting research in other parts of Africa.

Recently, Clintrid Pharma Services conducted a country-wide survey on trial sites and personnel and also concluded some site trainings. The Society of Quality Assurance (SQA) was also established in 2008, through the efforts of AGCPN, ZETA-12 and INBR. Today, Nigeria is ready for multi-centre clinical trials.

Universal standards for clinical trials in practice

Background

The ‘Switching the Poles’ Clinical Research Network brings together researchers from Belgium, Burkina Faso, Cambodia, Cuba, DRC, Indonesia, Nepal, Peru, Uganda and Zambia. It has the aim of jointly developing capacity, tools and procedures to apply universal standards for clinical research in resource-poor settings. The Network was officially launched in 2008 as part of a programme for institutional capacity strengthening funded by the Belgian Development Cooperation and is coordinated by the Antwerp Institute of Tropical Medicine. Its motto is ‘Switching the Poles’, and its explicit aim is to transfer not only expertise but also resources and decision-making to the South. Several network partners participate in EDCTP-funded projects, so far mainly in the field of malaria.

This satellite meeting focuses on the challenge of setting and implementing appropriate standards in externally funded clinical research projects, carried out in resource-constrained settings.



Programme

The gap between standards and resources: Lessons learned through the EDCTP-funded ABC malaria trial

*Ambrose Talisuna • Medicines for Malaria Venture (MMV)
Representative in Africa, Kampala, Uganda*

Double ethical review of externally funded clinical research: From recommendations to regulatory enforcement or accreditation

*Anne Buvé • Department of Microbiology, Institute of Tropical Medicine Antwerp, Belgium
Pascal Lutumba • Institut National de Recherche Biomédicale Kinshasa, and University of Kinshasa, Democratic Republic of Congo*

Informed consent and decision-making in vulnerable populations

Tinto Halidou • Institut de Recherche en Sciences de la Santé (IRSS) / Centre Muraz, Burkina Faso

Responsibilities of Northern sponsors of non-commercial clinical trials in resource-constrained countries: Gaps and challenges

Bruno Gryseels • Institute of Tropical Medicine Antwerp, Belgium

Please note: packed lunches will be available in the Mahale XL room for participants to this satellite meeting

PLENARY SESSION I

The Global Picture (cont.)

The need for clinical trials and EDCTP

14:00–15:45

Victoria Hall

CHAIRS

Dr Andrew Kitua

Dr Steven Shongwe

Dr Rafael De Andrés Medina

14:00–14:15

African commitment to health research: The case of the East African Community

Amb. Juma V. Mwapachu • Secretary General, East African Community, Arusha, Tanzania

For a period of over three decades between the years 1947 and 1977, institutional cooperation among the East African Community (www.eac.int) Partner States in the field of regional health research, health policy and practice, among other fields was facilitated through the defunct East African Medical Research Council (EAMRC) that was based in Arusha, Tanzania. However, with the collapse of the former East African Community in 1977, the regional health research organization set-up, including the East African Medical Research Council (EAMRC), also came to an end. This resulted in alternative national health research administrative set-ups being instituted in each of the three former Partner States to cater for each country's research needs. These institutions are the Kenya Medical Research Institute (KEMRI), Uganda National Health Research Organization (UNHRO) and the National Institute for Medical Research (NIMR) in Tanzania.

Following signing of the new Treaty for the Establishment of the East African Community (EAC) on 30 November 1999, the five EAC Partner States have resolved to cooperate with one another in the area of health, social and cultural fields and, in particular, in the field of health research, health policy and practice pursuant to Article 118 of the Treaty.

In this regard, the East African Community (EAC) has re-established regional institutional mechanisms to foster health research and the application of results of such research for policy formulation and improving health practice and delivery. One such mechanism is the Regional East African Community Health (REACH)-Policy Initiative. At the same time; the EAC is presently in the process of establishing an East African Health Research Commission. Once fully operationalised, the East African Community Health Research Commission (EACHRC) will be a body corporate charged with coordination and mapping of regional health agenda in collaboration with Ministries of Health and research institutions in the Partner States. However, the regional hub and Country Nodes of the REACH Policy Initiative will continue to add value to the operations and activities of the East African Community Health Research Commission (EACHRC) especially



with regard to the development of sustainable regional institutional mechanisms necessary to address health research issues with focus on sustainable health care delivery, and translation of health research findings into policy and practice.

These institutional developments attest to EAC's commitment to actively participating in fostering international, continental, regional and national collaboration in strengthening health research systems and knowledge management as part of Africa's strategy to attain the health-related United Nations' Millennium Development Goals (MDGs) and Targets as well as the accelerated continental fight against HIV/AIDS Tuberculosis, and Malaria in line with the Abuja Declaration of the Special Summit of the African Heads of State and Government held at the International Conference Centre in Abuja, Nigeria from 2 to 4 May 2006.

PLENARY SESSION I

The Global Picture (cont.)

The need for clinical trials and EDCTP

14:00–15:45

Victoria Hall

CHAIRS

Dr Andrew Kitua

Dr Steven Shongwe

Dr Rafael De Andrés Medina

14:15–14:30

**Higher education and capacity development as a means to
fight poverty and poverty-related diseases**

Ambassador Staffan Herrström • Swedish Embassy, Tanzania



14:30–14:45

Health Research Initiatives in West Africa

Dr Placido Cardoso • Director General, West African Health Organisation (WAHO)

The West African Health Organization (WAHO) is the health-specialised institution of the Economic Community of 15 West African States (ECOWAS). The objective of this communication is to highlight the health research initiative in the ECOWAS region.

We conducted a review of literature and visited the websites on health research. In West Africa, there are many health research initiatives on HIV/AIDS, tuberculosis and malaria, nutrition, epidemic diseases and neglected tropical diseases. The types of research conducted are biological research, clinical trials, epidemiological study, interventions trials, and social studies. The leaders of these major research projects are researchers located in Europe or America. The major funders of these researches are located outside the region.

We found multi-site research taking place in many West African countries. For example on 20 July 2009 in the WHO International Clinical Trials Registry Platform (ICTRP) search portal, we found 64 clinical trials actually in recruitment Phase in the 15 West African countries. The main diseases trialled are malaria, tuberculosis, neglected tropical diseases, maternal and child health. The main funders for these trials are National Institute of Allergy Disease, the Gates Foundation, African Malaria Network, Bandim Health Project, European Union and pharmaceutical industries. The West African Health Organization in its 2009–2013 strategic plan created a regional fund on health research.

In the West African region, there are many health research initiatives. A better exchange between researchers and translation of results into policy briefs for decision makers should contribute to improve the health of the population.

PLENARY SESSION I

The Global Picture (cont.)

The need for clinical trials and EDCTP

14:00–15:45

Victoria Hall

CHAIRS

Dr Andrew Kitua

Dr Steven Shongwe

Dr Rafael De Andrés Medina

14:45–15:05

Health research initiatives in the Central Africa Region

Dr Marlyse Peyou Ndi • Head of Studies, Planning and Training, OCEAC

The Organisation of Coordination for the Fight against Endemics in Central Africa (OCEAC) is the specialised public health institution of the Central African Economic and Monetary Community (CEMAC) which comprises 6 member states: Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea, and Gabon.

OCEAC's missions are to (1) coordinate policies and health actions, (2) participate in the training of health personnel, (3) coordinate research and the synergy of applied research carried out by national institutions (4) work on expertise missions in different fields of health sciences, (5) contribute to the promotion of health; and (5) bring support in sanitary emergency interventions.

The work focuses on its priority themes: HIV/AIDS, tuberculosis and malaria (diseases evitable by vaccination), African Trypanosomiasis and Hemorrhagic fevers (Ebola). This led to the development of several regional health research initiatives such as:

- RESNET: the HIV Drug Resistance surveillance (HIVDR) network which studies and evaluates the prevalence of transmitted HIVDR among recently infected patients, and assesses the feasibility and challenges for the implementation of generic protocols in Central African countries
- PPSAC: the HIV/AIDS and other sexually transmitted diseases prevention project which uses social marketing, information, education and communication, and studies different ways to increase the availability and use of condoms at lower prices
- CANTAM: the Central African Network on Tuberculosis, HIV/AIDS and Malaria for the conduct of clinical trials. Its goals are to develop human resources skilled enough to conduct safe clinical trials, to strengthen laboratories in performing relevant tests related to clinical research, to strengthen ethical review boards and regulatory authorities and to collect baseline data on future participants in clinical trials.



15:30–15:45
Discussion (Q&A)

15:05–15:30

SADC Health and HIV and AIDS Research Agenda

Steven Sianga • SADC Director of Human and Social Development

The Southern African Development Community (SADC) is a Regional Economic Community of 14 Member States. The main goal for SADC goal is to further socio-economic cooperation and integration as well as political and security cooperation among its members.

The SADC region continues to bear a disproportionate burden of HIV infection with HIV prevalence co-existing with TB and growing incidence of malaria. This places greater imperatives for the development of new research strategies and technologies to prevent the further spread of resistance and minimise the impact on the socio-economic status of the people. The magnitude of the impact of the three diseases and the limited resources especially due to the economic crisis, call for a more focused and evidence based response in the region. The long-term response to HIV and AIDS and other diseases of public health importance depends on progress made in research and biotechnological advancement.

SADC Secretariat and Partners have realised the importance of evidence based responses and the need to coordinate research in order to minimise duplication and maximise resources. This realisation is translated into a SADC Health Research Agenda which was developed in order to provide a regional framework for cooperation, sharing of experiences, collaboration in research and development that is aimed at improving health provision, planning and management and prevention of diseases. The Research agenda has identified priority areas for research in the SADC region and also defines roles and responsibilities. It has further put in place structures of research and monitoring and evaluation.

16:15–16:30

The EDCTP Networks of Excellence: An overview


Dr Andrew Kitua • WHO/TDR and Chairperson DCCC

Networks of Excellence were created as an African felt strategy to provide better research enabling environment, career opportunities, balanced sub-regional spread of capacities, raise the standards to forge better and equal partnership with the north, and allow partners to grow with complementing capacities that support each other.

An open was launched call inviting sub-regional institutions to partner together into single Networks of Excellence, linking institutions at different levels of development, allowing cross-mentorship and the creation of complementing expertise and competences among the partners. Each application was required to demonstrate how these conditions were being pursued and to demonstrate activities that would strengthen less endowed members of the partnership. One network per sub-region would be selected.

Central Africa was first winner fulfilling all the requirements instantly, while other regions struggled to coalesce. The DCCC acted decisively nudging them in the right direction. Finally four sub-regional networks have been established and some have secured additional support from their economic groups. The model uniquely integrates research capacity building and networking within African-owned and -led institutions. It is being emulated by reputable research funding agencies and is highly quoted as a model to emulate.

Involving institutions recognised by their governments and strengthening their ability to attract complementary research funding assures sustainability. A research-enabling environment is being created and career development of African scientists enhanced: a win-win situation to both south-south and north-south partnerships. African scientists can enjoy fellowship awards assured of facilities to go back and work in.



16:30–16:45

The Central Africa Network of Excellence on Clinical Research (CANTAM)

Prof. Francine Ntoumi • CANTAM Coordinator

In response to an EDCTP call for the support of regional Networks of Excellence in 2007, institutions from Cameroon, Congo, Chad and Gabon came together with the support of the University of Tübingen, the Multilateral Initiative on Malaria and OCEAC to establish the Central Africa Network on Tuberculosis, HIV/AIDS and Malaria (CANTAM) for the conduct of clinical trials. The strategy of CANTAM is to develop clinical research in the weakest institutions through the development or strengthening of collaborations and mentorship programmes with the regional established institutions to carry out future HIV/AIDS, tuberculosis and malaria interventions in compliance with ICH/GCP standards.

In the first implementation phase, a consultative meeting on tuberculosis financially supported by French institutions was convened in Brazzaville. Invited experts from Africa and Europe assisted regional TB groups in the development of a relevant strategy to initiate baseline studies and training programmes in Congo and Cameroon. Additionally, CANTAM is actively networking with African organisations which have already developed educational and training programs on clinical trials. Open calls for the recruitment of trainees have been launched and the groups are in the process of selecting the best students who will be enrolled in sandwich programs with African and/or European partners.

A poor research environment, lack of research culture in some cases and the great expectations from junior researchers and local authorities are part of the challenges that CANTAM will have to overcome so as to be able to move ahead; strengthening and not building local capacities.

16:45–17:00

**Harmonisation and strengthening of regulatory activities
in sub-Saharan Africa**

*Dr Liliana Chocarro • WHO/FCH/IVB/QSS Regulatory
Pathways*

Strengthening regulatory oversight of clinical trials in sub-Saharan Africa is key to ensure the quality of the clinical data for registration of priority vaccines. The African Vaccine Regulatory Forum (AVAREF) has been established as a platform to foster communication among regulators and ethics committees in the region, and between regulators from countries where vaccines are produced and from countries where trials take place. The forum serves to identify common challenges, and find solutions that will be sustainable through capacity building activities.

AVAREF was the result of the consensus of regulators of countries that are target for clinical trials of priority vaccines, to work together to deal with challenges relevant to the regulation of vaccine clinical trials. Its first plenary meeting took place in 2006 with the participation of representatives from regulatory authorities and ethics committees from 19 African countries. AVAREF functions through an annual plenary meeting and satellite activities to build capacity in participating countries, such as the joint review of clinical trial applications of meningitis A and malaria vaccines and joint inspections of trial sites, all this with the support from organisations like EDCTP and PATH.

AVAREF members endorsed an initiative that aims to integrate ethical review, regulation and registration of clinical trials in Africa. The Pan African Clinical Trial Alliance (PACTA) intends to create a shared interface among regulatory authorities, ethics committees and the Pan African Clinical Trial Registry (PACTR) to facilitate transparency and the highest standards for clinical trials in Africa. Harmonisation of regulatory procedures for submission, approval and inspection of clinical trials are an integral component of this project.



17:00–17:15

Mapping of ethics review and trial regulatory capacity in sub-Saharan Africa: The MARC project

Prof. Carel IJsselmuiden • Director, Council on Health Research for Development (COHRED)

Health research in general and clinical trials in particular are key to development, health and health equity in Africa. It builds evidence, supports innovation and creates new solutions, technologies and drugs. The conduct of clinical trials is complex - not only in terms of products being tested, but also in balancing scientific requirements with ethical obligations to study participants and to populations in which research is conducted. The ability to ethically review of study protocols for drug trials is a core competence of responsible research systems. Each country should have at least one research ethics committee (REC) able to ethically review proposals for clinical trials – and be able to do so effectively and efficiently.

Mapping African ethics Review Capacity (MARC) is an EDCTP-funded project aimed at creating an interactive map of (1) RECs, (2) programmes to increase capacity for ethics review, and (3) drug regulatory mechanisms in all countries in which EDCTP funds trials. The mapping is done on COHRED's Health Research Web platform (<http://hrweb.cohred.org>) which encourages RECs to upload and manage their own information aiming to generate a 'self-updating' resource. Following initial mapping, MARC will team up with other initiatives in Africa to facilitate an African debate about standards, accreditation and capacity building.

MARC started in January 2009 as a joint effort between COHRED and SARETI, the South African Research Ethics Training Initiative at the University of KwaZulu-Natal, and will last at least until December 2011. This paper provides the first report on progress in all three areas of the MARC project.

17:15–17:30

Transitioning from ATM to PACTR: Leading the way in prospective clinical trials registration in Africa

Amber Abrams • South African Cochrane Centre, Cape Town, South Africa

The Pan-African Clinical Trials Registry (PACTR, www.pactr.org) is a prospective clinical trials registry based at the South African Cochrane Centre and supported by EDCTP. This African-initiated registry publicly displays the 20-item minimum data set advocated by the World Health Organization (WHO). In August, 2009 PACTR was recognised as a WHO Primary Registry.

We searched the PACTR on 26 August 2009, and will present a descriptive and spatial analysis of registered applications.

Since May 2007 there have been 25 applications: 11 are registered trials, 10 applications were ineligible and 4 are incomplete. The focus of the registered trials are HIV/AIDS (6), TB (3), Malaria (1) and co-morbid TB and HIV/AIDS (1). Five trials are single-centre (Gambia 1, Kenya 1, Tanzania 1, South African 2); six multi-centre trials have sites in 11 African countries (Burkina Faso, Ethiopia, Gabon, Mozambique, Nigeria, Rwanda, South Africa, Tanzania, Uganda, Zambia, and Zimbabwe) and one in India. Principal investigators are from SA (4), the UK (3), Belgium (1), Netherlands (1), Sweden (1) and Tanzania (1). Trial funders are inter-government agencies, non-government organisations, governments, universities and partnerships between these. Nine trials had prior ethics approval. Of the HIV/AIDS trials, five focus on prevention (MTCT 1, vaccine 3, behavioural 1), and one on treatment.

Limited registration numbers likely reflect the lack of regulatory requirements for registration in African countries, identifying a need for better integration between ethics, registration and regulation. The receipt of WHO-endorsed primary register status, coupled with active promotion, will ensure that the PACTRs goals of comprehensive registration are realised.



08:30–10:30 **Plenary session III**

Recent advances in HIV/AIDS, Tuberculosis and Malaria (keynote addresses)

08:30–09:10 HIV/AIDS

09:10–09:50 Malaria

09:50–10:30 Tuberculosis

[VICTORIA HALL]

10:30–11:00 Coffee / Tea break

11:00–12:05 **Parallel sessions**

Clinical trials in sub-Saharan Africa

HIV/AIDS [MERU HALL]

Malaria [VICTORIA HALL]

Tuberculosis [MANDARA HALL]

12:05–13:05 **e-Poster presentations**

[CANE RESTAURANT]

All day **Poster presentations**

[BANQUETING LOBBY]

12:30–14:00 **Satellite meeting**

Ownership of research outcomes in sub-Saharan Africa

[MAHALE XL ROOM]

13:00–14:00 Lunch

[KILIMANJARO RESTAURANT]

14:00–16:00 **Parallel sessions**

Clinical trials in sub-Saharan Africa (cont.)

HIV/AIDS [MERU HALL]

Malaria [VICTORIA HALL]

Tuberculosis [MANDARA HALL]

16:00–16:30 Coffee / Tea break

16:30–17:30 **Plenary session IV**

Summaries and recommendations

[VICTORIA HALL]

19:00–20:30 Cultural dinner

[KILIMANJARO RESTAURANT]



08:30–09:10

Recent advances in HIV/AIDS

*Dr Anatoli Kamali • Uganda Virus Research Institute (UVRI),
Entebbe, Uganda*

New HIV prevention technologies are being developed and evaluated using randomised controlled trials (RCTs) including male circumcision (MC), STI treatment, microbicides, Pre-Exposure Prophylaxis (PrEP), HSV-2 suppression and HIV vaccine. However, only 4 of 36 major RCTs to date have shown efficacy against HIV transmission, of which 3 were on MC showing approximately 60% protection among heterosexual males, but a recent trial reported no protection for female partners of circumcised HIV-infected men.

The results of a Phase III vaginal PRO2000 microbicide gel, expected in November 2009, are eagerly awaited since a smaller trial (HPT035) showed a non-significant 30% reduction in HIV-incidence. Future microbicides comprise antiretrovirals, but their efficacy is yet to be determined.

Several PrEP and two HIV vaccine efficacy trials are also ongoing. HIV vaccine research has had unique challenges and the few completed trials have shown no efficacy. Infected individuals do not elicit immune response against the virus due to short period before it hides in host cells. This is associated with its ability to mutate and destroy key cells of the immune system.

Different HIV treatment regimens and models have shown encouraging results. Most recent results indicate that antiretroviral therapy (ART) could be delivered safely and effectively in resource-limited settings, and regular laboratory services offer little clinical benefits compared to careful clinical monitoring by trained and supervised health workers. Major questions remain on when to switch ART and on when to initiate treatment. There is also growing interest on the possibility of using antiretrovirals to prevent HIV transmission.



09:10–09:50

Recent advances in Malaria

Dr Abdoulaye Djimdé • University of Bamako, Mali



Malaria is a complex parasitic disease that has shaped mankind. It was once an orphan disease because it is most concentrated in poor countries. Currently there is a renewed interest in both basic research and the control of malaria.

Recently, desperately needed funding has significantly increased from private foundations, governments, non-governmental organisations and public-private partnerships. New generations of insecticides and drugs are available, improved research has brightened the future of vaccine discovery/development and genetic modification of mosquitoes is now a reality. The entire genomes of the human host, the mosquito vector and the parasite have been sequenced. Recent major technological advances made it possible to sequence additional 1000 people and numerous new strains of parasites and mosquitoes. As a result, there is a sharp decrease in the burden of malaria in some areas, demonstrating that it is possible to eliminate and ultimately eradicate malaria.

Despite these success stories, malaria continues to impose an intolerable burden on many people. There are emerging reports of the parasite and mosquito resistance to artemisinin derivatives and to the new insecticides, and new human malaria parasite species have been reported. The optimal delivery of the current tools has proven to be much more difficult than expected.

The challenges ahead can be summarised in two questions: how can we effectively deliver the existing tools and how can we better exploit the post-genomics era to invent and develop the new tools that are required for the eradication of malaria? These challenges will be discussed.

PLENARY SESSION III
**Recent advances in HIV/AIDS,
malaria and tuberculosis**

08:30–10:30
Victoria Hall

CHAIRS
Prof. Peter Ndumbe
Prof. Olle Stendahl



09:50–10:30

Recent advances in Tuberculosis

Prof. Willem Hanekom • South African Tuberculosis Vaccine Initiative, University of Cape Town, South Africa

The overview of advances in tuberculosis (TB) will focus on 4 areas: HIV-associated TB, drug-resistant TB, new diagnostics and new vaccines. New data on the importance of integrating HIV and TB care in high incidence areas will be emphasised. New advances in understanding TB-immune reconstitution inflammatory syndrome (IRIS), and how to manage these complications, will be discussed.

The epidemiology of and problems associated with multidrug and extensively drug resistant TB will be described, as well as interventions planned. Exciting new advances in microbiological diagnosis of TB will be discussed, including LED-based fluorescence microscopy and integrated nucleic acid amplification systems.

Finally, novel vaccination strategies against TB, and current status of development of new vaccines, will be discussed. This will include new data on biomarkers of protection against TB, following newborn vaccination with BCG.



PARALLEL SESSIONS | HIV/AIDS
Clinical trials in sub-Saharan Africa
11:00–12:05
Meru Hall

CHAIRS
Dr Simon Agwale
Prof. Eric Sandstorm

11:00–11:05
Brief introduction
from the Chairs

11:05–11:20
Safety and immunogenicity of a multigene
multiclade HIV-1 DNA plasmid vaccine
boosted with heterologous HIV-1 MVA among
healthy volunteers in Dar es Salaam, Tanzania

*Said Aboud • Muhimbili University of Health and Allied
Sciences and Muhimbili National Hospital, Tanzania*

Introduction | A Phase I/II trial HIV vaccine (HIVIS 03) employing a multiclade, multigene HIV-1 DNA prime and heterologous MVA boost vaccine among healthy volunteers in ongoing in Dar es Salaam, Tanzania.

Methods | Sixty healthy HIV negative volunteers, 15 females, randomised to 3 groups, were injected with plasmid DNA vaccine of 1 mg i.d. (n=20) or 3.8 mg i.m. (n=20) or placebo (n=20) using the Biojector. At months 0, 1 and 3, DNA plasmids were given. At month 9, a single i.m. injection with HIV-MVA 10^{6.8} pfu or placebo was administered. Interferon (IFN)- γ ELISpot responses were measured using peptide pools representing HIV-1 p17B, p24A, p55A, gp120A/B, gp120 B, gp41B, gp160E and PolA. T-lymphoproliferative (TLP) responses to AT-2 inactivated HIV-1 antigen were tested by a standard ³H-thymidine uptake assay.

Results | There has been excellent adherence of volunteers to the study schedules and the vaccines were well tolerated. Eleven serious adverse events unrelated to vaccination occurred. Two weeks after the third DNA/placebo injection, 23 of 59 (39%) volunteers had positive IFN- γ ELISpot responses and 24 of 52 (46%) volunteers had positive TLP responses. Two weeks after the HIV-MVA/placebo boost, 34 of 50 (68%) volunteers had positive ELISpot responses and 35 of 48 (73%) volunteers had positive TLP responses. The study still remains blinded.

Discussion | Excellent safety profile and high immunogenicity of HIVIS03 DNA-MVA vaccine is consistent with the previous Phase I study in Sweden. Capacity built paves the way for EDCTP-funded TaMoVaC 01 Project aimed at optimising DNA vaccine delivery.



II:20–II:35

Safety profile of a multigene, multiclade HIV-1 DNA plasmid vaccine boosted with HIV-1 MVA among healthy volunteers in Dar es Salaam, Tanzania



Joel Francis • National Institute for Medical Research, Tanzania

Introduction | A Phase I/II HIV vaccine trial (HIVIS 03) among healthy volunteers employing a multiclade, multigene HIV-1 DNA prime/HIV-1 MVA boost is ongoing in Dar es Salaam, Tanzania.

Methods | Sixty healthy HIV negative volunteers (15 females), randomised to 3 groups, were injected with plasmid DNA vaccine of 1 mg i.d. (n=20) or 3.8 mg i.m. (n=20) or placebo (n=20) using the Biojector at months 0, 1 and 3. At month 9, a single i.m. injection with MVA-HIV-DNA 108 pfu or placebo was administered. Safety evaluations were done two weeks following each vaccination and in additional visits if indicated.

Results | A total of 323 clinical adverse events (AE's) were reported. Among these 264 (82%) were of grade 1 severity of which 154 (73%) were unrelated, 10 (4%) probably related, 57 (22%) possibly related and 43 (16%) remotely related to vaccinations. Fifty (15%) grade 2 AE's reported of which 47 (94%) were not related to vaccination. Nine (3%) grade 3 or higher adverse events were reported none of which were related to the vaccination. Clinical malaria (mostly diagnosed at the peripheral hospitals) was the commonest 71 (31%) of the reported events out of which 43 (61%) were reported after 1st MVA/Placebo vaccination. A total of 82 (6%) episodes of abnormal Laboratory parameters reported, all were of grade 1 severity. No noted trend in laboratory abnormalities. The study remains blinded.

Discussion | The HIVIS03 DNA-MVA vaccine products have so far demonstrated excellent clinical and laboratory safety profiles and qualify for further improvements and trial after completion of this trial.



11:35–11:50

Heterologous vaccination regimen using recombinant BCG, ovine adenovirus and modified vaccinia virus Ankara induces potent HIV-specific T cell responses in macaques

Max Rosario • University of Oxford, UK

Introduction | Most children in Africa receive *Mycobacterium bovis* bacillus Calmette-Guérin (BCG) as their tuberculosis vaccine at birth. Those infants, who are born to HIV-1-positive mothers, are at high risk of acquiring HIV-1 infection through breastfeeding in the first weeks of their life. Thus, recombinant BCG expressing HIV-1-derived immunogen such as HIVA may prime HIV-1-specific T cell responses at or soon after birth and these can then be boosted by a heterologous vaccine such as rMVA delivering the same immunogen and/or through natural exposure to HIV-1 in the breastmilk. The hypothesis is that these early primed responses will decrease mother-to-child transmission of HIV-1 during breastfeeding and/or improve control of breakthrough virus replication.

Methods | Gene coding for HIV-1-derived immunogen HIVA was inserted into BCG (B), ovine adenovirus (O) and modified vaccinia virus Ankara (M) vaccine vectors. These vaccines were used for immunisations of rhesus macaques in heterologous prime boost combinations using BOM and BMO regimens and the T cell immunogenicity was assessed.

Results | Strong, polyfunctional HIV-1-specific T cell were induced.

Discussion | These results are discussed in the context of developing both pediatric and adult vaccine against HIV-1 transmission.

11:50–12:05

Tolerance and viral dynamics after short-course of nevirapine, tenofovir disoproxil fumarate and emtricitabine (TDF/FTC) to delivering women and neonates:

TEmAA ANRS 12109 Trial – Step 2

Elise Arrivé • Université Victor Segalen Bordeaux, France

Background | The safety and viral response of the TDF/FTC combination in HIV-1 infected pregnant women for PMTCT have been shown to be good. It is unknown whether this drug combination can be administered to neonates as well.

Methods | A Phase I/II trial conducted in Africa and Asia. All women received antenatal zidovudine, single-dose nevirapine (sdNVP) plus 2 tablets of TDF/FTC at the onset of labour (Ho) and one week of TDF/FTC. All infants received sdNVP, sdTDF (13 mg/kg) and sdFTC (2 mg/kg) plus one week of zidovudine. During a 2-month follow-up, serious adverse events (SAEs), kinetic of maternal plasma HIV-1 RNA and neonatal HIV-1 plasma RNA at 3 and 28 days of life were assessed.

Results | Among 36 enrolled: median age, 28 years; median CD4 count, 462 cells/mm³. All women received TDF/FTC 6 hours before delivery in median. One grade 3 leucopenia at Ho and one grade 4 neutropenia at Day-7 postpartum were reported. Among 29 women with HIV-1 RNA >2.6 log₁₀ copies/ml at enrolment, viral load decreased by a median of 0.5 log₁₀copies/ml at Day-2 postpartum. The 36 live-born infants (median birth weight: 3000g) received sdTDF and sdFTC. Two infants had clinical SAEs, including 1 death (postnatal infection). One transient grade 3 neutropenia and two grade 3/4 hyperbilirubinemia were reported. Plasma HIV-1 RNA was detected in 1/34 infants at 3 and 28 days of life.

Conclusion | Giving the combination of TDF/FTC for PMTCT to women as well as to their neonates appears to be well tolerated in both populations.

PARALLEL SESSIONS | MALARIA

Clinical trials in sub-Saharan Africa

11:00–12:05

Victoria Hall

CHAIRS

Prof. Alioune Dieye

Prof. Peter Kremsner

11:00–11:05

Brief introduction from the Chairs

11:05–11:20

Artemisinin combination therapies (ACTs) for uncomplicated malaria in African children: The 4ABC trial, preliminary results

*Umberto D'Alessandro • 4ABC study group, Institute of
Tropical Medicine, Antwerp*

Introduction | This study aims at making a head-to-head comparison between 4 available ACTs.

Methods | The study is carried out at 10 sites in 7 African countries (Burkina Faso, Gabon, Mozambique, Nigeria, Rwanda, Uganda and Zambia) with the involvement of local and European institutions (Belgium, UK, Germany, France and Spain). More than 4,000 children (6–59 months old) with clinical malaria were randomised to either amodiaquine+artesunate (AQAS), dihydroartemisinin + piperaquine (DHA-PQ), artemether + lumefantrine (AL) or chlorproguanil-dapsone + artesunate (CDA), the first three co-formulated combinations and the last one co-administered. Children were actively followed up for 28 days and then passively for the next 6 months; any second clinical episodes were treated with the same drug used for the first one and a 28-day active follow-up.

Results | DHA-PQ was administered to 1,450 children, AL to 1,199, ASAQ to 994 and CDA to 403. CDA treatment was prematurely stopped when GSK decided to stop the development of this treatment. PCR-corrected data are not available yet. Overall, within the 28-day first active follow up, 71.4% (2932/4105) children had an adequate clinical and parasitological response, 82.5% (1197/1450) for DHA-PQ, 67.0% (804/1199) for AL, 71.4% (710/994) for ASAQ and 54.8% (221/403) for CDA. There were only 6 early treatment failures, 253 late clinical failures and 493 late parasitological failures. During the 6-month passive follow up, 889 children (21.6%) had a second clinical episode. During the whole trial, including beyond the 28-day first active follow up, 142 serious adverse events, including 11 deaths, were reported.

Discussion | These are preliminary results as the last patient has been recruited at the end of December 2008. The passive follow up will end in July and the final database will be locked at the end of October 2009.

11:20–11:35

A randomised trial of the efficacy and safety of PQ in combination with DHA or SP for seasonal IPT in Senegalese children



Badara Cisse • University of Dakar, Senegal

Introduction | In the Sahel, malaria transmission is seasonal with a disease burden limited to three months a year. Seasonal IPT has been found very effective in reducing malaria morbidity (Cisse *et al.*, 2006). In 2006 we compared several antimalarial combinations for seasonal IPT. Sulphadoxine-pyrimethamine (SP) + amodiaquine (AQ) was most efficacious but presented the highest rate of adverse events (Sokhna *et al.*, 2008). We therefore assessed the efficacy and safety of piperazine (PQ) when used for seasonal IPT.

Methods | This trial recruited children <5 years living in the responsibility zone of Keur Soce, rural Senegal, who met inclusion criteria. The intervention consisted of administration of treatment doses in September–November of either Dualkin® (sulfalene-pyrimethamine + AQ) over 3 days, Duocotexin (PQ + dihydroartemisin (DHA)) over 3 days, or SP + PQ over 3 days. For pragmatic reasons, drugs were delivered by health post volunteers, dosage based on age and doses on days 2 and 3 unsupervised. Cumulative incidence of malaria, safety, prevalence of parasitaemia, SP-resistant mutations and anaemia in December were the major endpoints. The trial was powered for non-inferiority in incidence of malaria (5% non-inferiority margin) and superior tolerability.

Results | Coverage of monthly rounds and compliance with daily doses was similar in all groups. 90% of children received at least 2 monthly doses. PQ combinations were better tolerated with a significantly lower risk of common mild adverse events. Incidence of malaria was lower in the PQ groups. Prevalence of parasitaemia and the proportion of Pfdhfr and Pfdhps mutations were low in all groups.

Discussion | Seasonal IPT with SP+PQ in children is highly effective and well tolerated. The combination of two long-acting drugs is optimal for malaria prevention and is most effective against emergence of resistant parasite genotypes.



11:35–11:50



Efficacy and safety of quinine vs. artemether-lumefantrine in uncomplicated malaria during pregnancy, Mbarara, Uganda*Patrice Piola • Epicentre, Paris, France*

Introduction | ACTs are recommended by WHO in the second and third trimesters of pregnancy. This study aimed to examine the efficacy and safety of artemether-lumefantrine (AL) compared to oral quinine (SQ7) for treating uncomplicated *falciparum* malaria during the 2nd and 3rd trimesters pregnancy in Mbarara, Uganda.

Methods | An open-label, randomised, prospective, non-inferiority trial in which pregnant women were followed weekly until delivery. The cure rate at day 42 (primary outcome) and at delivery were confirmed by PCR genotyping. Adverse events, pregnancy outcome and newborn growth and development at 1 year of age were assessed.

Results | Overall 304 women, 152 in each arm, were enrolled. In the Per Protocol analysis, AL efficacy was high: 99.2 [95.7–99.9]% at D42 and 98.1 [93.3–99.8]% at delivery. SQ7 efficacy was 97.4 [92.1–99.3]% at D42 and 95.7 [88.7–98.6]% at delivery. In the PP analysis AL efficacy was non inferior to SQ7 at D42 (+1.8% difference with 95%CI lower limit at –0.9%), and at delivery (+2.4% difference with 95%CI lower limit at –1.7%). The trends and significance in the Intention to Treat Analysis were similar. There were no serious adverse events. Intolerable side effects were significantly higher with SQ7, resulting in 2.6% interrupted treatment in this arm (0% in AL). Birth outcomes were similar between treatment arms.

Discussion | The high efficacy and better tolerability of AL compared to SQ7 adds further reassuring information to the data published on pregnancies treated with artemisinins. The lumefantrine pharmacokinetic data currently being analysed are important to fully interpret these results.



11:50–12:05

Intermittent preventive therapy post-discharge (IPTpd): An innovative approach in the prevention of rebound severe malaria anaemia and mortality in young children

Kamija Phiri • College of Medicine, Malawi–Amsterdam–Liverpool (CoMMAL) Initiative

Introduction | Severe malarial anaemia requiring blood transfusion is a major cause of in-hospital childhood morbidity and mortality in sub-Saharan Africa. Previous follow-up studies from high malaria transmission areas in southern Malawi and western Kenya have shown that transfused children with severe malarial anaemia are also at high risk of dying after discharge from the hospital. We hypothesise that failure to clear the initial malaria infection due to ineffective antimalarial treatment and the acquisition of new infections after discharge, negate the initial improvements in haemoglobin concentrations that result from the blood transfusion. The study aims to compare the efficacy of a single treatment course with lumefantrine-artemether (Coartem®) at discharge to three treatment courses with Coartem® given at discharge, 1 and 2 months (IPTpd) in the post-discharge management of children who have recovered from severe malarial anaemia.

Methods | This is a randomised double-blind placebo controlled trial in which children aged between 4–59 months will be randomised to receive IPTpd with Coartem or with placebo. Children are followed up for a period of 6 months with the primary efficacy end-point being the incidence of recurrent severe anaemia or death.

Results | The study is ongoing with 1300 participants recruited to date and being followed up. 85 children have had a recurrent severe anaemic episode or died during follow-up.

Discussion | This study shows that preventing recurrent severe anaemia and death in this vulnerable group of children would lead to important policy recommendations. At the forum, we shall present important preliminary results.

PARALLEL SESSIONS | TUBERCULOSIS

Clinical trials in sub-Saharan Africa

11:00–12:05
Mandara Hall

CHAIRS

Prof. Tumani Corrah,
Prof. Joseph Odhiambo
Dr Hulda Swai

11:00–11:05
Brief introduction
from the Chairs

11:05–11:30
An international multicentre controlled
clinical trial to evaluate high-dose rifapentine
and a quinolone in the treatment of
pulmonary tuberculosis (RIFAQUIN)

Andrew Nunn • Medical Research Council Clinical Trials
Unit, London, UK

Introduction | RIFAQUIN assesses whether a regimen using intermittent rifapentine and moxifloxacin in the continuation Phase can reduce treatment duration to 4 months and can simplify treatment administration from daily to once or twice weekly. A second objective is to assess whether high dose rifapentine will eliminate acquired rifamycin resistance among HIV-infected relapses.

Methods | Patients with pulmonary tuberculosis, with two microscopy positive sputa are randomised to: Control Regimen: 2 months of daily ethambutol, isoniazid, rifampicin, and pyrazinamide followed by 4 months of daily isoniazid and rifampicin (2EHRZ/4HR). Study Regimen 1: 2 months of daily ethambutol, moxifloxacin, rifampicin, and pyrazinamide followed by 2 months of twice weekly moxifloxacin and rifapentine (2EMRZ/2P2M2). Study Regimen 2: 2 months of daily ethambutol, moxifloxacin, rifampicin, and pyrazinamide followed by 4 months of once weekly moxifloxacin and rifapentine (2EMRZ/4P1M1). Primary outcome measures: (1) Failure during treatment or relapse by 18 months. (2) Acquired rifamycin resistance in relapse cultures of HIV infected patients. (3) Grade 3 or 4 adverse events during chemotherapy. Follow-up: 18 months from start of chemotherapy.

Results | Participating countries are Botswana, South Africa, Zambia and Zimbabwe. The design of the study will be discussed, including limitations and the process for the choice of an acceptable margin of non-inferiority. Excessively long delays were encountered in obtaining regulatory approval.

Discussion | Non-inferiority study design presents particular challenges and there is an urgent need for more rapid approval mechanisms.



11:30–11:50

Partnering to support research capacity in TB endemic countries

Anthony Hawkridge • Aeras Global TB Vaccine Foundation, Cape Town, South Africa

Introduction | Several new tuberculosis vaccine candidates are already in clinical trials with others expected to enter trials in 2009/10. As they advance to larger-scale trials, multiple sites capable of participating in these studies will be needed. Aeras and EDCTP share the objective of accelerating the development of safer and more efficacious TB vaccines by forming partnerships with research institutions in high burden countries, building capacity at potential Phase III trial sites and promoting networking between these trial sites.

Methods | Development and licensure of a new TB vaccine requires building clinical research capacity in preparation for clinical trials which are ICH-GCP compliant. An important part of the Aeras/EDCTP partnership with local research institutions is to support a network of active or potential sites which are interested in TB vaccine trials, known as TBVACSIN, to facilitate the sharing of information and expertise related to TB vaccine studies, harmonisation of protocols, assays and methods as well as the promotion of better communication with the communities in which trials are conducted.

Results | Currently five sites in Africa are members of the TBVACSIN network. Researchers from these sites meet at least annually to share information and experiences, which enhances the capacity at each site and helps ensure that the infrastructure and expertise for large-scale trials is in place in multiple sites.

Discussion | Clinical site development, capacity building and networking for vaccine clinical research foster both South-South and North-South collaborations that will lead to more effective partnerships and strengthened research capacity in endemic countries.

PARALLEL SESSIONS | TUBERCULOSIS

Clinical trials in sub-Saharan Africa

11:00–12:05

Mandara Hall

CHAIRS

Prof. Tumani Corrah,

Prof. Joseph Odhiambo

Dr Hulda Swai

11:50–12:05

Similarity between pulmonary tuberculosis and pulmonary nocardiosis

Mugahid Elhassan • College of Medical Laboratory Sciences, Khartoum, Sudan

Introduction | The present study aimed to determine the occurrence of *Nocardia* spp. among Sudanese patients suspected with tuberculosis and to investigate all proteins expressed by the genome of *Nocardia africana* (formerly isolated from patients with pulmonary infection misdiagnosed as MDR) compared to *Mycobacterium tuberculosis*.

Methods | Three hundred twenty nine patients, presented with pulmonary infection were included. Patients were examined for the presence of acid-fast bacilli. (LJ) medium was inoculated with sputum sample. Cultures were incubated for 8 weeks. Phenotypic and genotypic characterisations were performed.

Results | Ten isolates showed rapid growth pattern within 2–3 days, suggesting belonging to family *Nocardia*. Confirmation was conducted by 16 rDNA for phylogenetic analysis. (2D-PAGE) using pH strips 3–10 revealed that soluble proteins were visible in a much smaller pI range. Prominent spots were excised from the gels and assigned. The original data and spectra can be downloaded from the NoDaMS (<http://ifg-izkf.uni-muenster.de/proteomik/nodamsa>) database. Heat shock factors, chaperones and metabolic enzymes, dominate the visible proteome.

Discussion | *Nocardia* revealed considerable occurrence among patients with pulmonary infections giving clinical symptoms similar to those occur by *M. tuberculosis*, may be due to similarities in functional proteins. This suggested that pulmonary nocardiosis occurs in patients suffering from chronic lung disease in Sudan. Therefore, clinicians should consider this condition, especially when patients with respiratory infections fail to respond to classical anti-tubercular therapy.





HE 09

Hepatitis B and C viral co-infections among HIV-infected treatment naïve participants recruited in HIV-1 molecular diversity cross-sectional survey, Western Kenya

Micah Oyaro • University of Nairobi, Kenya

Introduction | Similar to HIV, hepatitis B and C viruses (HBV and HCV, respectively) can be transmitted through blood or sexual contact. We examined the prevalence of HBV or HCV co-infection in HIV positive individuals participating in HIV-1 molecular surveillance study in Western Kenya.

Methods | Investigations included detection of serological markers for HBV (HBsAg) and HCV (anti-HCV antibodies) infections with standard ELISA technique. HIV seropositive status was confirmed with fourth generation ELISA-based kit, Vironostika Uniform I & II. All testing procedures were done according the manufacturers' instructions. Socio-demographic data were obtained and entered into a database and analyzed using the EPI-INFO 2003 statistical software package (CDC). Fisher's test was used to determine statistically significant differences. The study was approved by Kenyatta National Hospital Ethics and Research Committee (KNHERC).

Results | 150 HIV infected adults, 96 (74%) females and 34 (26%) males were enrolled. In total, 10 (7.69%) samples had hepatitis co-infection. Seven samples (5.38%) were co-infected with HBV while three samples (2.3%) were co-infected with HCV respectively. None of the participants was co-infected with three viruses. Co-infection was not associated with any of the investigated risk factors (number of sexual partners, condom use and history of blood transfusion).

Discussion | Our data show a high seroprevalence (7.69%) of hepatitis co-infection in HIV infected patients in Western Kenya suggesting that interventions are required to prevent the infections and routine screening of hepatitis viral co-infection is vital for proper care and management of HIV patients.

HE 010

Prevalence and risk factors for HIV and syphilis among fishing populations of Uganda: A capacity development project for HIV prevention research

Gershim Asiki • MRC/UVRI Uganda Research Unit on AIDS and UVRI-IAVI, Uganda

Introduction | Recent evidence suggests increasing rates of HIV infection in fishing populations. Robust data on prevalence and risk factors for HIV and other STIs needed for designing biomedical and behavioural interventions is lacking in such populations. The EDCTP-funded Fisher folk study is investigating HIV-prevalence, incidence and risk factors (main cohort study), HIV molecular epidemiology (virology sub-study), and behavioural characteristics (social science study) to establish the suitability of fishing communities for future HIV prevention research. We present preliminary findings.

Methods | A structured questionnaire on demographic variables and sexual behaviour including history of STIs was administered to 192 individuals. We analysed 280 and 216 sera for HIV and syphilis infection rates respectively from volunteers aged 13–49 years in two fishing villages in Masaka district, Uganda.

Results | HIV and syphilis prevalence was 30.7% (95%CI: 25.2–36.8) and 5.1% (95%CI: 2.6–8.9). Syphilis (OR 4.9 P=0.007) and history of STI (OR 2.1; P=0.041) were closely associated with HIV infection. Alcohol intake (OR 1.13 P=0.114), absence from home (OR 1.38; P=0.324), multiple sex partners (OR 1.84 P=0.196) and condom use (OR 0.34 P=0.140) showed no significant association with HIV infection.

Discussion | HIV prevalence in these populations is higher than that of the general population (11.4%). HIV incidence is also likely to be high. Such high risk populations urgently need behavioural and biomedical interventions and make them suitable for future clinical trials. Additional epidemiological and social science data are now being collected to provide more detailed information on associated risk factors and on the feasibility for future HIV prevention research.



HE 011

Expanding the world's largest HIV drug resistance database, EuResist, into an African context

Francesca Incardona • EuResist Network GEIE, Muhimbili National Hospital (MNH), Tanzania

Introduction | Drug resistance is a major threat to the long-term benefits of antiretroviral therapy. It is most often determined by genotyping requiring access to molecular biology techniques and laboratory facilities. EuResist has developed the world's largest HIV drug resistance database including both clinical and virological data and a freely available web-based prediction tool of which drug combinations to use after a therapy failure. The prediction engine outperforms existing similar tools. However only data from Europe are included.

Methods | Collaborations have been established with several African countries in order to enrich the EuResist database with new African data and to provide decision support to doctors in Africa. As intermediate objective, IT education to local personnel is being organised.

Results | Assessments of the IT-infrastructures at the collaborating hospitals showed the feasibility to use EuResist database and a bioinformatic prediction engine adapted for low-income countries.

Discussion | Transferring important parameters to the new expanding EuResist database from medical treatment into an R&D context in a structured and simple way creates new opportunities for doctors to contribute to clinical HIV research and care of African patients with drug resistance. Developing cross-border systems such as an adapted EuResist database and a new prediction tool means that we can achieve synergistic effects in trials performed in Africa and optimisation of the use of HIV drugs. We will evaluate whether prediction of the best new ART regimens after a therapy failure can be done with our bioinformatic engine without performing genotypic resistance testing.

HE 012

Reducing loss to follow-up in the Comtru Project

Mercy Chiduo • National Institute for Medical Research, Tanga Centre, Tanzania

Introduction | ComTru project is a preventing mother-to-child transmission (PMTCT) study being conducted in Tanga, Tanzania. Due to a larger than anticipated loss to follow-up, the study paused during 2007; restructured and resumed enrolment again in March 2008.

Methods | Follow-up was improved by making tracing acceptance mandatory, obtaining precise addresses using GPS, addition of study nurses to the team, purchasing of study car, and addition of a third study site. The number of patients was found in the database and percentages were calculated accordingly.

Results | During the first study period, 63% of recruited patients were enrolled, out of whom 56% delivered at the hospital. 30% came for day 7 follow-up visit, 28% and 27% week 4 and week 6–8 respectively; and only 4% showed up for the month 9 visit. From March 2008 to March 2009, we were able to enrol 183 patients, out of which 117 patients have thus far delivered. 82% of the enrolled patients came for day 7 visit, 84% were seen for week 4 visit and 93% came for week 6–8 visit. By March 2009, 50% of the patients who had completed 9 month post delivery came for the month 9 visit.

Discussion | The changes implemented in the study have had a marked impact on loss to follow-up. Home visits by study nurses have now improved due to having residential address aided by GPS.



HE 013

Association between HIV-infection and infertility in Rwanda: A case-control study

Ammiel Gasarabwe • Projet Ubuzima, Kigali, Rwanda

Introduction | Infertility in sub-Saharan Africa is frequently caused by STIs. HIV and infertility share the same determinant of high risk sexual behaviour, which explains the finding by some studies of a higher HIV prevalence (up to 3 times) in infertile couples. The aim of this study is to examine whether HIV is associated with infertility independent of these common risk factors.

Methods | This study was conducted in the main university hospital in Kigali, Rwanda. Cases were recruited from women presenting themselves with infertility problems to the study clinic. An unmatched control group of fertile women (defined as women who recently delivered) were sampled from the same geographical area. A total of 312 women were enrolled in each group. Data were collected on demographics, sexual behaviour and STIs in the past and blood was drawn for HIV testing.

Results | HIV prevalence was 16% in fertile woman and 32% in infertile women (crude OR=2.47, 95%CI 1.67–3.66). HIV prevalence remained associated with infertility (adjusted OR=1.72, 95%CI 1.04–2.82) in a multiple logistic regression model including age, income, marital status, divorce in the past, sexual violence, transactional sex, lifetime sexual partners and self-reported past STI (genital ulcer and/or combination of abdominal pain and vaginal discharge).

Discussion | HIV prevalence is high in this urban group of infertile women compared to the fertile women. HIV is associated with infertility independent of self reported high risk sexual behaviour and STIs in the past. Further research is needed to elucidate the mechanisms of this association.

HE 014

Prevalence of HPV and association with other STIs among high-risk women in Kigali, Rwanda

Lambert Mwambarangwe • Projet Ubuzima, Kigali, Rwanda

Background | Persistent high risk human papilloma virus (HR-HPV) infection is strongly associated with the development of cervical (pre) cancerous lesions. Over 80% of cervical cancer cases occur among women in developing countries. However, there is a lack of HPV prevalence data from these countries. Furthermore, there are conflicting results about the association between HR-HPV infection and other prevalent sexually transmitted infections (STIs).

Methods | Cross-sectional analyses were performed on the month 6 visit of a prospective HIV incidence study among 400 high-risk, HIV-negative women in Kigali. Endocervical samples were tested for HPV, *Neisseria gonorrhoeae* (NG) and *Chlamydia trachomatis* (CT); vaginal samples for *Trichomonas vaginalis* and syphilis RPR/TPHA serology were performed. Positive NG/CT results were confirmed with a second PCR. Associations were evaluated using univariate models.

Results | HPV results from 381 women were available. Of these, 15 women were excluded from these analyses as they were found HIV positive. Overall HPV prevalence was 48.1%. Prevalence of HR-HPV types was 33.9% and 32.8% for low-risk (LR) HPV. The prevalence of HPV16 and 18 was 9.0%. The five most prevalent HR-HPV types were HPV52/33/35/58 (38.7%), HPV16 (17.7%), HPV53 (14.5%), HPV45 (13.7%) and HPV68 (12.1%). The prevalence of NG, CT, TV and syphilis was 7.7%, 4.4%, 15.2% and 7.6% respectively. No significant difference in the prevalence of these STIs between HR-HPV positive women and HR-HPV negative women was found on univariate analyses.

Conclusions | HR-HPV infections are highly prevalent among these high-risk, HIV-negative women. No association was found between HR-HPV infections and other STIs.



HE 015

Anti-inflammatory cytokines and haematological indices in HIV and HBV seropositive adults with uncomplicated *Plasmodium falciparum* malaria

Mirabeau Tatfeng • College of Health Sciences, Niger Delta University, Nigeria

Introduction | The biological functions anti-inflammatory cytokines appears crucial in immune response. The aim of this study is to determine the role of anti-inflammatory cytokines, IL-4 and IL-10, in a heterogeneous group of HIV seropositive patients with uncomplicated *Plasmodium falciparum* malaria.

Methods | Levels of IL-4 and IL-10 of 111 malaria infected, 97 HIV/malaria co-infected, 79 HIV seropositive subjects and 73 controls were determined by Enzyme Linked Immunosorbent Assay. CD4 and CD8 cells were counted using the Dynabeads T4-T8 Quantification protocol while haematological parameters were estimated using standard haematological techniques.

Results | The mean IL-4 was significantly higher in malaria patients than the levels obtained in HIV and malaria-HIV co-infected subjects ($P < 0.05$). IL-10 in malaria patients was significantly higher than the levels obtained in HIV and malaria-HIV co-infected subjects ($P < 0.05$) while in control subjects, the level was significantly higher when compared to values obtained in HIV and malaria-HIV co-infected subjects ($P < 0.05$). The mean haematological parameters revealed a significant high difference in the CD4 count (1434 ± 331.05 cells/ μ l) of malaria infected individuals when compared to values obtained in HIV (274 ± 465.0 cells/ μ l) and malaria-HIV (207.0 ± 841.09 cells/ μ l) co-infected subjects respectively ($P < 0.05$). The CD8 count was significantly higher in malaria infected subjects than in controls, HIV and malaria HIV co-infected subjects ($P < 0.05$).

Discussion | Impaired production of Th2 cytokines in an infective process could indicate an immunosuppressive state as observed in HIV infection.

HE 016

Molecular detection of chemokine ligand 3-like 1 (CCL3L1, MIP-1 α Or LD78 β) gene copy number amongst HIV-1 positive patients in Khartoum, Sudan

Elias Onyoh • Institute of Endemic Diseases (IEND), University of Khartoum, Sudan

Introduction | There is evidence that gene copy number (CN) variation of chemokines influences phenotypic variation in HIV-1 infection. Chemokine ligand 3-like 1 binds to CCR5 co-receptor thereby preventing the R5 strains of HIV-1 to some extent from infecting the host CD4 cells. Individuals with more copies of CCL3L1 (CCR5 ligand) than the median CN of their population have been found to be less susceptible to HIV-1 infection.

Methods | A case-control study was conducted in order to estimate the median copy number (CN) of CCL3L1 gene within Sudanese population comparing to HIV positive Sudanese patients. We measured CCL3L1 gene CNs per diploid genome (pdg) in 76 individuals from different regions of the Sudan using the Strata-gene MxP 3000 real-time PCR after extracting genomic DNA from whole blood. The 76 recruited were 36 HIV-1 seropositives and 40 seronegatives.

Results | The median CCL3L1 CN pdg amongst Sudanese was found to be 3, and was the case (i.e. 3) in both the Nilo-Saharan and Afro-Asiatic speaking groups, with a case-control Kruskal-Wallis test p-value=0.001, a 2-tailed t-test p-value of 0.004 ($P < 0.05$) with a 95% confidence interval of between -2.13 and -0.43. More than 70% of HIV infected participants had an estimated CCL3L1 CN lower than 3 and in stage III of the disease.

Discussion | Sudanese with CCL3L1 CNs lower than the median population-specific CN pdg have a higher chance of acquiring HIV-1 infection if exposed to the virus.



ME 09

Pfhrh polymorphisms and *Plasmodium falciparum* sensitivity to quinine in Mali

Aminatou Kone • University of Bamako, Mali

Introduction | Quinine is the drug recommended for severe malaria treatment. The mechanism of *P. falciparum* resistance to quinine is not known. Recently described, the low-level quinine resistance in parasites is related to genetic loci on several chromosomes including polymorphisms in a *Plasmodium falciparum* Sodium-Hydrogen Exchanger (PfNHE) on chromosome 13.

Methods | Prospective *in vivo* study was conducted in two hyperendemic villages in Mali assessing the quinine in efficacy. Kollé and Faladié. Consenting cases of non-per os malaria were included, treated with quinine standard doses of 5 days during 28 days follow up. Treatment outcome (ETF, LCF, LPF and ACPR) were classified using modifications of the WHO's 2003 protocol for the assessment of antimalarial efficacy. Molecular markers of polymorphisms msp1, msp2 and CA1 have been used to distinguish recrudescence from new infections.

Results | Overall 87 patients were included for Kollé with 0%, 12.8%, 46.8% and 40.4% of ETF, LCF, LPF and ACPR, 63 patients for Faladié with 15% LCF and 21.9% LPF. Molecular correction showed 100% of ACPR in two villages. The prevalence of microsatellite resistant form in post treatment parasites increased for the two villages. Faladié's samples (n=30) showed statistical difference between parasites collected before and after Quinine treatment ($P=0.006$) χ^2 Mc Nemar. Kollé's samples (n=49) also showed a significant difference ($P=0.0006$).

Discussion | From patients presenting day 21 parasitemia and positive PCR by day 14, two had positive PCR at day 7 showing that the drug may select the less sensitive parasites.

ME 010

Haemoglobin S and C protect children under five 5 years living in the Saponé Health District (Burkina Faso) against the malaria infection

Edith Christiane Bougouma • Centre National de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso

Introduction | To assess the protective role of haemoglobin C in relation with malaria, we have conducted a genotyping study in children aged 0–5 years living in the Saponé health district located at 50 km south of Ouagadougou, the capital city of Burkina Faso.

Methods | The study was performed as transversal survey done during the high malaria transmission season. During the survey, we realised for each child a clinical examination. Blood smears were taken for thick and thin film and a venous sampling was taken for human genetic tests. The haemoglobin genotypes were identified by PCR restricted fragment length polymorphism (RFLP) on malaria patients.

Results | A total of 909 subjects (630 HbAA, 176 HbAC, 15 HbAS, 17 HbCC, 5 HbSC, 3 HbSS) were taken into account during the transversal survey. We have noted 203 malaria episodes: 57 (28, 08 %) episodes for the haemoglobin C and S groups and 146 (71.92%) episodes in haemoglobin A group ($P<0.0001$). The parasitaemia mean was 8656 parasites/ μ l for the bearers and 10870.73 parasites/ μ l for the non bearers ($P<0.0001$). The gametocyte carriage rate was 45.96 % for the bearers of haemoglobin C and S; 34.18% for the other group; ($P=0.0001$).

Discussion | Our hypothesis that bearing the haemoglobin C could allow a favourable interaction man-parasite with low morbidity, mortality and probably a very high transmission for the parasite is confirmed.



ME 011

Genetic identification of *Plasmodium falciparum* parasite virulence markers according to local populations

Else Carole Moukoko Eboumbou • University of Buea, Cameroon

Introduction | The mechanisms of the heterogeneous courses of severe malaria (SM) are not clearly understood. They are thought to involve a complex combination of human host factors under the influence of their genetic background and parasite specific factors. SM incidence varies greatly among people and epidemiological conditions. Our study aimed to identify *P. falciparum* genetic factors associated with pathogenicity in three countries with various transmission rates.

Methods | We are performing a combined epidemiological, clinical and genetic analysis of more than 160 *falciparum* isolates which include uncomplicated malaria (UM) and SM cases from Cameroon, Gabon and Mali. Parasite loci associated with pathogenicity will be identified using a genome wide gene mapping approach.

Results | The *P. falciparum* genotypes associated with severity and clinical manifestation will be presented.

Discussion | Linkage disequilibrium blocks and susceptibility haplotypes will be characterised and linked to SM pathogenesis. These findings could be clinically relevant by allowing early identification of clinical cases which may progress toward severity. In addition, it may also generate new hypothesis on the pathogenesis of SM and suggest new therapeutic approaches.

ME 012

Decrease of malaria prevalence in the paediatrics services of Franceville's hospitals between 2004 and 2008

Ulrick Bisvigou



ME 013

Regulatory T cells in sympatric ethnic groups with different susceptibility to malaria in Burkina Faso

Issa Nébié • Polytech University of Bobo,
Burkina Faso

Introduction | Regulatory T cells have been reported to decrease human specific immune responses against *P. falciparum*. To evaluate the role of these T cells, we carried out 2 case control studies comparing regulatory T cells in two ethnic groups (Mossi and Fulani) living in sympatric with different susceptibility to malaria in Burkina Faso.

Methods | Two cross-sectional surveys were carried out at high and low transmission season of 2007 and 2008 respectively in a hyper-endemic malaria transmission area. Peripheral blood mononuclear cells were isolated from 60 Mossi and 72 Fulani and stained for cell surface antigens expression and intracellular cytokine secretion profiles using flow cytometry.

Results | The prevalence of *P. falciparum* was higher in Mossi compared to Fulani (27.1% and 8.8% at high transmission season) and (12.2% and 0% at low transmission season). The frequency of CD3+CD4+CD25+ T cells was lower in Fulani at high transmission season compared to Mossi (60.4% and 64.2% respectively) as well as at low transmission season (47.6% and 50.7% respectively). Seasonal was related CD3+CD4+CD25+ T cells frequency either in Mossi or Fulani with a peak frequency during the high transmission season. Similarly, CD4+CD25+TGFB+ cells was found less frequent in Fulani compared to Mossi at high transmission (9.8% and 12.3% respectively) without an evident difference at low transmission season.

Discussion | In this study, regulatory T cells markers associate with ethnicity and season. These findings confirm the hypothesis that the resistance of Fulani to malaria might be linked to a deficit in regulatory T cells.

ME 014

Overuse of artemisinin combination therapy in Mto wa Mbu (River of mosquitoes), an area misinterpreted as high endemic for malaria

Charles Mwanziva • Tumaini University,
Kilimanjaro Christian Medical College, Tanzania

Introduction | Adequate malaria diagnosis and treatment remain major difficulties in rural sub-Saharan Africa. These issues deserve renewed attention in the light of first-line treatment with expensive artemisinin combination therapy (ACT) and changing patterns of transmission intensity. This study describes diagnostic and treatment practices in Mto wa Mbu, an area that used to be hyperendemic for malaria, but where no recent assessments of transmission intensity have been conducted.

Methods | Retrospective and prospective data were collected from the two major village health clinics. The diagnosis in prospectively collected data was confirmed by microscopy. The level of transmission intensity was determined by entomological assessment and by estimating seroconversion rates using anti-malarial antibody responses.

Results | Malaria transmission intensity by serological assessment was equivalent to <1 infectious bites per person per year. Despite low transmission intensity, >40% of outpatients attending the clinics in 2006–2007 were diagnosed with malaria. Prospective data demonstrated a very high over-diagnosis of malaria. Microscopy was unreliable with <1% of slides regarded as malaria parasite-positive by clinic microscopists being confirmed by trained research microscopists. In addition, many 'slide negatives' received anti-malarial treatment. As a result, 99.6% (248/249) of the individuals who were treated with ACT were in fact free of malaria parasites.

Conclusion | Transmission intensity has dropped considerably in the area of Mto wa Mbu. Despite this, most fevers are still regarded and treated as malaria. There is obvious discrepancy of problem studied.

ME 015

Complement utilisation in children with severe malarial anaemia

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Medical Research Institute, Kisumu, Kenya



Introduction | The complement system plays an important role in both innate and adaptive immunity and complement can be activated and depleted during malaria infection, thus potentially compromising overall immune defences. Activation of complement also leads to production of potent pro-inflammatory mediators such as C3a and C5a, which may explain the genesis of pro-inflammatory cytokines seen in children with severe malarial anaemia (SMA).

Methods | In a case control study, we compared the levels of complement haemolytic activity (CH50) in cases of SMA and in asymptomatic controls with malaria infections.

Results | The CH50 in SMA (16 ± 10 U/ml) were below normal ($34-70$ U/ml) and were half the levels in controls (34 ± 8.2 U/ml ($P=0.001$, paired t test). The levels of C3a were 10 times higher than normal (normal ranges= $257-690$) in both the cases (mean= 3489 ± 650 ng/ml) and in controls (3852 ± 555 ng/ml), indicating a high degree of complement activation in both groups. Similar trends were obtained for C4a and C5a. PCR detection of C4 null genes (C4AQ0 and C4BQ0) found 5 homozygous individuals for C4BQ0 (1 case and 4 controls), but no patients expressing the C4AQ0 allele in either group.

Discussion | Collectively, these results indicate: (1) Profound uncompensated utilisation of complement in patients with SMA; (2) Equal formation of pro-inflammatory complement fragments in cases and controls, indicating that the pro-inflammatory cytokines commonly seen in children with SMA cannot be accounted for by these anaphylatoxic agents; and (3) Complement deficiency observed in SMA does not appear to be associated with genetic defects.



TE05

A Phase II, randomised study to evaluate the protective efficacy against TB disease of MVA85A in HIV-infected adults in South Africa, Senegal, and The Gambia

Nathaniel Brittain • University of Oxford, UK

Introduction | MVA85A is the most clinically advanced new TB vaccine and has recently entered into Phase IIb efficacy trials in infants in South Africa, the first TB vaccine to do so in over 80 years. MVA85A is a modified Vaccinia virus Ankara that expresses the 85A antigen from *Mycobacterium tuberculosis* and is designed to enhance the immune response to BCG.

Methods | We are currently planning a randomised, double-blinded Phase IIb efficacy trial in HIV-positive adults in three sites in Africa – South Africa, Senegal and The Gambia, which will commence in 2010. This trial will look at efficacy against TB disease and *M.tb* infection, and will also include expanded safety and immunogenicity studies.

Results | MVA85A has been safely given to over 500 subjects to date, including 57 HIV-positive adults in the UK, South Africa and Senegal. There have been no significant changes in either CD4 counts or HIV viral load in these subjects. We see a significant induction of polyfunctional, antigen specific CD4+ T cells, as in our studies in HIV-negative subjects.

Discussion | To date, MVA85A is safe and immunogenic in HIV-infected subjects and the next step is to evaluate efficacy in this important target population. The EDCTP-funded efficacy trial will commence in 2010.

TE 06

A Phase I TB vaccine trial in Ethiopia as a platform for capacity building for TB vaccine trials in east Africa

Rahel Iwnetu • Armauer Hansen Research Institute (AHRI), Addis Ababa, Ethiopia

Introduction | The global effort to develop a more effective TB vaccine has taken the important step from pre-clinical discovery into clinical development, including clinical trials in Africa. One leading candidate TB vaccine currently under Phase I clinical trial in Ethiopia includes the strongly immunogenic secretory antigen ESAT-6 together with Antigen 85B and the adjuvant IC31. A second clinical trial of this same vaccine candidate in HIV +ve and HIV –ve volunteers is serving as a platform for capacity building for future TB clinical research and vaccine trials in East Africa.

Methods | A cGCP clinical trial protocol for testing the vaccine in HIV+ve individuals is under development at AHRI, based on the current Phase I clinical trial undergoing testing in normal Ethiopian individuals. Over the last 18 months, capacity building activities in the area of ethics, clinical immunology, assay development/standardisation and GCP have been conducted jointly in the three African collaborating centres: Ethiopia, Tanzania and Madagascar.

Results | Three courses in GCP and research ethics have been completed, with over 50 participants trained. A Phase I trial protocol for testing safety and immunogenicity with the adjuvanted TB subunit vaccine administered in different antigen/adjuvant formulations in 24 HIV negative and 24 HIV positive Ethiopian adult volunteers at 0 and 2 months has been developed and submitted for ethical review in May 2009.

Discussion | Capacity building for the development and conduct of GCP clinical trials in Africa remains a challenge. Considerable progress has been made to date in this East African initiative focused on TB vaccine testing.

TE 07

Low rate of antituberculosis drug-induced hepatotoxicity in Tanzanian hospitalised pulmonary tuberculosis patients

Hadija Semvua • Kilimanjaro Christian Medical Centre (KCMC), Moshi, Tanzania

Introduction | Tuberculosis is treated with an antibiotic course of at least six months, containing isoniazid, rifampicin, pyrazinamide and ethambutol. Hepatotoxicity is the most serious adverse effect of TB treatment. Data on hepatotoxicity in sub-Saharan Africa is limited. We conducted a study in Tanzanian hospitalised TB patients and monitored their liver function closely.

Methods | The liver function was monitored during the intensive Phase of TB treatment. Alanine aminotransferase (ALT), aspartate aminotransferase and total bilirubin were determined at baseline and after 2, 4, 6 and 8 weeks of treatment. Patients were treated according to the guidelines of the Tanzanian Tuberculosis Program. Liver toxicity was defined as ALT more than five times the upper limit of normal (ULN) without symptoms of toxicity (jaundice, abdominal pain, nausea, vomiting) or >3 times the ULN with symptoms.

Results | The maximal ALAT value was 87 U/l and the maximum ASAT was 98 U/L, which is not more than two times the ULN. One patient experienced liver toxicity symptoms but did not have increased liver function parameters. Ten patients had increased bilirubin levels; this was related to hepatitis B (risk ratio 5.7; 95%CI 1.7–18.6).

Discussion | None of the patients developed hepatotoxicity according to international definitions. Only one case of liver toxicity was observed in the study, since the patient experienced symptoms of liver injury in relation to the TB drug intake. This concludes a low rate of hepatotoxicity in African patients. This is a reassuring message in the light of upcoming trials with a high dose of rifampicin.

TE 08

Assessment of DNA stability in urine from healthy adults in Mbeya, Tanzania

Gaspari Mwanyika • NIMR-Mbeya Medical Research Programme, Tanzania

Introduction | Molecular diagnosis of infectious diseases like Tuberculosis using urine is becoming increasingly utilised. However the storage of urine prior to nucleic acid analysis is a paradox.

Methods | We examined the stability of human and cell free DNA in urines collected from 20 healthy adults (10 males) at Mbeya Medical Research. The urines were stored for 7 days with preservatives, EDTA, K₂EDTA, Sodium azide and Guanidine isothiocyanate at 4°C. Cell free DNA was added as *M. tuberculosis* spike of IS1081. The urines were extracted at days 0, 1, 3 and 7 after storage. Human DNA content was measured using ALU target and *M. tuberculosis* DNA spike by IS1081 real time PCR assays.

Results | Human DNA content in extracted urines was on average slightly greater than previously reported in Italy and Zambia at base line with less human DNA in males, 3.2x10⁸ copies/ml against 2.5x10⁸. *M.tb* DNA IS1081 copies/ml was on average equal in both sex. Generally, after initial decline in amount, DNA in urine is stable at 4°C with all four preservatives.

Discussion | As we found that, the stability of DNA in urine from healthy adults in Mbeya was good regardless of urine preservative employed. For low hazard, cost and ease of use, EDTA is adequate to store urine at 4°C for a week in Mbeya.



CE 09

Ownership and stewardship of outcomes of clinical research conducted in sub-Saharan Africa

Adamson S. Muula • University of Malawi, Chichiri, Malawi

Introduction | Despite the fact that sub-Saharan Africa suffers a significant burden of diseases, especially communicable diseases, the continent has lagged behind in clinical research. The situation however continues to change for the better as there is a growing interest in clinical research conducted on the continent by both local and international researchers.

Methods | A qualitative systematic review of published reports was reviewed to explore and identify current guidelines and opinions on disposition and beneficiaries of clinical research and research outputs and outcomes from sub-Saharan Africa.

Results | Communities in sub-Saharan Africa have benefited from clinical research through access to high-quality ancillary care provided by the research industry but not yet available in the existing general clinical services. There is no congruency of opinions regarding how sub-Saharan communities should benefit from research outcomes. While some authors have suggested the appropriation of benefits of research to 'owners' of the data, establishing who are and who may not be 'owners' of information is fraught with problems. Discussions and opinions in appropriating the fruits of clinical research often appear to weigh one group's contribution to the research enterprise more than the others.

Discussion | The lack of adequate consensus in defining who the 'owners' of the outputs and outcomes of clinical research limits an informed discussion regarding the appropriation of benefits. There is need to suggest and test definitions of ownership of research outcomes in order to appropriate the outcomes of clinical research conducted in Africa. Just as researchers, funding agencies and study participants (patients) contribute to the outcomes of research, and all these and other groups should participate in the identification of beneficiaries of research.

CE 010

An IT platform to support clinical research in East Africa

Fonju Fausta • Cineca Inter-University Consortium, Bologna, Italy

Introduction | Poverty-related diseases such as HIV/AIDS, tuberculosis and malaria are still heavily affecting African sub-Saharan population and economy. Access to treatment is fortunately improving, but long-term monitoring of treatment efficacy and safety and systematic epidemiological data collection is still very poor. Another concern comes from the ethical and scientific implications of the globalisation of clinical research.

Methods | Cineca, a consortium of 36 Italian universities, is the lead partner of Medishare, a European project funded within the Edulink Programme to provide an IT platform for a shared knowledge registry of patients, clinical trials and health programmes in East Africa. The platform, developed by Cineca, offers web-tools to collect homogeneous and standardised data to grant clinical data transparency and integrity, to improve the quality of medical care and to monitor patients' safety and access to treatment. The African partners of the project are the University of Nairobi, the University of Makerere, and the Muhimbili University.

Results | At the Medishare Kenyan National Conference in March 2009, Cineca presented the IT platform and the tools for a population-based registry for HIV/AIDS, TB and malaria. The aim is to monitor and measure appropriate prevention and intervention programmes and to plan new studies and avoid duplication of efforts in Kenya, Tanzania and Uganda. The platform also offers e-learning opportunities and networking tools for participants.

Discussion | The ultimate goal of the Medishare Project is to perform training activities to create capacity and new expertise in Africa in the field of epidemiology/clinical trial methodology.



CE 011

A new tool for quantifying laboratory commodities: The Botswana experience

Phetogo Phoi • Supply Chain Management System (SCMS), Gaborone, Botswana

Introduction | Strengthening health commodity logistics management systems is a priority for the Botswana Ministry of Health for a sustainable national ARV programme. Scale-up has been challenged by persistent stock-outs of critical reagents and commodities. Lack of technical capacity and automated tools to quantify laboratory commodities further hindered scale-up attempts. In 2008, SCMS in collaboration with the Clinton HIV/AIDS Initiative (CHAI), the Botswana Ministry of Health and BOTUSA sponsored the country's first-ever training and national quantification exercise for laboratory commodities for the HIV/AIDS programme. Key to the programme's success was piloting a new laboratory commodity quantification tool developed by SCMS, CHAI and USAID.

Methods | A national forecast was conducted for the ART programme using morbidity-based methods. Data from the National HIV/AIDS Programme, Botswana National HIV/AIDS Treatment Guidelines 2008, laboratory commodity price lists, Central Medical Stores and National Health Laboratory was used.

Results | The new tool enabled the ART programme to forecast the country's commodity needs and reduce stock-outs by 95%. Consumption data remains a challenge, as is adequate dry and cold storage facilities. SCMS will work with CMS and NHL to design a logistics management information system (LMIS) to integrate commodity quantification procurement, warehousing and distribution.

Discussion | Laboratory quantification tool has addressed persistent commodity shortages and overstocking in Botswana's national ART programme and will be updated annually to accommodate future. Lessons learned here can be applied to strengthen systems for other health programmes, with an emphasis on automated quantification tools.

CE 012

Networking for research capacity development: TASO Uganda

Christine Nabiryo • The AIDS Support Organisation (TASO), Kampala, Uganda

Introduction | The AIDS Support Organisation (TASO) is an indigenous non-governmental AIDS service organisation established in 1987 with a cumulative clientele of over 100,000 people living with HIV receiving care and treatment at the 11 service delivery centres. TASO has developed a database that has routine data on follow-up visits of all clients. TASO rolled out its 2008–2012 strategic plan which has a focus on in-house operational research (OR) capacity development beyond implementing specialised collaborative research with partners. TASO research partners include CDC, MRC (UK), Canada Africa Prevention Trials Network, University of Washington (PrEP trial), KIT (Netherlands).

Methods | Collaborative research partners on specific research projects with TASO and others mobilised to support TASO OR capacity building have run workshops in basic research, abstracts and manuscript writing, research proposal development and undertaken mentoring of selected staff in publishing with international peer reviewed journals.

Results | Since January 2008, 4 scientific papers have been published in international peer reviewed journals, 5 participants have been supported to attend an international HIV/AIDS conference and made presentations, and 30 TASO staff have been oriented to basic research methods. Over 30 abstracts have been developed by TASO staff, 10 OR proposals have been developed in-house, seed funding for operational research and equipment have been mobilised and efforts are underway to attract more.

Discussion | Through north-south and south-south networking, organisations in Africa can develop OR capacity and strengthen their programming with support of well-established research partners.

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CE 013

Alternative strategies for ensuring quality research ethics: The case of Uganda*Julius Ecuru • Uganda National Council for Science and Technology, Kampala, Uganda*

Introduction | Research ethics in Africa is fairly new but rapidly evolving. Recent policy reforms in many countries are yielding new research ethics guidelines, and human research protection programmes have been set up in some countries such as training in research ethics and establishment of Institutional Review Committees (IRCs). The challenge is to ensure that rights and welfare of research participants is not compromised in the increasing quest for new knowledge. Uganda developed national guidelines for research involving humans as research participants in 1997 and revised them in 2007. Thus, all human subjects research should undergo ethical review. Currently, twenty institutional review committees have been established in Uganda compared to only two in 1997.

Methods | Consultations through meetings and workshops; review of policy documents and group discussions.

Results | A network of IRC chairpersons, an Annual Research Ethics Conference (AREC), and an IRC accreditation scheme were established.

Discussion | With 20 committees on board and others in the pipeline, the establishment of a network of IRC Chairs, the AREC and IRC accreditation scheme will ensure that IRCs are credible, function optimally to meet national and international standards for research ethics, do not hinder research and the whole system of scientific and ethical review is well coordinated.

This decentralised approach, coupled with a strong networking and coordination mechanism such as a network of IRC Chairs and the Association of Research Ethics Committees (AREC) and IRC accreditation scheme, is necessary given the increasing volume of research and the need to ensure an efficient and predictable research ethics regime.

CE 014

Professional Development Program (PDP) for clinical research staff in Kisumu, Kenya in preparation for future TB vaccine trials*Steve Wandiga • KEMRI/CDC, Kisumu, Kenya*

Introduction | Lack of research skills is a hindrance to site development for clinical trials. This deficit may result in inadequate explanation of studies to participants, potential risks for ethical violations and suboptimal data quality. Within a TB vaccine site development project at KEMRI/CDC in Kisumu, Kenya, funded by EDCTP and Aeras Global TB Vaccine Foundation, we established the Tiegruok Professional Development Program (PDP) in 2007.

Methods | The PDP has 3 staff members. Training methods include: a train-the-trainer model to deliver pre-existing basic training modules shared by Aeras, site visits to similar projects, clinical research trainings, and specialised trainings facilitated by TB Vaccine Network (TBVACSIN) partners. One-hour post training assessments evaluate specialised courses and utilise a classroom environment.

Results | 50 to 65 staff members took four basic research training modules. Evaluation of clinical research knowledge among staff revealed that epidemiology and biostatistics was significantly greater on post-test than pre-test (means: pre-test=59.74, post-test=85.93 & $P<.000$, paired samples t-test). PDP team and study coordinators visited similar studies and PDP programmes in Cape Town. Specialised trainings include: four laboratory technicians trained in TB culture methods for 2 weeks at San Raffaele Laboratory in Italy. Nine clinical staff trained in administering Mantoux, seven in reading chest radiographs, and eighteen in sputum collection. The Vienna School of Clinical Research delivered three courses including Good Clinical Practice (GCP) to 70 participants including 7 from other TBVACSIN sites.

Discussion | Embedding staff development within clinical research can contribute towards bridging the gap in Africa's ability to conduct clinical trials.



CE 015

The importance of introducing quality practices in clinical research

Emma Hancox • Medical Research Council (UK), Banjul, The Gambia

Introduction | There is an increasing recognition that quality practices play a vital role in demonstrating the credibility of clinical research data. An implemented Quality Management System (QMS) can provide assurance to an external source like a funding body or regulatory agency that an institution meets accepted international standards and that the data generated is reliable and reproducible.

Discussion | At the end of 2008 the Medical Research Council (UK) in The Gambia introduced the role of a quality manager to the Unit with the objective of establishing a QMS. The implementation of a QMS will ensure the clinical research data produced at the Unit in West Africa meets similar quality standards to data produced internationally. The QMS model introduced at the early stages of drug development needs to be unique. It needs to both consider and encourage experimental activity whilst also introducing controls to ensure the data is integral and reproducible to allow for further research. A QMS should consider the quality of the research is also dependent on the quality of the available resources and other supporting services which provide the platform for the research. A QMS should be built up of different elements that work together to ensure all activities meet the quality expectations. This paper describes the model being applied at the MRC in The Gambia and discusses the different elements of the QMS, how they interact and how the QMS will allow for the Unit to continuously improve and be confident that their research data meets international quality expectations.

CE 016

Towards a Clinical Research Organisation (CRO) – Major considerations and challenges

Niresh Bhagwandin • South African Medical Research Council (MRC), Cape Town, South Africa

Introduction | The South African Medical Research Council (MRC) sees the need for a national Clinical Research Organisation operating at the highest level for drug and vaccine development with potential public health benefit. We are advised that there is a considerable need for this; a need that is not fully met by the pharmaceutical industry. In order to address this gap, the MRC held a workshop in May 2009 with invitees from the South African public and private sector, as well as international experts.

Discussion | In this paper we present the outcomes of the workshop in the key areas of capacity development, Good Clinical Practice (GCP), ethical considerations, costing and the proposed business model.



HP 011

Microbicide availability knowledge among fishermen along Lake victoria in Kenya, impact on sexual, demographic and behavioural characteristics

Enos Omondi Ochieng • Kenya Medical Research Institute, Kisumu, Kenya

Introduction | The objective of the study is to determine the impact of knowledge on availability of a microbicide by fishermen along Lake Victoria in Kenya on their sexual, demography and behavioural characteristic.

Methods | This study was a pre-clinical Phase of a trial testing the efficacy of 62% ethanol in emollient gel as a potential topical male microbicide among fishermen along Lake Victoria in Kenya. Data was collected by structured interviews on sexual, demographic, behavioural and STI/HIV infection among sexually active fishermen (n=250, age ≥ 18 years) from 18 beaches. Risk factors associated with knowledge of availability of microbicide was investigated using bivariate and multivariate logistic regression analyses.

Results | Overall, 48 (19.2%) reported awareness of availability certain products they would call a microbicide, which ranged from medicated soaps 29.2%, methylated spirit 29.2%, hydrogen peroxide 6.25%, ethanol emollient gel (2.08%). In bivariate analyses those with knowledge were likely to be polygamous (PR 1.09; 95%CI 1.02–1.17), engage in casual sex partnerships (PR 1.08; 95%CI 1.02–1.14) and single (PR 1.06; 95%CI 1.01–1.12). Those aged 26–30 years (PR 0.89; 95%CI 0.82–0.97) or 31–40 years (PR 0.90; 95%CI 0.83–0.97) were unlikely to be aware. Independent risk factors associated with microbicide knowledge were HSV-2 infected (PR 1.21; 95%CI 1.01–1.46), polygamy (PR 1.17; 95%CI 1.03–1.33). They were unlikely to be aged 26–30 years (PR 0.87; 95%CI 0.76–0.95) or 31–40 years (PR 0.87; 95%CI 0.78–0.97).

Discussion | This knowledge and subsequent microbicide usage could lead to alteration of sexual, demographic and behavioural characteristics.

HP 012

Contraceptive use among women participating in a microbicide feasibility study in north western Tanzania

Tony Trong Ao • London School of Hygiene & Tropical Medicine

Introduction | The EDCTP Women's Health Project is conducting a microbicide feasibility study among a cohort of women at high risk of HIV infection. Information about contraceptive use is crucial in the planning of future intervention trials. We report preliminary evidence of contraceptive use in the study population.

Methods | From July 2008 to March 2009, we enrolled 434 women working in bars/hotels into an observational prospective cohort study (we expect to enrol a total of 1000 women by the end of the recruitment period). Structured questionnaires were conducted at baseline asking about reproductive health and family planning. Multivariate logistic regression was used to identified independent factors associated with contraceptive use.

Results | Contraceptive use prevalence was 61.4% (95%CI=56.8–66.2). The main reason for not using family planning was wanting to be pregnant (26.5%). Among those who reported using contraception, 65% use condoms, 11.6% use pills, 26.6% use injectable, and 2.3% use implants. After adjusting for age and education, women were found to be at decreased likelihood of using contraception if they are from Shinyanga site compared to Geita site (AOR=0.41, 95%CI=0.24–0.73), if they report to be a cook compared to a waitress (AOR=0.47, 95%CI=0.24–0.91) or if they are a manager (AOR=0.37, 95%CI=0.14–0.99).

Discussion | Low level of contraceptive use in this population indicates need for improved access to family planning services. The methods of contraception also can inform planners on strategies to increase coverage as well as tailor family planning counselling services to meet the needs of trial participants.



HP 013

Mobilisation strategies in a feasibility study to evaluate the population and the study sites of Manhica and Mavalane in preparation for a Phase III randomised controlled trial of a vaginal microbicide for the prevention of HIV

Khátia Munguambe • Centro de Investigação em Saúde da Manhica (CISM), Mozambique

Introduction | As part of the Microbicide Development Program (MDP), two sites in Mozambique are involved in a microbicide feasibility study to evaluate site preparedness for a Phase III randomised controlled trial of a vaginal microbicide gel for the prevention of HIV. The objective of this study was to describe and evaluate the mobilisation strategies in the context of the microbicide feasibility study in Mozambique.

Methods | A cohort of 500 women was enrolled and followed up between October 2007 and August 2009, in Manhica and the peri-urban area of Mavalane (Maputo City). The recruitment, retention, clinical and behavioural follow-up procedures were similar to those that would be employed in a future microbicide randomised controlled trial. Also included were: (1) training seminars with community representatives who were mobilizers, (2) General health talks at usual community gathering places and recreational spots, (3) Focus group discussions with selected members of the community, (4) Recruitment talks targeted at potential participants at health centre facilities, (5) Messages through mass media channels.

Results | Interest to participate varied throughout the course of the recruitment period, with a moderate rate in the first 2 months followed by a rapid decrease in the subsequent 2 months. The rates oscillated markedly in the following 6 months, as a result of short-term reinforcements to the mobilisation strategy in the periods of low recruitment rates. The rate finally picked up and stabilised at high levels in the final 5 months of recruitment. The most effective channels of communication were

health talks at the hospital and word of mouth in the communities.

Discussion | It is possible to keep communities involved and committed not only with the objectives of study but also with the global effort of developing a safe, effective, and accessible vaginal microbicide gel. Ways of recruiting and maintaining a cohort of volunteers without resorting to direct material incentives to the participants. The fluctuating rates of participant flow demonstrated that community involvement in studies of this nature depends on continuous mobilisation effort.



HP 014

Developing an HIV vaccine research unit from scratch, the Walter Sisulu University experience in South Africa

Jimmy Chandia • Walter Sisulu University HIV Vaccine Research Unit, South Africa

Introduction | South Africa has about 5.4 million people living with HIV infection. Coupled with its relatively developed infrastructure it is a minefield for HIV-related research. The search for an affordable and effective HIV vaccine is one of the national strategies to scale the pandemic. Walter Sisulu University joined the search from scratch in May 2006 with the objective of developing an HIV Vaccine research unit comparable to any of the best in the country.

Methods | The Medical Research Council (MRC) through its mandated unit the South African AIDS Vaccine Initiative (SAVI) provided some initial seed money. A local task team was set up. A building to house the unit was secured. Stakeholders which included the Community, the Department of Health and the University were capacitate on HIV in general and HIV Vaccine research in particular through workshops, presentations at community meetings, radio programmes, posters, faith-based organisations, etc. Formal presentations were made at national and international conferences to market the unit.

Results | The stakeholders were very receptive to the methods used for capacitation. The necessary infrastructure including the renovation of the building to house the unit is work in progress but is not holding us back. The unit is currently involved in one of the EDCTP projects i.e. the preparation of adolescents and their parents for future participation in HIV vaccine trials, an Italian vaccine trial project and a Human papilloma virus vaccine trial for prevention of carcinoma of the cervix.

Discussion | The Walter Sisulu University experience of successfully developing HIV Vaccine Research Unit is having a recipe which includes money, a task team, involvement of stakeholders and marketing the unit.

HP 015

Phase I/II HIV vaccine trial in Dar es Salaam, Tanzania: Study volunteers' experiences

Saida Mmbaga • HIVIS03 Study Volunteers, Dar es Salaam, Tanzania

Introduction | An ongoing HIV vaccine trial in Tanzania started in February 2007. Prior to commencement of the trial, baseline HIV/AIDS epidemiological and socio-behavioural studies were conducted among Dar es Salaam police officers. The trial is the first of its kind in Dar es Salaam and posed unique challenges to volunteers. The objective here is to report on volunteers experiences in participating in the HIV vaccine trial.

Methods | Two of the 60 volunteers were randomly selected to compile a report on advantages and challenges of trial participation from their point of view. The initial draft on the experiences was discussed at a meeting with a majority of the volunteers for their further inputs. Furthermore, self-administered questionnaires on suggested benefits and challenges were filled in by the volunteers. Data was analysed using Stata version 10.

Results | Forty-four of the 60 enrolled volunteers including 12 (28%) females and 32 (72%) males attended the volunteers' meeting to discuss the report. They agreed participating in the trial increased their knowledge on HIV/AIDS and HIV vaccine research, fidelity to their spouses, enabled them to know their general health status, appreciated usefulness of the trial's medical insurance cover. The main challenge faced by the volunteers was dealing with stigmatisation from community's wrong perception that they had been implanted with the HIV. Some volunteers had concerns with vaccines safety and the delay before they could have babies.

Discussion | The volunteers faced challenges through participation in the trial however continuous educational sessions and frequent updates from the study team helped to clear their doubts.



HP 016

Cohort development and collection of epidemiological data in fishing communities in Wakiso District, Uganda

Juliet Mpendo • UVRI-IAVI HIV Vaccine Program, Entebbe, Uganda

Introduction | Fisher folk are considered as high HIV risk populations due to mobility, alcohol consumption, risky sexual behaviour and inadequate HIV health education services. Uganda Virus Research Institute, Entebbe with partner research organisations are recruiting 1000 HIV-negative individuals into a 2-year prospective study and 250 HIV-positive individuals into a virology sub study among fishing communities along shores of Lake Victoria. This is part of the EDCTP funding in preparation for future HIV vaccine trials. We describe challenges in setting up this cohort.

Methods | House-to-house mapping was done followed by socio-demographic census of all residents. A community-based research clinic was set up where screening of volunteers and HIV risk assessment are conducted after informed consent, followed by medical history, physical examination and blood drawn for HIV and syphilis testing. Eligible participants are then enrolled.

Results | To date 1,286 households have been mapped and 2,436 residents (all ages) censused. 203 volunteers have been screened and 133 enrolled (screening/enrolment ratio=1.3:1 for males and 1.6:1 for females). Challenges include few potential volunteers especially men coming for screening. Reasons for these are unavailability of men during clinic hours; community expectations such as provision of routine health care; long informed consent process due to low literacy rate, hence long waiting time at the clinic; misconceptions and stigma that the study recruits only HIV-infected individuals.

Discussion | We have observed unique challenges in setting up HIV cohort in these marginalised communities. Consultation with community leadership has been done and helped in designing better recruitment strategies.

HP 017

Hepatitis C virus infection in people living with HIV/AIDS: Seroprevalence and genetic diversity

Marceline Djuidje Ngounoue • University of Yaoundé, Cameroon

Introduction | HIV/AIDS ranks as one of the prevalent infectious disease facing mankind in the 21st century. Sub-Saharan Africa remains the critically affected region, with AIDS being the principal cause of mortality. The pandemic of AIDS is associated with HCV-infection, another public health problem throughout the world.

Methods | Prospective cohort study was carried out within Public Hospital, Douala from January 2005 to February 2006. A total of 14,742 blood donors and 311 people living with HIV/AIDS were screened for antigens/antibodies to both HIV and HCV using ELISA technique. Viral isolates were used for molecular studies that involved RT-PCR, DNA-Sequencing, and bio-informatics methods for phylogenetic analysis.

Results | 5.77% were obtained for HIV seroprevalence, 2.45% HCV seroprevalence, 2.58% HIV/HCV co-infection among blood donors, and 4.50% among people living with HIV/AIDS. Phylogenetic analysis of co-infected isolates showed that HIV-1 strains were all circulating recombinant forms, CRF02_AG. Different genotypes and subtypes 1a-1b-1c-2a-2c-2k-4a were observed with HCV-NS5B and E2 genes. Phylogenetic analysis showed that Cameroonian strains cluster with Gabonese and French strains, whereas they differ from Ghanaian and Canadian strains. Subtype-1b that is mostly found in developed countries was identified in Douala-Cameroon.

Discussion | 27 years into HIV/AIDS pandemic, this seroprevalence explains the trend of HIV infection in Cameroon. It is an indicator to evaluate the effectiveness of measures undertaken to fight against HIV/AIDS in Africa. HIV/HCV co-infection is less prevalent, but represents serious threat in patients. There is evidence of HIV/HCV genetic diversity in Cameroon, and therefore a tremendous need for sequencing of more isolates.



HP 018

Prevalence of sexually transmitted infections at enrolment in a feasibility study to prepare for future HIV prevention trials in north west Tanzania

Joseph Chilongani • Mwanza Intervention Trials Unit, Mwanza, Tanzania

Introduction | The EDCTP Women's Health Project intends to evaluate the feasibility of establishing a cohort of women at high risk of HIV/STIs to explore key indicators for planning of future microbicide trials. The study is enrolling 1000 women working in recreational facilities in northwest Tanzania.

Method | Women aged 18–44 years were recruited, screened, and enrolled if eligible. Blood and genital samples were collected during enrolment visit and tested at the reference laboratory. Information on sexual risk behaviour was collected using structured questionnaires.

Results | As of April 2009, we have enrolled 462 women. The prevalence of STIs was as follows: HSV-2, 74.4% (95%CI=70.3–78.5); chlamydia, 11.1% (8.2–14.0); gonorrhoea, 14.2% (11.0–17.4); active syphilis 12.2% (9.2–15.3). In multivariate analyses adjusting for age and education, HSV-2 infection was associated with working in a hotel, being divorced/separated, and age at first sex; gonorrhoea infection was associated with history of transactional sex; chlamydia was associated with type of work and age at first sex.

Discussion | STI prevalence is high, suggesting a need for intervention. Safe sex knowledge and other preventive intervention is needed to reduce the burden of infection in this cohort.

HP 019

The molecular epidemiology of HIV-1 in the fishing communities of Lake Victoria, Uganda

Jamirah Nazziwa • Uganda Virus Research Institute, Entebbe, Uganda

Introduction | The high HIV prevalence rates in the fishing communities could be a reflection of the high-risk characteristics of the community. There is evidence associating risk of infection with migration, and in addition, sexual network studies have shown mixing patterns between fishing villages, nearby trading towns and its rural hinterland. In this study, we analysed the molecular epidemiology of HIV in these communities.

Methods | 75 HIV+ individuals who screened out at enrolment into the EDCTP Fisher folk study determining incidence, social and behavioural characteristics, were consented into the virology sub-study. Proviral DNA was extracted from EDTA-treated blood; and PCR carried out in gag-p24 (460bp) and env-gp41 (405bp). PCR products were cloned and sequenced. Phylogenetic trees constructed using neighbour-joining method, and reliability of topologies estimated with bootstrapping.

Results | 67% (24/36) of samples were sequenced in the gag region, analysis showed; 42% (10/24) were subtype A1, 54% (13/24) subtype D, and 4% (1/24) subtype C. 50% (18/36) of samples were amplified in the env region; 67% (12/18) were subtype A1, 22% (4/18) subtype D, and 11% (2/18) subtype C. For 39% (14/36) of the samples, sequences of both gag and env gene were analysed and this showed 57% (8/14) to be recombinants with subtype A1 and D. One was subtype A1/ C recombinant, 7% (1/14), 29% (4/14) were subtype A1 and 7% (1/14) subtype D.

Discussion | Preliminary data of the randomly selected samples shows a significant number of recombinant viruses in this community. The virology data will be related to the social science data to enable us to better model the impact of migration.



HP 020

Which HIV-infected mothers choose to exclusively breastfeed their babies in Burkina Faso? Preliminary findings from a cross-sectional survey in Ouagadougou, 2008–2009



*Eric Nagaonlé Some • Site ANRS Burkina,
University of Ouagadougou, Burkina Faso*

Introduction | The national prevention programme of mother-to-child HIV transmission (PMTCT) is implemented at peripheral level by primary healthcare facilities. These facilities have artificial milk in stock that they offer free of charge to HIV-infected mothers. The study objective was to identify factors associated to the choice by HIV-infected mothers to exclusively breastfeed their babies despite the pressure to formula-feed their babies.

Methods | Cross-sectional study in Ouagadougou. The subjects were children included in the national PMTCT programme run in 22 primary healthcare facilities from 1 January 2008 to 28 February 2009. We have extracted data from medical files. The HIV-infection of children aged 0–24 months was diagnosed using HIV DNA PCR or HIV rapid tests.

Results | Among 182 children selected, 78 (43%) were exclusively breastfed. Factors positively associated with exclusive breastfeeding were: first feeding counseling at the second antenatal visit vs first antenatal visit ($P=0.0015$), follow-up in a second level healthcare facility vs first level ($P=0.0222$), in urban healthcare facility vs rural one ($P=0.0254$), in public healthcare facility vs private one ($P=0.0427$), where healthcare workers with particular dispositions are able to identify at first glance, an HIV-infected mother and her infant vs where they cannot ($P=0.0332$).

Discussion | The majority of HIV-infected mothers in Ouagadougou choose to formula-feed their babies. It will be useful to verify if formula feeding is really affordable, feasible, acceptable, safe and sustainable in this group. Those who choose to exclusively breastfeed their babies present various characteristics dominated by the fear of stigmatisation and discrimination.



MP 09

Glucose-6-phosphate dehydrogenase deficiency protects against severe malarial anaemia in Nigerian male children

Adebola Orimadegun • University of Ibadan, Nigeria

Introduction | Supporting data that G6PD deficiency (Gd-) protects against severe malaria are mainly from areas where malaria is less endemic and Gd- less common than Nigeria. We hypothesised that, being a haemolytic factor, G6PD deficiency makes severe malarial anaemia (SMA) commoner and more severe.

Methods | In 930 children aged 0.5–12 years (458 boys), with microscopically-proven *P. falciparum* malaria, G6PD and haemoglobin were typed by the fluorescent spot test and electrophoresis, respectively. Molecular typing by PCR and restriction enzyme digestion was also carried out on 15% of randomly selected samples. All patients were treated according to WHO/Nigeria protocol. Severity of malarial was compared between G6PD-normal and deficient children.

Results | The prevalence of Gd- was 16.4% and 8.1% among boys and girls with malaria, respectively. Mean (SD) haematocrits (PCV) of 22.8% (7.9) in Gd- was significantly higher than 21.0% (8.9) in Gd+ ($P=0.041$). In boys, 2.7% of Gd- had PCV $\leq 10\%$ compared with 13.6% in Gd+ (OR=0.17, 95%CI: 0.04, 0.73, $P=0.005$). Also, 21.3% of Gd- had PCV $\leq 15\%$ compared with 39.4% in Gd+ (OR=0.42, 95%CI 0.23, 0.75, $P=0.003$). However, no such contrast was found among girls. Overall, Hb AS was typed in 7.6% and was similar between Gd- (13.0%) and Gd+ (6.8%), $P=0.058$. The geometric mean parasite counts (GMPC) was significantly lower in Gd- (15477.5/ μ l) than in Gd+ (19784.4/ μ l), $P=0.013$, and it is independent of HbAS.

Discussion | Gd- male was unlikely to develop severe malarial anaemia. This prediction could not be made in female. Thus Gd- protects against emergency blood transfusion and its related risks in male.

MP 010

Risk factors associated with severe malaria among under-five children attending Seventh-Day Adventist hospital, Ile-Ife, Nigeria

Idowu Senbanjo • Lagos State University College of Medicine, Nigeria

Introduction | Over 90% of the burden of malaria occurs in sub-Saharan Africa. Children, especially the under-fives, are the most vulnerable. In Nigeria, it accounts for 25% and 30% of infant and childhood deaths respectively. The aim of this study is to determine the prevalence and risk factors associated with the development of severe malaria.

Methods | This is a cross-sectional, hospital-based prospective study of under-five children with severe malaria seen at the Seventh-day Adventist Hospital, Ile-Ife, Nigeria during the months of May to September 2005.

Results | Out of the 668 under-five children that were managed in the hospital during the study period, 176 (26.3%) children were diagnosed both clinically and parasitologically to have malaria. 116 (17.5%) children and 60 (9.0%) children had severe and uncomplicated malaria infections respectively. Of the seventeen variables examined, high malaria parasite density, non-use of mosquito-bite preventive measures, poverty, low maternal education, low-ranking paternal occupation, rural domicile and low social class were each associated with severe malaria ($P<0.05$). Multivariate analyses show that only parasite density and poverty were the significant predictors of severe malaria.

Discussion | Progress in stemming the burden of malaria depends on accurate knowledge and understanding of the epidemiology and control of the disease in the affected populations. The non-use of mosquito bite preventive measures might be as a result of ignorance and poverty. These factors should be considered in the design of sustainable and effective locally relevant strategies for the prevention of malaria.



MP 011

Reference biochemical parameters for Mpongwe district, a malaria vaccine trial site

Justin Chileshe • Tropical Diseases Research Centre, Ndola, Zambia

Introduction | Mpongwe, a rural district in Zambia, was characterised as a site for malaria vaccine trials. Among the various activities conducted was the determination of some biochemical parameters. Biochemical testing is the mainstay of drug and vaccine safety tests that underlie clinical trials. This was conducted in both the dry and wet seasons, during which periods malaria transmission varies significantly.

Methods | This was a cross-sectional study nested in the main survey conducted to characterise Mpongwe as a vaccine trial site. Two surveys were conducted in dry season of 2005 and in wet season of 2006. A total of 1200 samples were analysed (600 from each season) for selected clinical chemistry parameters as well as malaria related data. Data was entered and analysed using Epi Info and STATA.

Results | For both wet and dry seasons over 90% of the samples were found to have urea, albumin and total bilirubin parameters within normal range. Creatinine values were normal in 54.50% and 53.48% in the wet and dry seasons respectively. Alkaline phosphatase was within normal range in 55.33% and 50.47% in the dry season and the wet season respectively. When tested against malaria the parameters showed a significant statistical difference in the wet season for creatinine ($P < 0.001$), albumin ($P = 0.017$) and alkaline phosphatase ($P < 0.001$) whereas in the dry season only creatinine ($P < 0.001$) and alkaline phosphatase ($P = 0.006$) between the malaria infected and non-infected individuals.

Discussion | These results show that the population at our chosen site characterised for vaccine trial gave a normal statistical distribution for clinical chemistry parameters.

MP 012

Non-traumatic coma

Rebecca Kivumbi • Makerere University, Uganda

Introduction | Acutely ill children with impaired consciousness contribute 10–15% of all hospital admissions. In sub-Saharan Africa the most common causes of coma are cerebral malaria and meningitis with an overall mortality of 23.4%. In Uganda cerebral malaria is a common cause of coma, and neurological sequelae have been found in 1.5–29% of the survivors. The aim of the current study is to determine the prevalence, causes, and factors associated with immediate adverse outcome of children admitted with non-traumatic coma.

Methods | Hybrid of cross sectional design and unmatched cohort study design.

Results | The prevalence of non-traumatic coma among children admitted in ACU was 3.5% (95%CI = 0.65–6.35). The most common causes of NTC were cerebral malaria (57.6%) and acute bacterial meningitis (11.5%). Of the 142 study patients recruited 111 (78.2%) survived while 31 (21.8%) died. Factors that were significantly associated with death on a bivariate analysis included younger age, male sex, long duration of illness, incomplete immunisation, dehydration, depth of coma, hyperreflexia, hypertonia and respiratory distress. Independent predictors of death included deep coma, dehydration, hyperreflexia, hypertonia and pupil dilatation.

Discussion | The prevalence of NTC among children admitted to ACU was 3.5%, the main causes of NTC were infections with cerebral malaria being the commonest and acute bacterial meningitis being the second most common cause. Other important causes included TBM, Diabetic Keto acidosis, hypertensive encephalopathy, poisoning, and metabolic disturbances. Children with modified Glasgow coma scale of 8 and below should be managed and monitored closely till they stabilize. More studies should be done to follow the children for longer periods to find the long-term outcome of NTC.



MP 013

Pfcr 76T allele is associated with clinical severity of malaria in children of rural villages of Mali

Mamadou Wele • *Malaria Research and Training Center, University of Bamako, Mali*

Introduction | The pathogenesis of severe malaria is the result of complex interactions between parasites, host and environmental factors. As the risk of malaria death among children has increased with the emergence of chloroquine resistance, we hypothesised that the key determinant of CQR, Pfcr 76T may be involved increasing the risk of severe malaria.

Methods | In two Malian villages hyper-endemic for *P. falciparum* malaria, Kangaba and Kella, the relationship between Pfcr 76T allele and the clinical severity of malaria was investigated in a case control study. In total, 193 children were diagnosed as severe malaria cases. Each of them was matched by age and sex with a control from uncomplicated malaria cases. For all cases clinical and laboratory observations were made and Pfcr 76T was identified using nested PCR. In order to eliminate the impact of red blood cells disorder on clinical severity of the disease, only children with normal G6PD and normal haemoglobin were taken into account. Then the prevalence of Pfcr 76T was compared in the case and control groups to find out any association with severe malaria.

Results | Our data have shown that Pfcr 76T allele is significantly associated with malaria severity in endemic rural villages of Mali ($P < 0.0001$). In contrast, no significant association was observed between Pfcr 76T allele and severe malarial anaemia or cerebral malaria ($P > 0.5$).

Discussion | Pfcr 76T is associated with malaria severity. Because of low sample size in our study we found lack of association with severe anaemia or cerebral malaria.

MP 014

Estimation of malaria transmission in malaria endemic area, Central-East Sudan using enzyme-linked immunosorbent assays (ELISAs)

Zeinab Elmahdi • *Institute of Endemic Diseases, University of Khartoum, Sudan*

Introduction | Malaria continues to be a major health problem, especially Africa. Malaria is a focal disease, which differs from country to country and even within the same country, and therefore there has to be a regular assessment of each country's malaria situation. Objectives of this study are (1) Identification of malaria vector in the study area; (2) Estimation of malaria transmission intensity via two entomological parameters: i. Sporozoite rate (SR). ii. Entomological inoculation rate (EIR); (3) Using advanced immunological and molecular biological techniques to achieve the previous objectives; (4) Determination of feeding preference for the vector.

Methods | The study was conducted in a high-risk region with malaria. Samples were processed as follows: (1) Morphological identification; (2) PCR for species-specific detection; (3) Csp ELISA to detect malaria sporozoite; (4) Blood meal ELISA to detect host blood meal.

Results | *Anopheles arabiensis* is the only vector of malaria in the study area, with a high anthropophilic behavior; more than 85% feeding on humans. Sporozoite rate was in average ranging between 2.2–3.6%. EIR, showed an average rate according to data from different African countries, its overall range was 3.2–6.6 infective bites / person / transmission season.

Discussion | Indoor spraying for insecticide and impregnated bednets will be good for mosquito control, also larval control. Focusing of control activities in the transmission season is highly recommended in attempt to save the environment. Another study in the dry season is needed because *Anopheles arabiensis* can survive in this period.



MP 015

Dynamics of spread of the malaria protective polymorphisms in Sudanese village populations

Niven A Salih • Institute of Endemic Diseases,
University of Khartoum, Sudan

Introduction | The rise and maintenance of balancing selection as an evolutionary trend has its best example in the role of the S haemoglobin in protection from malaria. Yet, the dynamics of such processes remain poorly understood, particularly in relation to various transmission levels and under population effects.

Methods | We investigate the association of the abnormal haemoglobin HbS in protection from clinical episodes of malaria in two populations where malaria is endemic, but mostly presented with mild clinical forms. A number of 470 individuals comprising 65 and 82 families from Hausa and Massalit tribes respectively were genotyped for HbA and HbS. Allele and genotype frequencies were estimated in the total sample as well as for different age groups. Departure from Hardy Weinberg Expectation was calculated and the age group frequencies were used to calculate the coefficient of fitness and to simulate the expected frequencies in future generations.

Results | Genotypes were within Hardy-Weinberg expectations in Hausa and Massalit in the total sample but not within the different age groups. There was a trend for increase in allele frequencies in Massalit and decrease of frequencies in Hausa. Although the haemoglobin S allele were able to confer significant protection from clinical malaria in the two populations as suggested by Odd Ratios, the overall fitness of the S allele seem to decline in Hausa.

Discussion | Apparently such loss of balancing selection is due to combined effect of preponderance of non-clinical malaria in Hausa, the deleterious effect of the homozygote S under circumstances of endogamy.



TP 03

Tuberculosis at a tertiary referral hospital in Rwanda: Short-term outcome and risk factors

Osee Sebatunzi • Kigali University Teaching Hospital, Kigali, Rwanda

Introduction | The reason for the poor short-term outcome of patients on tuberculosis (TB) treatment in low-resource settings remains unclear.

Methods | We conducted a prospective cohort study with all patients starting first-line TB treatment at the Kigali University Hospital from May 2008 onwards. Those with at least three months follow-up were included in this analysis. Cox-proportional hazard modelling was used to explore risk factors of TB-related mortality.

Results | We report on 161 patients: 85 (53%) men, median age 34 years (IQR 28–41). Of these, 60 patients (37%) had pulmonary TB, 68 (42%) extrapulmonary TB and 33 (20%) a mixed form. Nineteen (12%) were on re-treatment. One hundred and four (65%) were HIV-seropositive with a median CD4 count of 100 (IQR 42–240). Median body mass index (BMI) and haemoglobin were 18.3 kg/m² (IQR 16.2–20.4) and 11.2 g/dl (IQR 8.8–13.5) respectively. Ninety-four (59%) were admitted. So far, 63 (39%) patients completed TB treatment, 14 (9%) were lost to follow-up and 36 (22%) died. Prior TB treatment (HR 2.80; 95%CI 1.19–6.62), hospitalisation (HR 9.92; 95%CI 2.01–48.97) and low BMI (HR 0.85 per unit increase; 95%CI 0.74–0.98) were independently associated with increased mortality.

Discussion | TB-related mortality is high in a setting with a high HIV co-infection rate. Besides markers of severity such as low BMI and hospitalisation, a prior history of TB treatment, a well-known risk factor for multidrug resistant TB, is associated with higher risk of mortality. This study subscribes the need for wider availability of TB culture and drug susceptibility testing.

TP 04

Drug susceptibility patterns among new and previously treated pulmonary tuberculosis patients from a high HIV prevalence urban setting in Zambia

Chanda Mulenga • Tropical Diseases Research Centre, Ndola, Zambia

Introduction | Zambia is among the top-10 countries with the highest tuberculosis incidence rates in the world. With such high levels of disease it is important to monitor levels of drug resistance to inform policy. We set out to determine the level of *Mycobacterium tuberculosis* resistant to first and second-line treatment drugs in an urban population.

Methods | Sputum samples were collected consecutively, from all new and previously treated patients, with a smear-positive result at four selected diagnostic centres in Ndola District between January and July 2006. Drug susceptibility testing was performed using the proportion method on Löwenstein-Jensen medium against four first-line drugs and two second-line drugs.

Results | Among 157 new cases, combined resistance was 7.6%, mono-resistance to isoniazid and rifampicin was 4.5% and 1.3%, respectively. Of 30 re-treatment cases, combined resistance was 13.3%, mono-resistance to isoniazid and rifampicin was 3.3% for each drug and 1 resistant to all four drugs (multidrug resistance) case was detected. No resistance to second-line drugs tested (kanamycin and ofloxacin) was found.

Discussion | Zambia appears to have maintained low levels of resistance; a plausible indication of a well functioning tuberculosis program. However, appearance of mono-resistance to rifampicin, not previously seen, and sustained levels of isoniazid resistance, may be cause for concern. Although described in HIV, mono-resistance to the two drugs may predispose the population to development of multidrug resistance, which would complicate effective management of patients.





CP 05

Lessons learnt from stakeholder consultations on research on the transmission dynamics of HIV and STIs in fishing communities in Malawi

John Sadalaki • Malawi–Liverpool Wellcome Trust, Mangochi, Malawi

Introduction | A combined social science and prospective epidemiological study aims to assess the transmission dynamics of HIV and STIs and the feasibility of conducting future preventive trials in the fishing communities of lakeshore Mangochi in Southern Malawi.

Methods | Consultations on the aims and objectives of the research were undertaken with key stakeholders, such as district heads of government, NGOs and the community leadership structure. Consultations involved presentations and discussions, which were recorded and analysed qualitatively – through mapping out key thematic concerns and linking them to different stakeholder groups (stakeholder analysis).

Results | All stakeholders welcomed the project, explaining that fisher folk – a highly mobile and often elusive group – have been largely neglected in interventions and research in lake-shore Malawi. In a context of extreme poverty and high HIV prevalence, local leaders were most concerned with tangible benefits, such as income generating activities and nutritional support for people living with HIV. Government officials' concerns related to ethics, and ensuring proposed MK250 transport allowance for those involved in the study did not constitute an inducement or impacted negatively on other health services in the area – a concern echoed by NGOs.

Discussion | Consultations enabled the research team to understand diverse stakeholders' multiple and often contradictory concerns and enabled them to clarify the aim of the research and inform the process for constituting a Community Advisory Group. Consultation takes time and resources but is an important investment at the beginning of a long-term clinical study.

CP 06

Identifying candidates for post-doctoral re-entry grants using PubMed automated search utilities

Paterne Lessihuin Dibacka • Albert Schweitzer Hospital, Lambaréné, Gabon

Introduction | Several funding bodies, among them EDCTP, offer re-entry grants for senior researchers. Scientists and research institutions may not be aware of each other if they are not specialised in exactly the same research area. We tried to identify Gabonese post-doctoral using search utilities made available by PubMed.

Methods | A database of local names was established, based on patients seen at the paediatric ward of the Albert Schweitzer Hospital, Lambaréné, Gabon. A Python programming language script was developed using Biopython's Entrez library and PubMed's e-search utility. It extracted all articles in the field of infectious diseases published within the last 5 years and having a local name as the first author.

Results | A total of 4108 unique family names were searched for and 561 articles with 224 unique author names were retrieved. Seventy-seven of these names were considered representative of local names. Forty-one authors had published three or more articles. Of these, the seven authors having articles containing Medical Subject Headings HIV, tuberculosis or malaria, all were either known personally to the authors or were unlikely to be Gabonese.

Discussion | PubMed's e-utilities are a promising way to identify post-doctoral candidates. In the case of Gabon, candidatures with fields of interest lying outside of the three EDCTP disease areas need to be solicited.



CP 07

The re-emergence of vaccine preventable diseases due to poor cold chain management in health facilities in Lagos, Nigeria

Munir Bankole • Ministry of Health, Nigeria

Introduction | Efforts have doubled by researchers all over the world to improve on available vaccines as well as develop new ones. In Nigeria, the Lagos State Government has intensified efforts to monitor and ensure that vaccines are adequately managed in Health Facilities (HFs). Despite this, vaccines are still poorly managed in many of the HFs. As a result, non-potent vaccines are administered to the populace, especially the children, with the ultimate (re-)emergence of those diseases thought to be under control, causing a rise in morbidity and mortality rates in the country. This work aims to review the Cold Chain Management in HFs and evaluate the knowledge of Health Workers (HWs) in vaccine management in Lagos, Nigeria.

Methods | 1,000 private HFs in Lagos, Nigeria were visited between September 2007 and March 2009. A Cold Chain assessment form was completed for each HF visited, and a total of 2,100 HWs were interviewed to evaluate their knowledge on vaccine storage temperature, Vaccine Vial Monitor (VVM) indicator and expiry date of vaccines. About 15,000 vaccine vials were screened to ascertain the expiry dates, presence or absence of VVM indicator and VVM stage.

Results | About 900 (90%) of the vaccine storage equipment in the HFs visited either had mechanical failure or virtually non-existent electricity supply. A total of 2000 (95%) HWs had little or no knowledge of VVM indicator. A significant ($P < 0.05$) value of 12,000 (80%) vials were either in stage 3 or 4 of VVM or had VVM indicators removed.

Discussion | Regular education on vaccine management would need to be given to HWs with very strict measures put in place by the government to ensure compliance in HFs, which would guarantee administration of potent vaccine to the populace.

SATELLITE MEETING
Ownership of research outcomes
in sub-Saharan Africa

12:30–14:00

Mahale XL (3rd floor)

ORGANIZERS

EDCTP
NACCAP

Background

Many African researchers and institutions have limited expertise with protecting their intellectual property, data or research outcomes which may hamper a healthy balance between ownership and utilisation of research outcomes, including data. This area is becoming even more critical as African institutions are beginning to assume sponsorship responsibilities which require compliance with ICH-GCP guidelines. In view of this EDCTP in collaboration with NACCAP will hold a satellite meeting on ownership of research outcomes, including data management, in sub-Saharan Africa.

Objectives

- To review the current situation and to sensitise researchers on the importance of legal ownership of knowledge and research outcomes
- To identify of gaps, challenges as well as potential solutions
- To identify the role that EDCTP, NACCAP and other partners can play in strengthening sub-Saharan the capacity for negotiating fair ownership of pre-existing knowledge and research outcomes.

Target audience

This satellite meeting will be open to all interested European and African project coordinators of EDCTP grants, especially those who are directly involved in contract negotiations, heads of research institutions, scientists and research administrators who deal with ownership issues or data management. Representatives from (public-) private partnerships who have experience in sharing legal ownership are encouraged to share their experiences.



Programme

Welcome: Objective of the meeting

Chair: Charles Mgone • EDCTP

Responsibilities of partnerships with regard to fair ownership

Marta Catarino • Universidade do Minho, Portugal

Data ownership: The responsibilities of all parties involved in product development

Janis Lazdins • WHO-TDR, Head Research & Development

Experiences with shared ownership of data: Capacity needs of African institutions

Elly Katabira • Makerere University, Uganda

Panel discussion on shared experiences and formulation of ideas for action

Moderator: Charles Mgone • EDCTP

Please note: packed lunches will be available in the Mahale XL room for participants to this satellite meeting

PARALLEL SESSIONS | HIV/AIDS
Clinical trials in sub-Saharan Africa (cont.)
14:00–16:00
Meru Hall

CHAIRS
Prof. Omu Anzala
Dr Rosemary Musonda

14:00–14:05
Brief introduction
from the Chairs

14:05–14:20
Strategies for nevirapine initiation in HIV-
infected children taking paediatric fixed-
dose combination 'baby pills' in Zambia:
A randomised controlled trial

*Veronica Mulenga • University Teaching Hospital,
Lusaka, Zambia*

Introduction | Fixed-dose combination scored dispersible tablets of stavudine/lamivudine/nevirapine (Baby/Junior Triomune, Cipla Ltd) provide a simpler alternative to liquid formulations and have correct dose ratios for children. However, to dose escalate nevirapine, separate drugs are required initially. We evaluated the need for dose-escalation in HIV-infected Zambian children.

Methods | Children were randomised to start antiretroviral therapy with full-dose (FD) nevirapine (Triomune am/pm) versus dose-escalation (DE), an initial 14 days of half-dose nevirapine (Triomune am; Lamivir-S (combined stavudine/lamivudine) pm) followed by full-dose. Primary endpoint was clinical/laboratory grade 3/4 adverse events (AEs) related to nevirapine.

Results | 211 children (median 5 (IQR 2–9) years; CD4% 13% (8–18%); WHO 3/4 65%/34%; weight- and height-for-age z-scores both -3.3) were enrolled and followed for median 92 weeks. There were 31 grade 3/4 AEs definitely/probably or uncertain whether nevirapine-related in full-dose (18.0/100 child-years) compared to 29 in dose-escalation (16.5/100 child-years: IRR=1.09 (95%CI 0.63–1.87) $P=0.68$). None of these were clinical AEs. 13 (12%) full-dose vs 2 (2%) dose-escalation had grade 1/2 disseminated skin rashes. 3 children (2FD, 1DE) substituted efavirenz (early in trial); 9 (8FD, 1DE) stopped nevirapine, followed by successful subsequent dose-escalation. Non significant predictors of nevirapine rash or grade 3/4 raised transaminases were being female (OR=1.5 $P=0.41$), older age (OR=1.09 per year; $P=0.14$), higher CD4-for-age (OR=1.06 per unit z-score, $P=0.38$). 22 children died (12FD, 10DE), 1FD and 5DE before 4 weeks, none considered drug-related.

Discussion | 90% children who started full-dose nevirapine continued uninterrupted. Although more reactions occurred than with dose-escalation, rashes were mild, and nevirapine was successfully re-started in the majority.

14:20–14:35

Pharmacokinetics of nevirapine in young children during combined ART and rifampicin-containing antituberculosis treatment



Mirjam Oudijk • Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands

Introduction | There is an urgent need to optimise co-treatment for children with TB/HIV. We investigated nevirapine pharmacokinetics in Zambian children <3-years old, co-treated with NVP/3TC/d4T in fixed-dose-combination and rifampicin-based anti-tuberculosis treatment.

Methods | Twenty-two children received anti-tuberculosis and ART regimens (using WHO weight band guidelines) concurrently for four weeks before pharmacokinetic sampling. Plasma nevirapine concentrations were determined in samples taken predose (Co) and at 1, 2 and 6 hours after an observed dose. Nevirapine pharmacokinetics were compared with those in 16 children without tuberculosis.

Results | One child with undetectable Co, assumed to be nonadherent, was excluded from analysis. Of the remaining 21 children, 10 were girls. Median (range) age, weight, and baseline CD4+% were 1.55 (0.66–3.18) years, 8.0 (5.1–10.5) kg and 12.9 (3.9–33.4)%. Mean (IQR) nevirapine and rifampicin daily doses were 353 (326–375) mg/m² and 12.2 (10.2–13.6) mg/kg. Median (range) Co, peak concentration and estimated AUC were 2.93 (1.06–11.4) mg/L, 6.33 (2.61–14.5) mg/l and 52.0 (22.6–159.7) mg×h/L. Co was <3.0 mg/l in 57% of children with vs none without tuberculosis. Multivariate linear regression described a 41% (95%CI: 24–55%) reduction in AUC for children with vs. without tuberculosis after adjusting for dose/m².

Discussion | We found substantial reductions in nevirapine concentrations in young children receiving rifampicin concurrently. The co-treatment approach should be used with caution until more efficacy and safety data is available. An increased nevirapine dose is likely to be necessary and requires further evaluation.

14:35–14:50

Single-dose fluconazole versus standard two weeks therapy for oropharyngeal candidiasis in HIV-infected patients: A randomised, double-blind placebo-controlled trial

Omar JM Hamza • Muhimbili University of Health and Allied Sciences, Tanzania

Introduction | Oropharyngeal candidiasis is the most common opportunistic infection in HIV-infected patients. Because of convenience, cost and reticence to complicate antiretroviral treatment regimens, a single-dose fluconazole may be a favourable regimen for moderate to severe oropharyngeal candidiasis. We conducted a prospective, randomised, double-blinded placebo-controlled trial to compare the clinical and mycological responses, relapse rates and safety of single 750 mg dose and a 14-day course of fluconazole.

Methods | 220 HIV-infected patients with clinical and mycological evidence of oropharyngeal candidiasis were randomly assigned in a 1:1 ratio to receive either a 750 mg single-dose of fluconazole (n=110) or 150 mg fluconazole once daily orally for two weeks (n=110). The primary efficacy analysis was based on clinical and mycological responses at end of treatment. Secondary parameters were safety and relapse rate.

Results | Single-dose fluconazole was equivalent to 14-day course fluconazole in achieving clinical and mycological cure, with a clinical cure of 94.5% and 95.5%, respectively (OR=0.825; 95% confidence interval is 0.244–2.789; P=1.000), and a mycological cure rate of 84.5% and 75.5%, respectively (OR=1.780; 95%CI=0.906–3.496; P=0.129). Drug adverse events were uncommon and not different for both treatment groups.

Conclusions | A single dose of 750 mg of fluconazole was safe, well tolerated and as effective as standard 14-day fluconazole therapy in HIV/AIDS patients with oropharyngeal candidiasis.



14:50–15:05

High prevalence of cervical squamous intraepithelial lesions in women on antiretroviral therapy in Cameroon: Is targeted screening feasible?

Julius Atashili • University of Buea, Cameroon

Introduction | Cervical cancer is the most common cancer in women in low-income countries. Although cervical cancer incidence and mortality is higher in HIV-positive women, resource limitations restrict the implementation of systematic screening programs in these women. We explored the potential for targeted screening by assessing the prevalence, severity and predictors of cervical squamous intra-epithelial lesions (SILs) in HIV-positive women in Cameroon.

Methods | We conducted a cross-sectional study of women on antiretroviral therapy in Cameroon. Socio-demographic, behavioural, and clinical information was obtained from eligible women. Cervical exfoliated cells were then collected, a conventional cytology performed and epithelial lesions classified according to the Bethesda 2001 system.

Results | A total of 282 women, aged 19 to 68 years, were enrolled in this study. The median CD4 count was 179 cells/ μ l (interquartile range: 100 to 271). SILs were detected in 43.5% of the 276 women with satisfactory samples: including atypical squamous cells of unknown significance (ASCUS) 0.7%, low-grade SIL (LSIL) 25.0%, atypical squamous cells, cannot exclude high grade lesions (ASC-H) 14.5%, and high-grade SIL (HSIL) 3.3%. None of the demographic or clinical characteristics considered significantly predicted the presence of any SILs or the presence of severe lesions requiring colposcopy.

Discussion | The prevalence of SIL in women on antiretroviral therapy in Cameroon was high underscoring the need for screening and care in this population. In the absence of any accurate demographic or clinical predictor of SIL, targeted screening does not seem feasible. Alternative affordable screening options need to be explored.

15:05–16:00

Discussion on possible new strategies

PARALLEL SESSIONS | MALARIA
Clinical trials in sub-Saharan Africa (cont.)
14:00–16:00
Victoria Hall

CHAIRS
Dr Christine Manyando
Dr Saadou Issifou

14:00–14:05
**Brief introduction
from the Chairs**

14:05–14:20
**Malaria vaccine GMZ2 pre-clinical selection
and clinical development**

*Michael Theisen • Statens Serum Institut, Copenhagen,
Denmark*

Introduction | The rational development of malaria vaccines is a formidable task: the *Plasmodium falciparum* genome contains more than 5000 genes, and the diversity of the malaria parasite and the genetic diversity of the human host are vast. However, the fact that individuals in malaria endemic areas can develop protective immunity is a lighthouse and a guiding principle for our selection of vaccine components.

Methods | The starting point was to compare the antibody and antigen profile in malaria immune parents and their children suffering from acute attacks of *Pf*-malaria. Screening a genome library, we applied sera from immune individuals from Africa, Indonesia and South-America to identify the antigens found in acutely ill children. Subsequently, numerous immune-epidemiological studies have identified specific regions of a late schizont antigen (GLURP) and a merozoite surface antigen (MSP3). The absence of clinical malaria in children from Africa and Asia has consistently been linked to the possession of high titres of antibodies to GLURP and MSP3. A multi-target hybrid vaccine employing these two conserved antigens have therefore been developed employing a novel large-scale friendly production system.

Results | The GMZ2 vaccine has successfully passed Phase Ia clinical trial in German volunteers and Phase Ib clinical trial in Gabonese volunteers and recently a paediatric dose-finding study in Gabonese children. With EDCTP support this vaccine will now, with AMANET as sponsor, enter multi-centre Phase 2b efficacy trials in Gabon, Uganda, Burkina Faso and the Gambia.

14:20–14:35

Phase Ib randomised controlled double-blind trial to evaluate the safety and immunogenicity of 30 and 100 µg GMZ2 candidate malaria vaccine in Gabonese children aged 1–5 years



Saadou Issifou • MRU ASH Gabon

Introduction | A blood stage malaria vaccine candidate, GMZ2 (hybrid protein GLURP and MSP3) has been shown to be safe and immunogenic in non-immune and semi-immune adults in Phase I clinical trials in Germany and Gabon. We conducted a Phase Ib clinical trial of the GMZ2 vaccine to assess safety and immunogenicity in children aged 1–5 years in Lambaréné, Gabon.

Methods | A Phase Ib randomised, controlled, double-blind clinical trial with two different dosages of the GMZ2 antigen (30 µg or 100 µg) and Verorab control vaccine administered in three groups of 10 children at a schedule of 0, 1, and 2 months. The primary endpoint was safety and reactogenicity within 28 days post-vaccination. Blood samples were obtained at different time points for immunological response with primary analysis done at 84 days post vaccination one.

Results | 30 children were enrolled, 10 in each group. There was no difference in safety or reactogenicity profile between the two GMZ2 dosages and Verorab. Immunologically, 100 µg dosage performed better in achieving statistically significant component immune responses.

Discussion | The GMZ2 malaria vaccine candidate was safe, well tolerated and immunogenic in Gabonese children aged 1–5 years. The findings underscore the need to conduct a Phase IIb clinical trial to evaluate the vaccines efficacy against *P. falciparum* malaria disease.



14:35–14:50

Baseline epidemiological study in preparation for a Phase IIb proof of concept efficacy study of GMZ2 candidate malaria vaccine in children aged 12–84 months old


Kalifa Bojang • Medical Research Council (UK), Banjul, The Gambia

Introduction | Designing large Phase IIb/III malaria vaccine clinical trials requires data on the epidemiology of malaria in the proposed study area. With changing malaria epidemiology in the endemic areas of Africa, and absence of validated surrogate markers for immunological/efficacy endpoints, such data are important to guide the design of efficacy clinical trials. In preparation for a multi-centre Phase IIb proof of concept efficacy clinical trial of GMZ2 candidate malaria vaccine in children, we proposed to conduct baseline epidemiological study in children aged 12–84 months living in the proposed study sites in Uganda, Gabon, The Gambia and Burkina Faso.

Methods | Primarily, to determine incidence rates of clinical malaria in the selected study areas during the main malaria transmission season. Secondary objectives include determining the main risk factors for malaria in the study area, piloting surveillance system to be used in the main efficacy trial and measuring prevalence of malariometric indicators.

Results | The study will be set up at each site as prospective cohort study, with passive and active case detection follow-up. Surveillance will be carried out by screening all study children presenting at health facilities with fever or history of recent fever during the main malaria transmission. Cross-sectional surveys will be conducted at the beginning and end of the malaria transmission season. Participant study duration is approximately 6 months.

Discussion | Baseline data will be obtained that will allow for optimal sample size calculations for the multi-centre Phase IIb efficacy clinical trial of the GMZ2 candidate malaria vaccine.



14:50–15:05

Facing the challenge of building malaria clinical trials site in developing country: Achievements and lessons from the Balonghin malaria vaccine trial centre in Burkina Faso

Sodiomon Sirima • Centre National de Recherche et de Formation sur le Paludisme (CNRFP), Ouagadougou, Burkina Faso

Introduction | Malaria remains a major public health problem in sub-Saharan Africa (SSA) after increase of resistance to most affordable and accessible drugs and insecticides resistance. The need for cost-effective drugs and vaccines is challenging with several drugs and candidate vaccines for testing in endemic areas. It is desirable to develop and maintain trial sites conforming to international standards. Declining malaria trends at established trial centres demand setting new sites with adequate transmission. These areas lack water, electricity and adequate vital statistics.

Methods | Since 2002, CNRFP Burkina Faso undertook development of a vaccine trial site in rural Balonghin, Saponé district, 45 km from Ouagadougou, Burkina Faso.

Results | Achievements of the initiative include established DSS covering 85,000 inhabitants, clinical trial facilities (buildings and equipment), a reliable communication system and a multidisciplinary team of 20 investigators implementing various SOPs. The outcome being 3 Phase IIb drugs trials and 2 vaccines trials under GCP and complying with GLP successfully conducted over last five years.

Discussion | A holistic capacity strengthening option is most appropriate for sites development in sub-Saharan Africa.

15:05–16:00

Discussion on possible new strategies

PARALLEL SESSIONS | TUBERCULOSIS
Clinical trials in sub-Saharan Africa (cont.)
14:00–16:00
Mandara Hall

CHAIRS
Prof. Mecky Matee,
Prof. Martin Grobusch

14:00–14:05
Brief introduction
from the Chairs

14:05–14:20
The prevalence of tuberculosis infection and
disease among adolescents in Western Kenya:
Preparation for future TB vaccine trials

*Videlis Nduba • KEMRI/CDC Research and Public
Health Collaboration, Kisumu, Kenya*

Introduction | The risk of tuberculosis (TB) disease following infection begins to increase in adolescence making this high risk population a target for new TB vaccines. In order to contribute to the design and implementation of future TB vaccine trials, we sought to determine the incidence and prevalence of TB infection and disease among adolescents in Western Kenya. **Methods** | A prospective cohort study of 5000 adolescents aged 12–18 years is being conducted by KEMRI/CDC in Western Kenya. Adolescents are enrolled and followed for one year. TB suspects are defined using clinical criteria, history of contact with a TB case and/or a positive Mantoux [(TST); TST positive = ≥ 10 mm or ≥ 5 mm if HIV+]. Suspects are investigated for pulmonary tuberculosis (PTB) through sputum examination (microscopy and culture), and chest radiography. **Results** | Out of 1429 adolescents enrolled by February 2009, 698 (49%) were female, median age 14 years. 578 (40%) were identified as TB suspects. 341 (24%) had a TST > 10 mm and, of the 6 HIV infected adolescents, all had a TST > 10 mm. Five definite PTB cases were identified (positive smears or culture) and 3 probable PTB based on clinical and radiological criteria, reflecting crude prevalence estimates of 350/100,000 (definite) and 560/100,000 (definite and probable) PTB respectively. **Discussion** | The prevalence of TB infection and pulmonary disease among adolescents in Western Kenya appears quite high. Although follow up to obtain incidence is still underway, these preliminary results suggest that this study population will be a suitable target population for TB vaccine trials.



14:20–14:35

A mobile field site as a model for enrolment and follow up in a tuberculosis incidence cohort in adolescents, Western Kenya, in preparation for future vaccine trials



Peter Nyamthimba Onyango • KEMRI/CDC Research and Public Health Collaboration, Kisumu, Kenya

Introduction | Adolescents are expected to be a critical target population for new TB vaccine candidates. An optimised approach to enrol both in- and out-of school adolescents in clinical trials is needed to maximise participation and adherence to study procedures. We are conducting a TB incidence cohort study targeting 5000 adolescents aged 12–18 years in an area under continuous demographic surveillance (DSS), using a mobile field site (MFS) approach. We report on our experiences with this approach.

Methods | The DSS facilitates the identification of potential subjects. After consenting and assenting, all parents and adolescents are invited to the centrally located MFS for enrolment baseline evaluations and follow-up activities including clinical procedures. The site comprises tents as workstations, a mobile generator, mobile chest x-ray truck and data capture equipment.

Results | Between August 2008 and April 2009 we enrolled 1997 (89.5%) of 2232 adolescents approached to participate. Of these 95.1% came for the Mantoux reading within 4 days. Of 1997 participants 823 (41%) are TB suspects of whom 816 (99%) had chest radiography done, 100% gave the first sputum sample and 94.7% also the second required sample. Over 97% completed the first 4 monthly follow-up visits.

Discussion | So far participation in the study, adherence to study procedures and retention has been high. The MFS eliminates the need of taking participants to hospitals and ensures that the research services are more accessible to community.

14:35–14:50

The magnitude of childhood tuberculosis in Kilimanjaro region, northern Tanzania: A retrospective study from regional TB program registry

Charles Mtabho • Kilimanjaro Clinical Research Institute, Moshi, Tanzania

Introduction | While Tuberculosis (TB) remains an important public health problem to both adults and children, the burden in children has not been sufficiently addressed. Calls have been made to recognise and pay attention to TB in this age group.

Methods | In order to determine the magnitude of childhood TB and characterise clinical parameters and treatment outcome, retrospective registration-based data on TB notifications in Kilimanjaro region were retrieved from the archive of the Regional Tuberculosis programme for the period 2002–2006 and analysed using SPSS version 14.

Results | Between 2002 and 2006 there were 1615 cases of childhood TB in Kilimanjaro region. These constituted 13% of total TB burden, and the case detection rate in these years ranged from 41 to 59 per 100,000 population. Of these 1615 cases 54.2% were males, and 75.2% had pulmonary TB. Of all cases, 24.9% were tested for AFB by ZN staining and this showed that 5.8% of all TB cases were AFB smear positive. The remaining 94.2% were presumptively treated for TB. Treatment success rate was 79.9%, case fatality rate 10.9%, and default rate was 7%. Unfavourable outcome was more common among the unconfirmed TB cases.

Discussion | Childhood TB in Kilimanjaro region is among the highest in the world. The proportion of children who undergo microbiological diagnosis for TB and AFB smear positivity are far less than in adults. Treatment outcome in this region is also poorer than all-age outcome. These findings argue for specific TB control strategies to be designed for children.



14:50–15:05

A prospective cohort study to evaluate incidence of tuberculosis in infants, Western Kenya

Grace Kiringa • Kenya Medical Research Institute, Kisumu, Kenya

Introduction | Tuberculosis (TB) in young children is frequently under-diagnosed in resource-constrained settings. New TB vaccines are likely to be administered to infants. Therefore, cohort studies which include comprehensive diagnostic methods to provide reliable estimates of the TB incidence and other epidemiological parameters in infants are needed to guide the planning of future TB vaccine trials. We set out to determine the incidence of TB, mortality rates and, to provide BCG vaccination within 96 hours of birth.

Methods | The study takes place in Karemo, Western Kenya, with ~3,600 births per year. To demonstrate a TB incidence of 0.5%, and make precise inferences for a Phase III trial ~2900 infants will be enrolled and followed up for a minimum of one year. Through 4-monthly follow up visits and health facility surveillance those determined to be TB suspects will be admitted to a case verification ward. Specimens will be collected for microscopy and culture by induced sputum and gastric aspiration. Chest radiographs, Mantoux, HIV tests will be done. Morbidity, mortality, migration and BCG adverse event surveillance will be performed.

Results | Specialised clinical training has been conducted, including gastric lavage, sputum induction and interpretation of paediatric chest radiographs. Enrolment of newborns starts in May 2009 through April 2010.

Discussion | The lessons learnt will inform programmatic decisions on algorithms for diagnosis of infant TB in a setting with high HIV and TB prevalence, and also provide critical updates to assumptions that need to be taken into account when planning for Phase III clinical trials.

15:05–16:00

Discussion on possible new strategies

PLENARY SESSION IV
Summaries and recommendations
16:30–17:30
Victoria Hall

CHAIRS
Prof. Juhani Eskola
Dr Carolyn Peterson

Future strategies for conducting HIV/AIDS, malaria and tuberculosis clinical trials in sub-Saharan Africa

16:30–17:00
Summaries and recommendations

HIV/AIDS
Dr Shabbar Jaffar and Prof. Walter Jaoko

Malaria
Prof. Peter Kremsner and Dr Christine Manyando

Tuberculosis
*Prof. Richard Adegbola, Prof. Mecky Matee and
Dr Hulda Swai*

17:00–17:30
Discussion



8:30–9:00 **Plenary session V**
Capacity development in sub-Saharan
Africa
[VICTORIA HALL]

9:00–10:20 **Parallel sessions**
Presentations of research findings
HIV/AIDS [MERU HALL]
Malaria [VICTORIA HALL]
Tuberculosis [MANDARA HALL]

10:20–10:50 Coffee / Tea break

10:50–12:00 **Parallel sessions**
Presentations of research findings (cont.)
HIV/AIDS [MERU HALL]
Malaria [VICTORIA HALL]
Tuberculosis [MANDARA HALL]

12:00–13:00 **e-Poster presentations**
[CANE RESTAURANT]

All day **Poster presentations**
[BANQUETING LOBBY]

13:00–14:00 Lunch
[KILIMANJARO RESTAURANT]

14:00–15:35 **Plenary session VI**
EDCTP and global partnerships
[VICTORIA HALL]

15:35–16:00 Coffee / Tea break

16:00–17:30 **Closing session**
EDCTP future perspectives
16:45–17:00 **Award ceremony**
[VICTORIA HALL]

19:00–20:30 Closing dinner
[KILIMANJARO RESTAURANT]

8.30–8.55

**Challenges of health research capacity development in
sub-Saharan Africa: The EDCTP strategy**

Dr Michael Makanga • EDCTP, Cape Town, South Africa

Health research capacity development is fundamental for achieving high-quality and sustainable research in Africa. It is an ongoing process in which individuals, institutions, organisations and countries:

- increase their abilities to perform core functions
- identify and prioritise problems systematically
- develop, analytically monitor and evaluate appropriate solutions
- share and apply the knowledge generated in an efficient and sustainable manner.

The challenges to this process will be discussed, with a focus on development and deployment of intervention tools in the fight against HIV/AIDS, malaria and tuberculosis.

Capacity development in sub-Saharan Africa is one of the main objectives of EDCTP. In order to achieve efficient and sustainable capacity, EDCTP embraces the spirit of balanced partnership encouraging mutual contribution, commitment and ownership from all partners. For example, EDCTP's Developing Countries Coordinating Committee (DCCC) provides strong African input and leadership in identifying and prioritising capacity needs.

EDCTP uses a combination of short-term and long-term strategies, directed at individual, institutional, country and regional levels. These strategies are implemented through a programmatic approach that integrates the conduct of clinical trials with capacity development and networking. This integration of activities creates an enabling environment for clinical trials, as it develops scientific leadership, career structure, critical mass, infrastructure, information access, and transfer of technology and expertise. Additionally, EDCTP links capacity development to its utilisation and strengthening of both existing networks and creation of new collaborations. In collaboration with other partners, EDCTP also supports strengthening of the African ethics and regulatory framework to ensure high-quality clinical trial activities in sub-Saharan Africa.



PARALLEL SESSIONS | HIV/AIDS
Presentations of research findings
09:00–10:20
Meru Hall

CHAIRS
Prof. Nkandu P. Luo
Dr Abraham Alaabi

9:00–9:05
Brief introduction
from the Chairs

9:05–9:20
Prevalence of intravaginal practices in EDCTP
cohorts in Uganda and Tanzania

*Bahati Andrew • Mwanza Intervention Trials Unit,
NIMR, Mwanza, Tanzania*

Introduction | A range of highly prevalent female behaviours termed intravaginal practices (IVP) are potential risk factors for HIV transmission. This project investigates the prevalence of IVP within EDCTP cohorts in Tanzania and Uganda at enrolment.

Methods | We recruited commercial sex workers in Kampala, Uganda, and female bar/hotel workers in northwestern Tanzania into two prospective cohort studies. IVP questions were included in the structure questionnaires which were administered by female staff members in the local language.

Results | Of 346 enrollees in the Uganda cohort, 327 (95%) reported cleansing inside the vagina in the past three months at enrolment, of which 193 (55%) use soap or soapy water. 218 (63%) reported inserting a substance, of which 84 (39%) inserted traditional substances, 61 (28%) inserted commercial soft drink (e.g. Coca Cola), 34 (16%) inserted detergent and 57 (26%) inserted of petroleum-based gels. Of the 291 enrollees in the Tanzanian cohort, 270 (90%) reported cleansing inside the vagina in the past three months at enrolment, of which 209 (77%) used soap or soapy water. Seventy-five (25%) reported inserting a substance inside the vagina, of which 20 (27%) inserted traditional substances, 10 (13%) inserted lemon, 15 (20%) inserted detergent, and 14 (19%) inserted petroleum-based gels.

Discussion | Cleansing inside the vagina is common in both the Ugandan and Tanzanian cohorts, compared to insertion practices. The Ugandan cohort reports more insertion practices, while the Tanzanian cohort reports more use of soap for cleansing. The differences could represent geographical, occupational or other differences between these study populations.

9:05–9:20

Sexual risk behaviour and risk perception among female sex workers enrolled in a microbicide feasibility study in Kampala, Uganda



Justine Bukenya • MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda

Introduction | The Good Health for Women Project (GHWP) in Kampala is recruiting a cohort of 1000 female sex workers to study the epidemiology of HIV and other STIs and to investigate new HIV prevention interventions. A microbicide feasibility study is being conducted among the enrolled HIV-negative participants. This abstract presents baseline risk perception and sexual risk behaviour characteristics.

Methods | Women involved in sex work were recruited from the red-light-areas in Kampala. HIV-negative women 18 to 44 years old, not pregnant and not intending to become pregnant in the first year were eligible for the microbicide feasibility study. Information on sexual risk behaviour was collected using structured questionnaires.

Results | By the end of February 2009, 346 HIV-negative sex workers were enrolled in the microbicide feasibility study. Consistent condom use in the last month was 4% with marital partners, 65% with paying clients and 53% with other non-marital partners (casual or regular non-paying partners). The main reasons for not using condoms during paid sex were: the client disliked condoms, participant could not negotiate condoms with client, participant knew and trusted client. Only 55% of our study population considered themselves at high risk of getting HIV infected, 26% perceived the risk small to moderate, 16% did not feel at risk at all and 3% did not have an opinion.

Discussion | The preliminary findings of this study demonstrated low condom use and low HIV risk perception among women engaged in high-risk sexual behaviour. Health education on HIV prevention needs to be strengthened urgently.



9:20–9:35

Perceptions and practices regarding
microbicides: A baseline survey of the Dakar
Institute of Social Hygiene



*Papa Gallo Sow • Institute of Social Hygiene, Dakar,
Senegal*

Introduction | The Institute of Social Hygiene is one of the medical centres in the south district of Dakar. Dakar has a population of 230,000 people. Knowing people's perceptions about microbicides would assist in developing a focused and effective microbicide that can be effectively used in a developing country, between March and June 2008 a cross-sectional descriptive survey was carried out in the Institute in order to establish the community's current knowledge levels, gaps, attitudes and practices around microbicides. The study was aimed at establishing baseline information to be used in setting up a programme for community education.

Methods | Quantitative data was called through a random household survey of 600 women in the 21–59 years age group using a structured questionnaire. Data was analysed using Epi-info version 2002.

Results | About 98% of women knew that HIV is transmitted sexually, 55% knew that transmission can occur on contact with infected blood and 28% through knew about mother-to-child transmission. Only 0.1% knew what a microbicide is and 80% mentioned that they had never heard about a microbicide. About 90% felt that it was good for women to prevent HIV transmission.

Discussion | From the finding we concluded that knowledge on microbicides was low among women. Microbicides as a new HIV prevention strategy requires a lot of community education and information.



9:35–9:50

Barriers to adherence to clinical appointments in a free urban HIV care facility. A case of the Infectious Diseases Institute Kampala, Uganda

Suzan Nakate • Makerere University, Kampala, Uganda

Introduction | Recent studies have shown that patients who do not attend regular HIV care are significantly more likely to die than those who maintain good contact with their HIV clinic, making it important to examine the barriers to clinic appointment adherence, particularly in a free urban HIV care facility in a resource-limited setting.

Methods | A descriptive cross-sectional survey was conducted with 126 adult HIV-infected patients who had missed at least 3 appointments in a period of one year. For comparison, in-depth interviews were conducted with 10 patients who had never missed an appointment and 9 health workers were interviewed as key informants. Two focus group discussions were conducted to elicit further insights.

Results | Eighty-eight (69.8%) of respondents were female, the median (range) age was 35 (20–56). In order of frequency, the reasons for missing appointments were reported as: transportation to clinic; work-related; forgetting; attending ill relatives; feeling ill themselves; stigma; and a preference to rely on divine healing. Disclosure and social support were related to adherence. All except one of the respondents disclosed to someone, and 63 (50%) disclosed to a sibling. However, 68 (54.4%) of respondents reported ever having been accompanied to the clinic by those to whom they disclosed.

Discussion | The effectiveness of the treatment of HIV/AIDS is very dependent on clinic adherence. Disclosure, social and financial support should be addressed to overcome the obstacles to clinic attendance which is an important aspect of the management of HIV/AIDS treatment in resource-limited settings.

9:50–10:05

The effect of pregnancy on adherence to HAART among HIV-infected South African women: A pharmacy claims-based analysis

Jean Nachega • Stellenbosch University, Tygerberg Campus, Cape Town, South Africa

Background | Little is known on the antiretroviral therapy adherence of HIV-1 positive pregnant women in sub-Saharan Africa.

Methods | In this observational cohort study we evaluated records from 32,187 HIV-infected women enrolled in Aid for AIDS, a private-sector disease management program in southern Africa, between 1998 and 2007. Women were categorised into 3 groups: (1) never-pregnant, (2) pregnant before starting HAART, and (3) became pregnant while on HAART. Adequate Pharmacy-refill adherence was defined as >80%. Bivariate and multivariable logistic and Cox proportional hazards regressions were performed to determine independent predictors of adherence.

Results | Of the 32,187 women included, 22,742 were in Group 1, 1,020 were in Group 2, and 3,437 were in Group 3. Overall, 53.2% of the study subjects had a total adherence rate of at least 80%. Non-pregnant women were significantly more likely to have adequate adherence compared to women who became pregnant (55% vs. 45%, $P < 0.001$). Among the pregnant women, those who were pregnant before starting HAART were significantly more likely to have adequate adherence compared to those who became pregnant while on HAART (61% vs. 42%, $P < 0.001$). In the multivariate regression women who became pregnant before starting HAART were about 75% more likely to have sustained virologic suppression compared to non-pregnant women ($P = 0.008$). Women who became pregnant while on HAART were about 35% less likely to have experienced virologic suppression compared to non-pregnant women ($P = 0.011$). Independent predictors of mortality were a baseline CD4 count < 200 copies/ml (HR 0.55 CI: 0.37–0.83, $P = 0.004$), $> \log 5$ baseline viral load (HR 1.75 CI: 1.20–2.55, $P = 0.003$), and a total adherence rate of less than 80% (HR 0.36 CI: 0.24–0.56 $P < 0.001$).

Discussion | There is a critical need for targeted HAART adherence interventions in this antenatal population to decrease likelihood of MTCT of HIV.

10:05–10:20

Risk of coronary heart disease based on ratio of total cholesterol to high density lipoprotein in HIV-infected ARV naïve patients

Mariam Adebukola Adetunji • Nigeria Institute of Medical Research, Lagos, Nigeria

Introduction | Abnormal blood lipid profiles may be observed in HIV-infected individuals who are untreated. A lot of work has been done pointing to abnormal blood lipid profiles in HIV-infected individuals receiving highly active antiretroviral therapy (HAART). However little or no work has been done on the impact of HIV on coronary heart disease based on the ratio of total cholesterol to high density lipoprotein (HDL) in Nigeria. Hence there is a need to assess the risk of coronary heart disease in HIV-infected ARV naïve individuals.

Methods | 30 HIV sero-positive treatment naïve and 31 sero-negative patients as control group, attending a HCT (Voluntary HIV Counselling and Testing) centre in Lagos State. Age, sex, weight, height, HIV Status and 12 hours fasting total cholesterol and high density lipoprotein (HDL) were measured and the ratio of total cholesterol to HDL was calculated in the two groups. Statistical analysis was done using Epi-info version 2.0. Randox kits were used for analysing total cholesterol and HDL. Determine kit, stat pak and GeneII kit were used for screening. Manufacturer specifications were followed.

Results | Five (16.67%) out of thirty HIV sero-positive patients had total cholesterol to HDL ratio above 3:1 and twenty-five (83.33%) had total cholesterol ratio below 3:1. In the control group 13 (41.94%) had total cholesterol to HDL-Cholesterol ratio above 3:1 and eighteen (58.06%) had total cholesterol to HDL ratio below 3:1. There is a significant difference in total cholesterol to HDL ratio among the test group and the control group $p=0.016$ p set at $p<0.005$.

Discussion | There is a need to monitor sero-positive HIV patients for coronary heart disease.



PARALLEL SESSIONS | MALARIA

Presentations of research findings

09:00–10:20

Victoria Hall

CHAIRS

Dr Andrew Kitua

Dr Klaus Winkel

9:00–9:05

Brief introduction
from the Chairs

9:05–9:20

Application of real-time quantitative
polymerase chain reaction ‘qPCR’ in anti-
malarial drug trial

*Davis Nwakanma • Medical Research Council (UK),
Banjul, The Gambia.*

Introduction | Slide microscopy is the standard method for malaria diagnosis and estimation of parasite density. However, in large-scale clinical trials where thousands of slides are usually generated, microscopy is slow, labour-intensive and unreliable for detecting low-grade infections. PCR-based methods which have higher sensitivity and are amenable to high throughput application would greatly facilitate field trials of anti-malarial interventions and disease surveillance.

Methods | We compared real-time quantitative PCR (qPCR) assay with microscopy for malaria diagnosis and measurement of parasite density in 1211 hospital patients and subsequently evaluated the performance of both methods in an efficacy trial of two anti-malarial drugs. Blood samples collected from 106 study patients at 8-hourly intervals over a 3-day period (~1060 blood samples) were analyzed by qPCR amplification of *Plasmodium falciparum* 18S rDNA and microscopy.

Results | Agreement between microscopic and qPCR diagnosis ($\text{Kappa}=0.86$; $95\% \text{CI}=0.83-0.90$) as well as concordance of parasite density estimates ($\text{rho}_c=0.97$; $95\% \text{CI}=0.96-0.97$) were very high. However, estimates of parasite clearance time (PCT) differed between the two methods with microscopy giving a median PCT of 16H compared to 24H by qPCR. All patients appeared to have cleared their parasites by day 3 post-treatment judging by microscopy, although 19% (16/83) still harboured asexual parasitaemia detectable by qPCR.

Discussion | These results suggest that applying a sensitive parasite detection method could lead to more precise determination of the relative efficacies of different anti-malarial interventions.



9:20–9:35

In vitro chemosensitisation of antimalarials by verapamil and probenecid in *Plasmodium falciparum*



Alexis Nzila • KEMRI-Wellcome Trust Collaborative Research Program, Kilifi, Kenya

Introduction | We have tested the effect of uricosuric agent probenecid and calcium antagonist verapamil in chemosensitising the *in vitro* activity of several antimalarials including chloroquine, desethylamodiaquine, piperaquine, quinine, mefloquine, lumefantrine, pyrimethamine.

Methods | We tested the activity of these antimalarials in presence of probenecid and verapamil against the multi-drug resistant strains V1S and the drug sensitive 3D7. *In vitro* activities were measured at fixed ratios of 0.8:0.2, 0.6:0.4, 0.4:0.6 and 0.2:0.8 and the effects were measured by computation of the minimum fractional inhibitory concentrations (FIC). FIC values <0.5 and between 0.5 and 1 were scored as pronounced and moderate chemosensitization or synergy, respectively. Verapamil has a pronounced effect on quinine followed by desethylamodiaquine (mean FICs of 0.28 ± 0.20 and 0.47 ± 0.09 , respectively).

Results | Verapamil chemosensitizes chloroquine only moderately (mean FIC of 0.52 ± 0.08). No effect was observed when the drug-sensitive strain 3D7 was used. The most pronounced probenecid-effect was found on piperaquine (mean FIC 0.12 ± 0.01), followed by pyrimethamine (mean FIC 0.20 ± 0.14). A moderate probenecid-effect was observed on chloroquine and mefloquine. When 3D7 was used, a pronounced probenecid-effect was observed on pyrimethamine (mean FIC 0.46 ± 0.06).

Discussion | These data indicate that some of the mechanisms of chemosensitisation differ between verapamil and probenecid. The pronounced piperaquine and quinine chemosensitization by probenecid and the good pharmacokinetic and pharmacodynamic properties of probenecid make it a potential chemosensitizer of piperaquine and quinine *in vivo*.

9:35–9:50

Towards understanding the mechanisms of lumefantrine resistance

Leah Mwai • KEMRI-Wellcome Trust, Kilifi, Kenya

Introduction | Lumefantrine (LM)/artemether (Coartem®) is now first-line treatment for uncomplicated malaria, and piperaquine (PQ)/dihydroartemisinin (DHA) [Artekin®] is being evaluated as an antimalarial. Reports indicate that resistance to LM and PQ could arise quickly. We investigated the relationship between polymorphism at Pfcrt76 and Pfmdr186 and *in vitro* activity of chloroquine (CQ), piperaquine (PQ), lumefantrine (LM) and dihydroartemisinin (DHA) in Kenyan *Plasmodium falciparum* isolates.

Methods | We adapted >100 *P. falciparum* isolates *in vitro* and assayed drug chemo-sensitivity using the hypoxanthine assay. Results are presented as inhibitory concentrations that kill 50% of parasitaemia (IC₅₀).

Results | The median IC₅₀ for CQ (n=162), LM (n=78), PQ (n=78), and DHA (n=78) were 41 (19–68), 48 (27–94), 27 (17–39), and 2 (2–4) nM respectively. As expected, DHA was the most active, followed by PQ, LM and CQ. However, about 20% of isolates had LM IC₅₀ >100nM, an indication of decreased LM susceptibility. Interestingly, we have found an inverse relationship between CQ and LM activity ($r^2 = -0.315$, $P < 0.01$). The presence of wild-type codons at both Pfcrt76 and Pfmdr186 was associated with decrease in LM activity and increase in CQ activity. DHA activity was associated with wild type Pfmdr186 genotype. Surprisingly, the use of Artekin® tended to select parasites with higher LM activity.

Discussion | Pfmdr186 and Pfcrt76 have a bearing on LM activity. The use of LM could lead to selection of CQ susceptible parasites.



9:50–10:05

Cytokine gene polymorphism analysis in children exposed to malaria and/or helminths infections in Zimbabwe

Takafira Muduluza • University of Zimbabwe, Harare, Zimbabwe

Introduction | Single nucleotide polymorphisms within the cytokine genes, TNF- α (-308 G/A), IFN- γ (+874 A/T), TGF- β (codon 10 and codon 25) and IL-10 (-1082 G/A and -819 T/C) associated with protection and susceptibility to parasitic infections were examined.

Methods | EDTA blood was obtained from 492 children between the ages of 5–16 years, of which 27.2% were not infected and 72.8% infected with either malaria and/or different helminths. Genotyping was carried out using ARMS-PCR.

Results | The prevalence of samples with wild type TNF- α (GG) associated with low cytokine production was 76.1%, while 22.2% and 1.6% were predictors of medium and high production, respectively. For IL-10 (-819) the distribution of wild-type, was 59.6%, 22.9% and 17.5%, respectively and a similar analysis of the polymorphisms on -1082 for IL-10 revealed that most of the samples were of the wild-type genotype. For IFN- γ (+874 A/T), 70.5% were wild-type (AA) which is associated with high cytokine secretion, with 4.4% (TT) and 25.1% (AT) associated with low cytokine production. Limited analysis on the sample population also revealed that at the TGF- β (T/C codon 10) 88.5% were homozygous (TT) which predicts high production of the cytokine whereas 9.2% were homozygous (CC). Similar analysis at another locus of TGF- β (G/C codon 25) showed that only 2.3% of the sample population was heterozygous (GC) predicting high TGF- β production. Equal distribution of IL-10 (-819 G/A) and the rare occurrence of allele associated with low IL-10 (-1082 AA) production would suggest moderate to high IL-10 responses in the population analysed.

Discussion | The high prevalence of TGF- β genotype (TT) predicting high cytokine production and the existence of homozygote for IL-10 (high producer) might suggest the dominance of an anti-inflammatory environment when faced with acute *P. falciparum* infection in samples analysed.



10:05–10:20

Ascais Lubricoides as a risk factor for *P. falciparum* malaria infection during pregnancy in Lambaréné, Gabon

Ayola Akim Adegnika • Medical research unit, Albert Schweitzer Hospital, Lambaréné, Gabon

Introduction | *Plasmodium falciparum* and helminth infections are often prevalent in the same populations. For both infections the risk is higher in pregnant women compared to non-pregnant women.

Methods | In Lambaréné and the surrounding area where *P. falciparum* and intestinal helminth parasites are both endemic, we conducted a longitudinal survey of malaria and intestinal helminth infection during pregnancy.

Results | Data from 388 pregnant women were analysed. 98 (25%) pregnant women were infected with *P. falciparum* with an incidence of 2.1 infections per woman per year. Three different stools examination using Kato Katz method were performed, and 213 (66%) were found to be infected with a helminth. *Ascaris lumbricoides*, *Trichirus trichiura*, and hook worm eggs were presents in 112 (33%), 83 (24%) and 34 (10%) of pregnant women, respectively. *A. lumbricoides* (Odds Ratio [95%CI]: 2.4 [1.4–3.8]) and primiparity (Odds Ratio [95%CI]: 2.1[1.3–3.5] were independent risk factors for malaria parasite infection during pregnancy.

Discussion | The vulnerability of women against malaria during pregnancy might be partly explained through a helminth-*Plasmodium* interaction. The effect on the outcome of pregnancy needs to be studied as a priority.



PARALLEL SESSIONS | TUBERCULOSIS

Presentations of research findings

09:00–10:20
Mandara Hall

CHAIRS

Dr Veronique N. Penlap
Prof. Martin Grobusch

9:00–9:05
Brief introduction
from the Chairs

9:05–9:20
New drugs against tuberculosis: Problems,
progress, and evaluation of agents in clinical
development

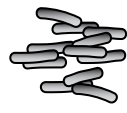
Gibson Kibiki • Kilimanjaro Clinical Research Institute
(KCRI), Moshi, Tanzania

Introduction | One-third of the world population is infected with *Mycobacterium tuberculosis*. 8.8 million patients are newly diagnosed with TB and 1.6 million of them die of TB every year. HIV/AIDS has fuelled the TB epidemic especially in sub-Saharan Africa. TB treatment is one of the cornerstones of controlling the disease. Current TB drugs are not optimal in controlling the epidemic. Rapid development of new drugs has been hampered by many obstacles.

Methods | In order to plan clinical trials in TB drugs this presentation gives an overview of: Problems with the current TB drugs, challenges of developing new TB drugs, remodifying the dose of the present TB drugs, and the overview on new drugs and their potential role in TB treatment.

Results | High doses rifamycins, and fluoroquinolones may shorten TB treatment duration. New drugs such as fluoroquinolones, diarylquinolines, nitroimidazopyrans, diamines, pyrroles though promising as anti-TB drugs will not be available as agents to shorten TB treatment within the near future.

Discussion | More clinical trials should continue using both old and new drugs to find a potent regime that will improve TB control strategies.



9:20–9:35

Response to treatment in sputum smear positive pulmonary tuberculosis patients in relation to HIV in Kano, Nigeria

Yusuf Mohammed • International center for AIDS care and treatment program (ICAP), Kaduna, Nigeria

Introduction | There is an association between tuberculosis (TB) and HIV infection. The immune suppression resulting from HIV infection confers the risk known for re-activation of latent or recent TB infection to active TB, and increase the rate of recurrence of TB. Therefore HIV infection has a great impact on the response to tuberculosis treatment.

Methods | In order to study the response to treatment, we enrolled 1,692 sputum smear positive pulmonary tuberculosis patients with or without HIV infection. The patients were followed-up and treated by directly observed chemotherapy short course (DOTS) with standard anti-tuberculosis drugs for 8 months. Treatment outcome were assessed using World Health Organization (WHO) indicators.

Results | A total of 1,046 were cured with 62% cure rate and in HIV negative the cure rate was 75% (785) with statistical significant difference ($P < 0.05$) of cure rate of 40% (216) in HIV positive. For treatment completion rate there was a statistical difference ($P < 0.05$) when the rate of 26% (172) in HIV seropositive is compared with only 9% (89) in seronegative. 188 deaths were recorded with death rate of 11%. 16% (103) death rate in HIV seropositive which was significantly higher ($P < 0.05$) than in seronegative with death rate of 8% (85). A failure rate of 4% (62) with 6% (39) in seropositive and 2% (23) in seronegative and the difference is statistically significant ($P < 0.05$).

Discussion | The tuberculosis treatment outcome routinely monitored can be grouped as favourable (cure and treatment completion) and unfavourable (death and failure) those associated with risk of ongoing TB transmission. Tuberculosis co-infected with human immunodeficiency virus is associated with unfavourable and poor treatment outcome.

9:35–9:50

Comparison of smear microscopy, solid culture and liquid culture for monitoring treatment response in pulmonary TB*Sven O Friedrich • University of Stellenbosch, Tygerberg, South Africa*

Introduction | Serial sputum samples are used to monitor treatment response in Phase III studies of novel anti-tuberculosis regimens. This study compared smear microscopy, liquid culture and solid culture in a cohort of patients participating in the REMox trial.

Methods | We collected serial sputum samples (baseline, weekly from week 1 to 8, week 12) from 195 patients and performed Ziehl-Neelsen microscopy (ZN), Löwenstein-Jensen (LJ) solid culture and BACTECTM MGIT960 liquid culture (MGIT) after standard NaOH based decontamination. Proportions of positive, negative and contaminated samples as well as semiquantitative (ZN and LJ: score 0–4) and quantitative (MGIT: time to positivity) measurements were compared with One-Way-ANOVA and Bonferroni's multiple comparison test.

Results | All measurements decreased statistically significant with $p < 0.0001$. ZN positive samples decreased from 93.9% (mean score 3.2) at baseline to 21.8% (0.4) after 12 weeks, positive LJ cultures from 83.1% (mean score 3.5) to 4.4% (0.13) and positive MGIT cultures from 93.2% (mean time to positivity: 127 hours) to 9.3% (850 hours). The contamination rate increased from 11.3% to 26.3% in LJ and from 5.7% to 20.1% in MGIT.

Discussion | All three methods showed steady conversion rates. The MGIT system was the most sensitive method and less susceptible to contamination than LJ.



9:50–10:05

Induction of antigen specific multifunctional T cells after vaccination with the live recombinant tuberculosis vaccine VPM1002 in a Phase I clinical trial



Bernt Eisele • Vakzine Projekt Management GmbH,
Hannover, Germany

Introduction | VPM1002 is a live vaccine against tuberculosis (TB). It is based on the well-known *Mycobacterium bovis* Bacille Calmette-Guérin (BCG) strain which has been applied approximately 4 billion times worldwide. As BCG is not sufficiently effective to stop the spread of TB, two modifications have been implemented in VPM1002 to improve its immunogenicity. Our Phase I study in humans used multiparameter flow cytometry to characterise the quality of the T cell response following immunisation with our VPM1002 tuberculosis vaccine candidate or BCG.

Methods | In a Phase I open label, randomised, controlled, dose-escalation study to evaluate safety and immunogenicity of VPM1002 in comparison with BCG. We enrolled 80 healthy male subjects stratified for history of BCG vaccination.

Results | Safety and tolerability revealed no serious adverse reactions from VPM1002 vaccination and only mild to moderate adverse reactions were reported. VPM1002 was very well tolerated in both cohorts the naïve and BCG pre-immunised volunteers. Higher total IFN- γ production was measured in the VPM1002 group vs. the BCG group. VPM1002 induced a good multifunctional CD4⁺ and CD8⁺ T cell response in comparison with BCG.

Discussion | VPM1002 induces multifunctional T cell subsets which are thought to play a crucial role in protection against tuberculosis. At the same time VPM1002 is very well tolerated and presents a safety profile that is similar or even better than BCG. VPM1002 shows all characteristics for a safe, well tolerated and efficacious tuberculosis vaccine, which could replace BCG immunisation in the future.



10:05–10:20

Mycolic acid antibody real-time inhibition test demonstrates that anti-mycolic acid antibodies are surrogate markers for active tuberculosis*Jan Verschoor • University of Pretoria, South Africa*

Introduction | There is currently no adequate test to diagnose active tuberculosis in human populations that are burdened with HIV infection, mainly due to insufficient mycobacteria in sputa of such patients. We have designed a biosensor method, dubbed the MARTI-test that accurately indicates anti-mycolic acid antibodies in patient sera as surrogate marker of active TB. Proof of principle has been published by Thanyani *et al.* in 2008. Here we assessed whether the test will indicate how the patient responds to anti-TB treatment.

Methods | Serum samples were collected from TB patients on day of diagnosis and then one week, five weeks, three months and one year after commencement of anti-TB treatment. The samples were analysed for the prevalence of anti-mycolic acid antibodies in the MARTI-test and the results correlated to the patient's clinical assessment.

Results | The prevalence of anti-mycolic acid antibodies on day of diagnosis was found to correlate with active TB in the patient. The signal increased after one week of anti-TB treatment and then decreased to almost zero after three months of treatment in patients that were eventually cured. When a patient turned out to be resistant to the treatment, the anti-mycolic acid antibody prevailed in the serum.

Discussion | The results imply a direct correlation between the presence of anti-mycolic acid antibodies in the serum and the state of active TB in the patient undergoing treatment. This confirms the hypothesis that the MARTI-test may be applied to determine whether a patient responds as expected towards anti-TB drug therapy, or whether the therapy should be reconsidered.



10:50–11:05

HLA alleles and KIR genes frequencies in HIV-2 infected individuals from two cohorts in West Africa

*Louis-Marie Yindom • Medical Research Council
Laboratories, Fajara, The Gambia*

Introduction | Several reports have implicated HLA molecules with favourable or unfavourable HIV disease outcomes with very little data from HIV-2 cohorts. More recent insights came from studies associating HIV-1 disease outcome with genotypes of Killer Immunoglobulin-like Receptors (KIRs) which are type I glycoproteins primarily expressed on NK-cells. HLA class I molecules are KIR ligands and their interaction modulate NK-cell activities. Here we report on the immunogenetic associations between HLA and KIR genotypes/haplotypes with clinical outcomes of HIV-2 infection in two West African populations in The Gambia and Guinea Bissau. Our major aim was to understand their roles in the preservation of immune functions observed in HIV-2 long-term non-progressors (LTNPs).

Methods | DNA samples were extracted from 1103 individuals (513 Manjako and 590 Gambians) including 379 HIV-2 infected, 35 duals (HIV-1&2) and uninfected controls. HLA typing was performed by sequencing HLA class I loci. KIR genotyping was performed by PCR-SSP (sequence specific priming) using a panel of 59 specific primers to detect the presence or absence 15 known KIR genes.

Results | HLA class I and KIR gene frequencies were determined. The most frequent alleles in Caio include HLA-A*3301 (18.6%), HLA-A*2301 (17.3%); HLA-B*1503 (12.7%); HLA-Cw*0701 (16.7%); and in Fajara HLA-A*2301 (17.6%), HLA-B*3501 (13.1), and HLA-Cw*0401 (18.6%).

Discussion | Activating KIR gene frequencies were low in both populations but that of KIR3DS1 was significantly higher in Caio than Fajara (18.3% vs. 6.4%, $P < 1 \times 10^{-6}$). HLA-B*1503 was associated with poor prognosis and B*0801 with susceptibility to infection.



11:05–11:20

Prediction of antiretroviral therapy outcomes in poor resource countries: Comparison between genotype resistance testing based vs. treatment history models

Mattia Prosperi • EuResist Network GEIE, Bologna, Italy

Introduction | In high income countries, guidelines recommend genotypic resistance testing (GRT) both before starting antiretroviral therapy (ART) and at ART failure. Appropriate funding and/or facilities to perform GRTs may be not available in low income countries, leaving physicians to switch therapy based solely on the clinical background. Treatment history is among most crucial factors to influence the response to a new treatment. We investigated a set of statistical learning models to optimise ART in the absence of GRT.

Methods | Treatment Change Episodes (TCE) were extracted from the EuResist (world's largest HIV resistance database) for analysis of 8-week and 24-week virological outcomes. Clinical markers, demographic information, GRT, current and experienced treatments, were linked to the outcomes. Random Forest (RF) classification was used to predict 8- and 24-week undetectable HIV-RNA, comparing GRT-based (i) vs. treatment-history-based (ii) models, using cross-validation and AUC goodness-of-fit.

Results | Virological success was reached in 68.2% and 69.8% of TCEs at 8 and 24 weeks ($n=2831$ and 2579). RF (i) and (ii) showed comparable performances (AUC 0.77 vs. 0.76 at 8 weeks, 0.84 vs. 0.83 at 24 weeks). When training on subtype B and validating on non-B, there was a drop in performance both for (i) and (ii).

Discussion | Treatment-history-based RF models are comparable to GRT-based for classification of virological outcome. These results may be relevant for therapy optimisation in areas where availability of GRT is limited. Further investigations are required in order to account for different subtype prevalence in African countries.



11:20–11:35

The effect of rifampicin on clinical outcomes in patients treated with efavirenz containing HAART


*Sabina Mugusi • Muhimbili National Hospital,
Dar es Salaam, Tanzania*

Introduction | Tanzania is highly affected with HIV and TB pandemic. TB notification has increased six-fold to 70,000 new cases of TB annually. 50% of TB patients are co-infected with HIV accounting for about 30% of overall mortality. The optimal management of TB-HIV co-infection has been a challenge due to drug-drug interactions. This study describes the effect of Rifampicin among patients receiving efavirenz containing HAART in Tanzania.

Methods | A prospective cohort study which recruited 254 ARV naïve HIV patients (Arm 1) conducted at MNH initiated on efavirenz-based HAART and 195 HIV/TB patients (Arm 2) initiated on both efavirenz-based HAART and rifampicin based anti-TB treatment, followed up at regular intervals. Clinical and laboratory characteristics were documented.

Results | A total of 449 patients were recruited. There were more males in arm 2 (49.22%) compared to arm 1 (33.9%) ($P = 0.001$). Arm 2 patients had lower BMI (BMI of 19.3) compared to Arm 1 (BMI of 22.03) ($P < 0.001$). During follow up nine (3.54%) patients in Arm 1 developed TB after HAART initiation. 1.6% of patients in Arm 1 experienced neuropsychiatry manifestations, with none reported in Arm 2. Greater proportion of hepatotoxicity was observed in Arm 2 compared to Arm 1. There was significant rise in CD4 counts in both groups and these were similar at 12 and 24 weeks.

Discussion | There were less neuropsychiatry manifestations in patients using rifampicin plus efavirenz. Hepatotoxicity was more in patients using rifampicin and efavirenz. CD4 counts at 3 and 6 months were similar in the two groups.



11:35–11:50

HIV prevalence and risk factors in a community-based sample of female sex workers, Kigali, Rwanda

Joseph Vyankandondera • *Projet Ubuzima, Kigali, Rwanda*

Introduction | Population-based data on HIV infection among female sex workers (FSW) in Rwanda is limited. This group is likely to benefit from prevention interventions and resources.

Methods | A cross-sectional survey of 800 FSW ≥ 18 years was conducted from 2006–2008, to gather data on HIV-1/2, HSV-2 and pregnancy prevalence, and sexual and other risk behaviours. Women were provided counselling, condoms, family planning, sexually transmitted infection (STI) treatment, and referral for HIV services as appropriate.

Results | Prevalence of HIV-1 and HSV-2 were 24% and 60%, respectively. Eight percent of women were pregnant. 93% of women received money/gifts from their last sex partner. Most (79%) reported inconsistent or no condom use with clients and casual partners. Only 8% knew their current HIV status, and 35% had never been HIV tested. Nearly one quarter (22%) of women had ≥ 1 genital symptoms in the last month. Current contraceptive use was high (92%), with male condoms being the most common method (80%). In multivariate analyses adjusted for age and district of residence, higher HIV prevalence was associated with: HSV-2 co-infection (OR=2.7); history of forced sex (OR=2.2); recent treatment for STI (OR=2.2); being widowed (OR=1.8); history of imprisonment (OR=1.6); recent AIDS-like symptoms (OR=1.6); alcohol consumption (OR=1.5); and vaginal cleansing before sex (OR=1.4).

Discussion | HIV prevalence among these FSW was nearly 4 times the 2005 DHS+ estimate of 6.6% prevalence in the female population in Kigali. Sexual behaviours, clinical factors, and factors indicating social vulnerability were positively associated with prevalent HIV.

11:50–12:00

Discussion

10:50–11:05

The Afro-immuno assay multi-centre network project and capacity building for malaria vaccine development in Africa

Daniel Dodoo • Noguchi Memorial Institute for Medical Research, University of Ghana, Legon, Ghana

Introduction | Antigen-specific antibody-mediated immune responses play an important role in natural protection against clinical malaria, but conflicting estimates of this association have emerged from studies in different geographical settings, and may be due to the use of different methodologies. In the attempt to render such studies more comparable, the Afro-Immuno Assay (AIA) network project was initiated, with the aim of developing and introducing standardised immunological assays that could form part of a set of criteria for validating promising malaria vaccine candidate antigens, provide essential baseline information for clinical trials and enhance quality assured laboratory capacity and capability.

Methods | In the Phase I project, 6 African and 3 European Institutions focused on using standardised ELISA and statistical methods to assess isotypes and IgG subclass levels against AMA1, GLURP, MSP1-19 and MSP3 in cohort samples in relation to protection from clinical malaria.

Results | Data from two of the study sites showed IgG1 [(0.80 (0.67–0.97), $P=0.018$)] and IgM [(0.48 (0.32–0.72), $p < 0.001$)] levels to MSP1-19 independently correlating with protection from malaria in Ghanaian children while IgG1 to AMA1 [0.87 (0.78–0.97), $P=0.013$] and IgG3 to GLURP [0.82 (0.72–0.94), $P=0.004$] were associated with reduced risk to malaria in Burkinabe children.

Discussion | The study has confirmed the importance of antibodies to MSP1-19, GLURP and AMA1 in reducing the risk of clinical malaria in Ghanaian and Burkinabe children, thus substantiating their potential as malaria vaccine candidates. The differing conclusions in the two studies may be due to the differences in malaria transmission that may influence induction of protective antibodies to different antigens. Parasite growth inhibition assays are required to confirm if these associations reflect functional roles of antibodies that correlated with protection from clinical malaria.



11:05–11:20

The ADRB assay: A new tool, correlated with clinical protection from *Plasmodium falciparum* malaria, to test malaria vaccine

Aissatou Touré • Institut Pasteur de Dakar, Senegal

Introduction | Effective vaccines to combat malaria are urgently needed, but have proved elusive in the absence of validated correlates of natural immunity. This study evaluated antibody dependent respiratory burst (ADRB) activity in polymorphonuclear neutrophils (PMN) induced by *Plasmodium falciparum* merozoites and antibodies in the sera of two different African endemic populations, and investigated its association with naturally acquired clinical protection. The role of antibodies specific for MSP1p19 malaria vaccine in mediating respiratory burst activity was also investigated.

Methods | Respiratory bursts by freshly isolated PMN were quantified by chemiluminescence readout in the presence of isoluminol. Using a standardised protocol, 230 sera were analysed from individuals of all age groups living in Ndiop or Dielmo, and enrolled in a cross-sectional prospective follow-up study. Isogenic parasite clones (D10–PcMEGF and D10–PfM3') and sera depleted of specific anti-BvMSP1p19 antibodies are used to test BvMSP1p19 vaccine. Statistical significance was determined using non-parametric tests and Poisson regression models.

Results | The most important finding was that PMN ADRB activity was correlated with acquired clinical protection from malaria in both high and low transmission areas. Complementary results showed that ADRB activity was only dependent on anti-merozoite opsonizing IgG (IgG1 and IgG3) and that anti-MSP1p19 antibodies reduced ADRB activity by an average of 30%.

Discussion | This is the first demonstration of an *in vitro* functional correlate of immune protection against malaria. These results strongly support the use of the ADRB assay to guide preclinical and clinical development and confirm the importance of BvMSP1p19 vaccine.



11:20–11:35

Decreased percentage of plasmacytoid dendritic cells and increased plasma levels of interferon α in Fulani children with *Plasmodium falciparum* infection in Mali

Charles Arama • Wenner-Gren Institute, Stockholm University, Sweden

Introduction | *P. falciparum* (Pf) infections are complex and involve both host and parasite interactions. Understanding the host's immune response in the protection of this disease may help to develop new strategies to control this infection. The innate immune response is the first line of defence. The bridge between innate and adaptive immune response is exerted by antigen-presenting cells such as dendritic cells (DC), which are critical to establish an efficient T cell response. The aim of this study was to investigate the role of plasmacytoid dendritic cells (pDC) in sympatric ethnic children undergoing malaria infection in Mali.

Methods | All the children included in this study belonged to either the Fulani or the Dogon ethnic groups. The children, aged between 2 to 10 years were divided on the basis of the presence or not of Pf infection. The DC subtypes were analysed *ex vivo* by FACS analysis. The cells were also stimulated *in vitro* with specific TLR ligands. Cytokines in plasmas and cell free supernatants were measured by ELISA and cytometric beads array assays.

Results | We observed that percentage of BDCA2+ pDC was significantly lower in the infected Fulani children than in the other groups ($P=0.04$). Conversely, the Mean Fluorescence Intensity of HLA-DR was higher on pDC of infected Fulani as compared to uninfected ($P=0.0092$). Interestingly, the secretion IFN- α in plasma was higher in Fulani than Dogon children ($P=0.003$) with the highest levels in the infected Fulani children.

Discussion | The pDC seen in the infected Fulani were more activated and could activate the acquired or innate immune responses more than the infected Dogon children, explaining why the Fulani have less clinical symptoms. We speculate that the lower number of circulating pDC in the Fulani might be because they already have migrated to the secondary lymphoid organs or that they have been depleted through apoptotic mechanisms.



11:35–11:50

HIV-1 infection increases the risk of severe malaria in semi-immune adults in Zambia

Victor Chalwe • *Institute of Tropical Medicine, Antwerp, Belgium*

11:50–12:00

Discussion

Introduction | The impact of HIV-1 infection on malaria is probably driven by the incapacity of the suppressed immune system to control parasite load, resulting in a higher parasite load, incidence of clinical malaria and treatment failure. We assessed if HIV-1 is an important risk factor for severe malaria in adults living in areas of stable malaria transmission.

Methods | In Luanshya, Zambia, a malaria meso-endemic area, each confirmed severe malaria case, 2 matched controls, an adult with uncomplicated malaria and a control with no evident signs of any disease, were selected. Matching criteria were gender, age and area of residence. HIV-1 infection and the related immune suppression were explored as risk factors.

Results | HIV-1 prevalence was 93.1% (27/29) among severe malaria cases, 51.7% (15/29) among uncomplicated malaria cases and 44.8% (13/29) in asymptomatic controls. HIV-1 was identified as a highly significant risk factor for severe malaria as compared to uncomplicated malaria (OR:12.6; IC95:2.0–78.8; $P=0.0005$) and asymptomatic controls (OR:16.6; IC95: 2.5–111.5; $P=0.0005$). Severe malaria cases were more likely to have a CD4-count $<350/\mu\text{l}$ compared to asymptomatic controls (OR: 23.00; 95%CI: 3.35–158; $P<0.0001$).

Discussion | In malaria-HIV-1 co-endemic areas, adults with severe malaria showing no clinical signs of immune suppression are likely to be co-infected with HIV-1.



10:50–11:05

Novel approach to address the tuberculosis treatment regime



Hulda Swai • Council for Industrial Scientific Research (CSIR), Pretoria, South Africa

Introduction | Tuberculosis (TB) is the leading cause of death in South Africa due to co-infection with HIV/AIDS. Although an effective therapeutic regimen is available, patient non-compliance (due to treatment length, dose frequency and side effects) results in treatment failure, while the emergence of drug resistance can lead to MDR-TB. The drawbacks of conventional chemotherapy necessitate the development of a superior nanotechnology-based delivery or carrier system. Nanotechnology has been used to deliver small drugs, proteins or genes, for example, to specific tissues and intracellular compartments.

Methods | To address the anti-TB treatment failure we encapsulated the drugs in polymer nanoparticles for oral delivery using a spray-drying technique. We determined the drug encapsulation efficiency, *in vitro* uptake and release.

Results | We have nano-encapsulated all four first-line anti-TB drugs, with an efficiency above 65% in 250nm size particles. We demonstrated a sustained release *in vitro* for several days with extra cellular clearance of bacteria by the encapsulated drugs. Subsequently, we have been able to illustrate *in vivo* particle uptake following oral administration of the particles. We observed a sustained drug release *in vivo* over a period of 6 days, maintaining the MIC for RIF and INH.

Discussion | Intracellular delivery of the drugs is feasible leading to the controlled and sustained release of drugs within the therapeutic window over long period of time. The nanoparticle high surface to volume ratio enables them interact with the mucosal surfaces of various tissues and permeate easily into cellular compartments.



II:05–II:20

Dominant *Mycobacterium tuberculosis* genotypes in Nigeria

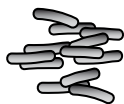
Agatha Ani • University of Jos, Nigeria

Introduction | There is rising incidence of tuberculosis in Nigeria due to limitations of diagnostic methods, poor treatment outcome and high HIV burden. Reports on epidemiological studies are scanty with poor indices of transmission pattern.

Methods | 111 *M. tuberculosis* from cases of pulmonary tuberculosis in Jos, Nigeria were genotyped by a PCR-based method that detects the presence or absence of 43 spacers between short direct repeat sequences on the *M. tuberculosis* genome. The isolates were assigned to family, subfamily and variant based on their spoligo patterns.

Results | The findings were highly homogenous with little genetic variation. Eighty-four (76%) of the isolates belonged to the Latin American Mediterranean (LAM) family, 78 of these were assigned to the LAM10 lineage. Among these, 59 carried identical spoligo patterns. Drug resistance data obtained for most isolates could not be correlated to the genetic clustering of the isolates.

Discussion | The dominance of few *M. tuberculosis* lineages indicate a high rate of transmission, high levels of synonymously import or a highly conserved genotype. It remains to be confirmed whether the large cluster of identical LAM10 represent an outbreak. Alternatively the low level of genetic variation among the non-identical isolates within this subfamily may indicate recent expansion of this group in Jos or simultaneous import from neighbouring countries. Similar patterns, yet less obvious, have been shown in other West-African countries. These findings suggest a recent local expansion of *M. tuberculosis* in West Africa. An extended population-based study is needed to confirm or discard.



11:20–11:35

Estimates of genetic variability of *Mycobacterium tuberculosis* complex and its association with drug resistance and treatment outcomes in Tanzania


Sayoki G Mfinanga • National Institute for Medical Research, Dar es Salaam, Tanzania

Introduction | This study aimed to provide estimates of genetic variability of *M. tuberculosis* complex and its association with drug resistance and treatment outcomes.

Methods | We conducted the study from 2006 to 2008, and the isolates were obtained from samples collected, cultured and stored from 2001 to 2007. A total of 487 isolates from 23 regions in the country were spoligotyped, and we were able to retrieve clinical information on 446 isolates.

Results | The spoligotype family assignment for the 487 isolates showed that 199 (40.9%) belonged to the Central Asian (CAS) family, 90 (18%) the Latin American Mediterranean (LAM) family, 56 (11.5%) to the East-African Indian (EAI) family, and 33 (6.8%) to the Beijing family. Other isolates included 1 (0.2%) for H37 Rv, 10 (2.1%) for Haarlem, 2 (0.45%) for LAM10 CAM, 4 (0.8%) for S family, 21 (4.3%) for TAN, 43 (8.8%) for T family not classified as TAN and 28 (5.7%) for unclassified. No spoligotype patterns were consistent with *M. bovis*. Cure rates were about 80% and no significant variation among the families. The level of MDR-TB was 2.5% (3/121), and the only significant difference we observed for the MDR-TB was in CAS family, whereby we report 4.1% (2/49) versus 1.6 (1/62) in others (Wald=238.2, P=0.001).

Discussion | Common families were the CAS, LAM, and EAI families, while the Beijing family was only about 7%, and all the families had good treatment outcomes. Drug resistance levels were low with an indication that MDR-TB was associated with the CAS family.



11:35–11:50

Spatial analysis of tuberculosis in an urban west-African setting: Is there evidence of clustering?

Kebba Touray • Medical Research Council (UK), Banjul, The Gambia

Introduction | Tuberculosis (TB) case notification has increased in Africa, even in countries where HIV is relatively low, such as The Gambia. In order to aid TB control activities in The Gambia, we used GIS and Spatial Scan Statistics (SaTScan) to identify whether there is significant TB case clustering.

Methods | In Greater Banjul, where 80% of all Gambian TB cases arise, all TB cases registered at chest clinics between March 2007 and February 2008 were asked to participate. Demographic, clinical characteristics and GPS coordinates for the residence of each consenting TB case were recorded. A spatial scan statistic was used to identify purely spatial and space-time clusters of tuberculosis among permanent residents.

Results | Of 1145 recruited TB cases, 960 (84%) are permanent residents and 844 (88%) were living in 37 settlements with a complete map available to settlement level. Significant high and low rate spatial and space-time clusters were identified in two districts. The most likely cluster of high rate from both the purely spatial analysis and the retrospective space-time analysis were from the same geographical area. A significant secondary cluster was also identified in one of the densely populated areas of the study region.

Discussion | Significant clustering of TB cases occurs in The Gambia. Systematic use of cluster detection techniques for regular TB surveillance in The Gambia may aid effective deployment of resources. However, there is an urgent need to conduct community-based active case detection in areas where significantly fewer cases than expected were found.

11:50–12:00

Discussion

HE 016

Ethnobotanical survey, cytotoxicity, *in vitro* study and identification of anti-HIV-1 active compounds from plants used in Congolese pharmacopoeia

Gelase Fredy Nsonde Ntandou • Université
Marien-NGOUABI, Brazzaville, Congo

Introduction | HIV/AIDS remains the second cause of mortality and morbidity after malaria in sub-Saharan Africa where 80% uses the traditional preparations of herbal medicinal products treatments. This study aims to improve the effectiveness of traditional plant-based treatments and the development of new drugs against HIV/AIDS.

Methods | An ethno-botanical survey has been used to identify plants used in Congolese traditional medicine against Influenza RNA virus disease. 10 µg/ml of selected plants extracts were assessed on mortality of cell line KB and Vero for their cytotoxicity. Triterpenoid rich fractions from dichloromethane none cytotoxic plants extracts were tested *in vitro* against HIV-1. The chemical identification of active compounds was made through the analysis by coupling HPLC/UV/mass and TLC.

Results | *Quassia africana* (FQa) is cytotoxic IC₅₀ ≥75%. *Uapaca paludosa* (FUp), *Cassia siamea* (FCs) and *Millettia versicolor* (FMv) barks fractions are not cytotoxic IC₅₀ ≤15%. Three fractions (FUp, FCs and FMv) showed a significant anti-HIV activity in cell culture of T-lymphoblastoid tumor cell line (CEM-4) IC₅₀=0.08, 0.4, 1.8 µg/ml respectively. FUP exhibited also a considerable protease (NF-κB and HIV Tat) and transcriptase reverse (RT) inhibitory activities IC₅₀= 0.5 and 1 µg/ml respectively. FCS showed good inhibitory activity of α-glucosidase IC₅₀= 1.2 µg/ml.

Discussion | This anti-HIV activity is related to betulinic acid and betulin in FPP, or to lupeol in FMv and FCs.

HE 017

Pattern of IFN-γ T cell responses to HIV-1 and their association to CD4 counts and viral load trajectory in acute and early HIV-1 infection

Daniel Bugembe Lule • MRC/UVRI Uganda
Research Unit on AIDS, Entebbe, Uganda

Introduction | In order to clarify correlates of protection against HIV-1 infection we evaluated T cell responses in acute/early infection against plasma viral load and CD4 counts to identify responses that could be harnessed for vaccine design.

Methods | Acute/early HIV-1 infections were identified through 3-monthly monitoring for P24 antigen and HIV-1 antibody EIA in a Ugandan cohort of 156 HIV-1 serodiscordant couples and in individuals within 12 months of seroconversion. Long term HIV-1 infected individuals with CD4 >500 were controls. HIV serostatus, CD4 counts, plasma viral load and HLA class I tissue types were determined. IFN-γ responses of cryopreserved PBMC to HIV-1 peptides spanning the entire consensus proteomes of subtypes A and D were measured in culture ELISPOT assays.

Results | Five acute/early HIV infections expressed IFN-γ responses to at least 1 peptide pool per HIV-1 protein (Gag, Pol, Env, Nef and pooled accessory proteins). Median time post infection at enrolment was 1 month (range 1–4) and viral load copies/ml and ranges at enrolment, month 3 and 6 were 31810 (738–750001), 12336 (912–482000) and 2836 (<400–424000) respectively. No association was observed with T cell responses at this stage. 36% of these patients have HLA class I allele B*5802 associated with rapid progression.

Discussion | The large scope of T cell response to HIV-1 pools observed in acute/early infections and the mixed HLA class I composition including alleles associated with both rapid and slow progression should allow us to identify response patterns associated with differences in progression and viral control as we refine the mapping of potential epitopes identified from pools.



HE 018

Prevalence of neutralising antibody responses in chronic clades A and D HIV-1 infections

Khamis Tomusange • MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda

Introduction | Characterising neutralising antibody (nAb) responses in non-B HIV-1 subtypes is essential, because the data may illustrate key genetic and antibody properties that could impact the design and testing of nAb vaccine candidates in countries where these subtypes circulate. We aimed to document the magnitude, breadth and prevalence of nAb in Chronic subtype A and D HIV-1 infections.

Methods | 45 treatment naïve patients were randomly selected from the rural clinical cohort (RCC), which recruits HIV-infected individuals with known date of sero-conversion. The average time of infection was 5–45 yrs (range 1–16 yrs). Two sample points were selected for each patient; T₁ (early) and T₂ (late), and tested against two tier-1 strains of HIV-1 (SF162.LS, MW965.26) and MLV negative control virus; in the standardized TZM-bl neutralisation assay. MLV positive samples were excluded from analysis.

Results | Magnitude of the nAb response against SF162.LS (subtype B) and MW965.26 (subtype C) varied but was relatively potent in a most cases (ID₅₀ titers >1,000; range 20–87,480). nAb titers against both viruses were closely associated and increased significantly ($P < 0.0012$) from the early to late time point. The magnitude of this increase was substantial in some subjects, whereas in a few the response decreased over time.

Discussion | A high prevalence of nAbs was detected. The magnitude and long-term kinetics varied between subjects. Further analysis with tier 2 viruses (4 As, 4 Bs, 4 Cs and 4 Ds) and association with Viral load and CD4 counts will be performed to document the prevalence and kinetics of cross-reactive neutralising antibody responses.

HE 019

Domestic violence among HIV/AIDS patients attending Nsambya Hospital HIV Chronic Care Clinic

Simon Peter Mayanja • St. Francis Hospital, Nsambya – Kampala, Uganda

Introduction | The magnitude of domestic violence remains unknown among HIV patients attending Nsambya Hospital - a missionary founded hospital, providing HIV care and treatment services to communities living within 21 km of peri-urban Kampala. Anecdotal reports however indicate increasing cases of domestic violence.

Methods | This was a cross-sectional descriptive study that randomly enrolled 117 men and 178 women attending the HIV chronic care clinic in September and October 2008. Structured questionnaires were administered during clinic exit interviews to collect self-reported data from participants.

Results | Domestic violence is very common among HIV patients. Women reported more violence than men. Acts of sexual violence and psychological violence were reported highest (56%) among female patients. Men were less likely (<3%) to experience sexual violence. 36% of women in the study reported ever been sexually abused by their partners, compared to 3% of their male counterparts. 60% and 49% of women and men respectively had been abused verbally by their current or most recent partners. The age of a woman, the rural-urban divide, level of education and history of extra-marital affairs were all significantly associated with domestic violence whether physical, sexual or psychological.

Discussion | Domestic violence is very common among HIV patients. Initiatives to address factors that are associated with violence should be put in force especially those that target women who are most hit. It is possible that domestic violence may impact negatively on issues of adherence as well as treatment outcomes on medication in the context of HIV.



HE 020

Assessment of awareness, attitude and perceptions of students on HIV vaccine trials at the University of Dar es Salaam (main campus), Tanzania

Fredrick Haraka • Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania

Introduction | HIV and AIDS is the major pandemic that has affected many people in the world. By the year 2006 the number of HIV and AIDS victims rose to almost 40 million. Effective vaccination could be employed as one of the primary prevention strategies in combating HIV and AIDS.

Methods | Descriptive cross-sectional study.

Results | A total of 384 were recruited in the study. Out of these 41.7% reported that HIV vaccine cannot prevent the spread of HIV. One hundred and four (26.8%) were of the opinion that an HIV vaccine can cause infection to the person vaccinated. A total of 317 (82.0%) perceived an HIV vaccine as an addition rather than a substitute to other existing preventive measures such as condom use, in the fight against HIV and AIDS. The attitude towards an HIV vaccine trial was generally positive in 87.5% of the students, but only 19.8% would be willing to participate in a vaccine trial with their current level of information. However, 48.2% would participate if they are better informed.

Discussion | The perception and attitude of University of Dar es Salaam students towards HIV vaccine trials were generally positive. However misconceptions were common. The community should be educated more on HIV vaccine trials, and more socio-behavioural studies need to be done among different social groups on HIV vaccine trials.

HE 021

Stigma related factors and patients' compliance on anti-retroviral therapy: Listening to the voices of the healthcare providers in Tanzania

Edith Tarimo • Muhimbili University of Health and Allied Sciences (MUHAS), Dar es Salaam, Tanzania

Introduction | Stigma is a discrediting attribute possessed by a person with an undesired difference. Evidence shows that stigma related to HIV affects compliance with treatment among AIDS patients but little is known about health care providers' perceptions. This study describes findings about stigma and antiretroviral therapy (ART) compliance as perceived by health care providers (HCPs) at Care and Treatment Centres (CTCs) in Tanzania.

Methods | Three Focus Group Discussions (FGDs) were conducted among health care providers at 3 CTCs. The purposive sample of 33 HCPs included 8 doctors, 17 nurse-counsellors, 3 pharmacists, 3 laboratory technologists and 2 social workers. Analysis followed thematic content approach.

Results | Key findings were: 1) the physical setup of the CTC led to a breaching of patient confidentiality. Patients tried to leave quickly and because of the rush sometimes picked up the wrong medicine. 2) The use of identifiable blue cards among patients led them to hide the cards or re-register themselves at another CTC to avoid those who could identify them at the initial clinic. During relocation they missed doses. 3) Sometimes when patients were given the ART in the container wrapped in the manufacturers' box, they kept the container but threw the box away. The instructions on how to take the ARVs were often written by the HCPs on the boxes. Some patients went home and used their medicines contrary to instructions.

Discussion | These findings indicate that simple interventions could have great impact on ART compliance. For instance, the 'Blue cards' could be replaced with less identifiable cards.



HE 022

Factors associated with HIV infection and pregnancy at screening in a feasibility study to prepare for future HIV prevention trials in northwest Tanzania

Asungushe Kayombo • Mwanza Intervention Trials Unit, Mwanza, Tanzania

Introduction | Development of female-controlled HIV prevention methods is crucial in the fight against HIV in sub-Saharan Africa. Novel interventions need rigorous safety and effectiveness evaluation in clinical trials. HIV infection and pregnancy are two common exclusion criteria for HIV prevention trials. Knowing factors associated with these criteria in a cohort will inform recruitment strategies in future preventative trials.

Method | Women working in bars/hotels in 3 districts in northwestern Tanzania were invited to screen for an observational prospective cohort study. At screening women were interviewed using structured questionnaires and were tested for HIV and pregnancy. Multivariate logistic analyses were performed to determine factors independently associated with these outcomes.

Results | As of March 2009, we have screened 920 women. The mean age was 27.8 years; 54% of women have completed primary schooling, and 45% are separated or divorced. Prevalence of pregnancy was 7.0% (95%CI=19.2–24.7) and of HIV was at 22.0% (95%CI=5.3–8.6). Adjusted for age and education, women working in a bar only were more likely to be HIV positive compared to women working in guest-houses (AOR=1.59, 95%CI=1.02–2.47); women working in Kahama town were more likely to be HIV positive compared to those from Geita town (AOR=1.8, 95%CI=1.2–2.8). No demographic factor was independently associated with pregnancy in this population.

Discussion | HIV and pregnancy prevalence at screening are high, indicating need for HIV-preventive interventions and family planning services. Recruitment strategies for future trials should consider type of facility where women are working.

HE 023

Ethical-legal challenges in conducting HIV prevention trial research with adolescents: A South African case study of tool development

Melissa Wallace • Desmond Tutu HIV Centre, University of Cape Town, South Africa

Introduction | Conducting HIV vaccine trial research with adolescents poses particular ethical-legal challenges. Anticipating and addressing these in advance of this research is essential. Examples of legal complexities include (i) establishing when adolescents can consent independently to research, (ii) the degree of privacy adolescents can enjoy within research, and (iii) establishing when reports must be made to authorities. As part of an EDCTP-funded project aimed at capacity building for adolescent HIV vaccine trials in South Africa, an explicit focus was building ethical-legal capacity of research staff to negotiate such complexities.

Methods | A partnership was formed with an ethical-legal research group and a consultative process of tool development and training was implemented, aiming at assisting researchers to recognise and apply their legal obligations when conducting research with adolescents.

Results | A legal directory, (partially developed by South African AIDS Vaccine Initiative (SAAVI)) was updated and finalised, resulting in a comprehensive overview of all laws in the South African setting affecting child research. Protocol development, consent form development, and standard operating procedures were influenced by this legal directory. Specific recommendations were made in relation to consent, privacy, mandatory reporting and ethics review.

Discussion | Ethical-legal requirements are a legitimate and often neglected area of inquiry. This ethical-legal research demonstrated that strategic partnerships are feasible, and can add ethical value to the implementation of research. Such research tools can add (in any setting) to national norm-setting around minimum standards for adolescent research.



ME 016

Variation in cytochrome P450 CYP2C19/CYP2C9 and efficacy of chlorproguanil and dapsone

Ramatoulie Janha • Medical Research Council (UK), Banjul, The Gambia

Introduction | Anti-malarial biguanides, proguanil and chlorproguanil, are metabolised by CYP2C19 to cycloguanil and chlorcycloguanil respectively. Dapsone is metabolised by the structurally related enzyme CYP2C9. Thus genetic variation in CYP2C19/CYP2C9 may affect treatment efficacy of chlorproguanil/dapsone for uncomplicated malaria.

Methods | CYP2C19/CYP2C9 polymorphisms in Gambians (43 adults and 621 children) treated with chlorproguanil/dapsone for uncomplicated malaria were assessed. Effects of CYP2C19/CYP2C9 alleles and CYP2C19 metaboliser groups on chlorcycloguanil pharmacokinetics in the adults and on treatment efficacy of malaria in the children were examined.

Results | Adult participants with CYP2C19*17 had significantly higher AUC_{0–24} (geometric means 317 vs. 216 ng·h/ml, ratio of geometric means 1.46, 95%CI 1.03 to 2.09, P=0.0363) and C_{max} for chlorcycloguanil (geometric mean ratio 1.52, 95%CI 1.13 to 2.05, P=0.0071) than non-carriers. CYP2C9*8 significantly reduced the geometric mean for T_{max} of chlorcycloguanil from 11 to 6 hours. Children with this allele showed a trend towards a lower drop in haemoglobin from day 0 to day 3 (mean drop in hb 1.1138 vs. 1.6638 g/dl, P=0.0555).

Discussion | CYP2C19*17 determines anti-malarial biguanide pharmacokinetic profile at the CYP2C19/CYP2C9 locus. CYP2C9*8 may confer some protection from anaemia which could be related to a reduction in dapsone toxicity. The findings can be utilised in future clinical trials involving the antimalarial biguanides and dapsone.

ME 017

Efficacy of a mosaic long lasting insecticide net; Permanet®3.0, against wild populations of resistant *Culex quinquefasciatus* in experimental huts in Togo, West Africa

Dominic Dery • University of Abomey-Calavi, Benin

Introduction | ITNs are recommended by WHO in malaria endemic countries. New developed techniques for long-lasting insecticide treatment of nets provide solution from regular re-treating difficulties. For acceptance in communities, these nets should offer protection against nuisance vectors such as *Culex* and *Mansonia* mosquitoes.

Methods | PermaNet®3.0 efficacy was tested in experimental huts. Field susceptibility was accessed by WHO test kits and protocol.

Results | 1,223 *Culex quinquefasciatus* females were collected within a six-week evaluation period (one Latin square rotation). The unwashed mosaic net (PermaNet®3.0) deterred 16.84% *Culex* mosquitoes. After 20 washes, it deterred 5.79% mosquitoes compared to 6.84% deterrence by the unwashed conventionally used net; PermaNet®2.0. PermaNet®3.0 induced mosquitoes to exit huts by 50.48% and inhibited blood feeding 70.97% in its unwashed state. After 20 washes, it induced 42.91% mosquitoes to exit and inhibited 67.06% mosquitoes from blood feeding. The new mosaic PermaNet®3.0 gave 76% personal protection at zero wash and 69% protection after 20 washes. Also, the net retained almost equal its insecticidal effect at zero wash (7.1%) and after 20 washes (6.5%). *Anopheles gambiae* ss populations in Akodesséwa were susceptible to chlorpyrifos methyl, deltamethrin and bendiocarb, but resistant to the organochlorine DDT. *Culex quinquefasciatus* species were resistant to all classes of tested insecticides.

Discussion | The efficacy of the new mosaic net is better explained by the overall personal protection it offers to an individual. Comparatively, it performed better in protection of sleepers from mosquito bites.



ME 018

Micronutrient deficiencies erratically induce polarisation towards either of the two arms of type I and type II cytokine response in *Plasmodium falciparum* infection

Erasto V. Mbugi • Wageningen University,
Wageningen, the Netherlands

Introduction | The balance between pro-inflammatory and anti-inflammatory cytokines which mediates innate and adaptive immune responses have been linked with effective human malaria protection and reduced dangers of development of pathology. This immunological balance in malaria endemic countries may be influenced by micronutrients deficiency.

Methods | We carried out an *in vitro* stimulation of peripheral blood mononuclear cells from preschool children using *Plasmodium falciparum*-infected red blood cells to determine T cell response to malaria antigens under different conditions of micronutrients deficiencies and malaria status.

Results | Our main findings indicate zinc deficiency to induce significant increase in production of TNF- α by 37% (95%CI; 14–118%) and IFN- γ by 74% (95%CI; 24–297%). Magnesium deficiency induced significant increase in production of IL-13 of 80% (95%CI; 31–371%) and reduction in IFN- γ production.

Discussion | These results reflect induction of a shift in cytokine profile to more of the type I cytokines and cell-cell mediated responses in zinc deficiency and a type II response in magnesium deficiency. The pathological sequel of malaria rests more on the state of balance between type I and type II arms of cytokine responses than suppression of production of these cytokines and may be influenced by different conditions of micronutrients and malaria status.

ME 019

Clinical diagnosis or microscopy under any circumstances? Outpatient case management of malaria in a rural African district

Evelyn Ansah • Dangme West District Health
Directorate, Ghana Health Service, Ghana

Introduction | There is evidence of massive over-diagnosis of malaria. This could result in a higher cost of treatment and ultimately unsustainable supply of ACTs. This study evaluated the accuracy of clinical diagnosis and routine malaria microscopy under normal operational conditions at some health facilities in rural Ghana.

Methods | A cross-sectional survey was carried out over a one-month period at four health facilities. Checklists involving data extraction from patient and laboratory records were used. Expert microscopists double-read research slides taken from patients suspected to have malaria to assess the accuracy of clinical diagnosis and local microscopy.

Results | We carried out analysis of 602 patient contacts with 22 clinicians in four health facilities. Laboratory tests were requested for 15.1% of the 602 patients. Of those with a negative test result, 21.9% still received an antimalarial. The sensitivity of clinical diagnosis was 99.3%; its specificity, 4.2%, its positive predictive value, 24.7%; and its negative predictive value, 95%. For local microscopy, its sensitivity was 75%; its specificity, 37.3%; its positive predictive value, 20.3% and negative predictive value, 87.5%. Slide positivity rate according to local microscopy was 64.8% compared to 17.6% from expert microscopy.

Discussion | Both clinical diagnosis and local microscopy were poor at identifying true malaria in this setting. Whilst clinical diagnosis results in over-diagnosis of malaria, poor quality microscopy does not improve the standard of clinical practice. There is a need to improve on the quality of microscopy and consider the use of alternative diagnostic methods with minimal requirement of technical expertise.



ME 020

Hematological parameters changes in children less than 6 years living in malaria endemic area: Implication for future malaria vaccine trials

Adama Gansané • CNRFP, Ouagadougou, Burkina Faso

Introduction | In malaria endemic areas, almost any children are infected by *Plasmodium* which targeted red blood cells and could have some impact on haematologies parameters. In order to describe these variations in a future malaria vaccine trials site, we examined immunological profiles of children less than 6 years living in an area where parasites diseases transmission is endemic and seasonal.

Methods | A cross-sectional survey has been conducted at the peak of malaria transmission season in rural area of Saponé Health District in Burkina Faso in September 2007. After informed consent and clinical examination, blood sample was obtained from all participants for malaria diagnostic and full blood count.

Results | From 414 children recruited, 192 were malaria negative and 222 were malaria positive. The mean age of infected children was 41.8 ± 15.4 months vs. 38.8 ± 16.4 months for control group ($P=0.06$). No significant differences were observed between the two groups in term of leucocytes count. However, parasitemic children tend to have significant lower haemoglobin level (10.8 g/dl vs. 10.4 g/dl $P<0.001$), lymphocytes count ($4592 \pm 1999/\mu\text{l}$ vs $5141 \pm 1846/\mu\text{l}$, $P<0.001$), platelets count ($266149 \pm 114995/\mu\text{l}$ vs. $379540 \pm 163263/\mu\text{l}$; $P<0.001$), red blood cells count ($4.388.106 \pm 535647/\mu\text{l}$ vs. $4.158.106 \pm 563356/\mu\text{l}$; $P<0.001$) and higher monocytes count ($1402 \pm 666/\mu\text{l}$ vs. $1192 \pm 534/\mu\text{l}$; $P<0.001$) as compared to non infected children.

Discussion | Special attention should be applied when interpreting haematological parameters and evaluating immune responses in vaccine trials since a high number of lymphocytes cannot be obtained in the assessment of immune responses in malaria-infected children. Assessment of subpopulation of lymphocytes count (CD4^+ , CD8^+ , CD3^+ , NK) in children from this site must be investigated.

ME 021

Antibodies to malaria vaccine candidates and chloroquine or SP treatment efficacy in an endemic area of Burkina Faso

Amidou Diarra • CNRFP, Ouagadougou, Burkina Faso

Introduction | During the assessments of malaria treatment efficacy, cure rates were reported to increase with age. In endemic areas, spontaneous clearance of *P. falciparum* is often the result of specific immunity. To evaluate whether the therapeutic response was associated with a specific immune response, antibodies to malaria vaccine candidates were measured before a longitudinal assessment of *in vivo* chloroquine (CQ) and sulfadoxine-pyrimethamine (SP) efficacy.

Methods | The target population was children from Balonghuin, aged 0.5–15 years. Prior to malaria transmission season, 5 ml venous blood were taken from each child and plasma used for antibodies measurement. The longitudinal assessment of CQ and SP efficacy of the study protocol was based on the 2001 WHO guidelines for antimalarial drugs efficacy monitoring. The level of antibodies (IgG subclasses, IgM) to MSP3, GLURP and MSP119 was assessed by ELISA.

Results | 195 children were treated with CQ and 53 with SP. Adequate clinical and parasitological response (ACPR) rates were 8.2% and 37.7% respectively for CQ and SP. Treatment failure rates (TFR) including early treatment failure and late treatment failure were 91.8% for CQ and 62.3% for SP. TFR was high in young children compared to elder. In both treated group, antibodies level were high in ACPR group except for IgM to MSP1 and IgG4 to GLURP in CQ treated sample and IgG1 to MSP1 and to GLURP in SP treated group. However the difference was statistically significant for IgG, IgG1, IgG2 and IgG4 to MSP3, IgM and IgG to GLURP for chloroquine treated patients and IgG3 to MSP3 in sulfadoxine treated patients.

Discussion | Our data suggested that efficacy of the therapeutic response seemed to be the result of the combined effects of treatment and the individual immune status of the patients at the time of drug cure.



ME 022

Malaria morbidity in a high and seasonal malaria transmission assessed through different methods



Alphonse Ouedraogo • CNRFP, Ouagadougou, Burkina Faso

Introduction | The incidence of clinical malaria is one of the key endpoints measures for malaria vaccine candidates' trials. These measures might be done either by active or by passive case detection (ACD, PCD) methods. This study aims to identify the most suitable method to be use in a site being prepared for future malaria vaccine candidates' trials.

Methods | Two cohort studies were conducted within the same study area of Saponé. The first cohort consisted (ACD cohort) of a group of 555 children aged 0–5 years followed up by biweekly home visit. The second cohort (PCD) included 945 children, whose parents were encouraged to report to the nearest community clinic should their child feel sick. Treatment was provided free of charge in both cohorts. At each visit, a malaria smear was obtained if fever. Study duration was one year. A malaria episode was defined as positive *Plasmodium falciparum* parasites density in presence of fever.

Results | In the PCD cohort, 3670 clinic visits were recorded with 1377 malaria episodes diagnosed. The incidence of clinical malaria was 1.26 episodes/child-year at risk (95%CI [1.06–1.46]). In the ACD cohort, total 56716 home visits were performed. The children were seen during 49672 visits. A total of 436 malaria episodes were diagnosed. The overall incidence of clinical malaria was 0.87 episodes per child per year at risk (95%CI [0.84–0.90]).

Discussion | These finding suggest that in our setting with a treatment provided free of charge PCD will be the efficient method to assess malaria morbidity in under-five children.



TE 09

Sharing experiences and optimising South-to-South collaboration in preparing resource-limited sites for vaccine trials: The TB vaccine sites

Anne Wajja • Makerere University Infectious Diseases Institute, Kampala, Uganda

Introduction | The TB vaccine project based in Iganga/Mayuge Demographic Surveillance Site (DSS) is one of 4 sites in Africa and 1 in India undergoing capacity building and site development by EDCTP and Aeras in preparation for Phase III TB vaccine trials. Under the TB Vaccine Sites Network (TBVACSIN), the sites vary in development ranging from well-established to limited experience in clinical research. Sites in similar settings face common challenges that may be addressed through sharing experiences and optimising south-to-south collaboration.

Methods | Optimising has been done through exchange visits, joint training sessions, annual networking events at one of the sites to share and harmonize protocols, SOPs etc.

Results | Ugandans visited the South Africa site to learn its setup and operations. Their staff trained Uganda staff in conducting Tuberculin Skin Testing, sputum induction and gastric lavage; the Uganda staff in turn trained Kenya staff on the latter investigations. In 2008, a consensus-building workshop for all sites on interpretation of infant chest x-rays was held. Uganda lab staff spent a month in the India site lab to learn how to run BSL₃ labs. Joint training sessions in clinical research methods, data quality management and professional development are planned or been done in Kenya and Uganda. All sites have learned practical lessons through these activities.

Discussion | This is a cost-effective way of building capacity in resource-limited settings offering practical lessons between sites. Already established sites still benefit from strengthening of such collaboration. Forming/joining similar networks should be encouraged.

TE 010

CDC's Tuberculosis Trials Consortium

Andrew Vernon • U.S. Centers for Disease Control and Prevention, Atlanta GA, USA

Introduction | The Tuberculosis Trials Consortium (TBTC) conducts programmatically relevant clinical research concerning treatment of latent TB infection (LTBI) and TB disease. Beginning in 1993, TBTC reorganised as a consortium in 1998, and has grown to include 28 study sites in North and South America, Europe and sub-Saharan Africa.

Methods | Beginning in 1993–94, TBTC reorganised as a consortium in 1998, and has grown to include 28 study sites in North and South America, Europe and Africa. Formal by-laws define a committee structure, relying on protocol teams and working groups, with an extensive system for communication, quality assurance, and attention to human subjects protection.

Results | TBTC has undertaken 9 major trials (TBTC Studies 22–30), and multiple sub-studies. These have included Phase II and III trials of TB disease, a large Phase III trial of a 12-dose, once-weekly isoniazid and RPT regimen for LTBI, and Phase IV trials in special populations such as HIV-TB patients treated with intermittent rifabutin-based regimens.

Over 12,000 persons have participated in TBTC studies, 8,000 of whom were in the United States. TBTC has focused recently on a series of Phase II studies including moxifloxacin or daily RPT, as part of the effort to identify a TB treatment regimen of 3–4 months duration.

Discussion | TBTC is one productive member of the growing global network of groups conducting TB clinical trials. The consortium is eager to coordinate and collaborate with other groups in the rapid pursuit of improved therapies for TB infection and disease.

TE 011

Complementary role of *Mycobacterium w* immunotherapy for treating tuberculosis: A systematic review

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Introduction | Systematic review to investigate the complementary role of *Mycobacterium w* immunotherapy for treating tuberculosis was conducted.

Methods | We searched MEDLINE, EMBASE and LILACS, and hand-searched journals, unpublished literature, abstracts and proceedings of the conferences (International Union Against Tuberculosis and Lung Disease World Congress (IUATLD) and European Respiratory Society World Congress (ERS)) using search terms: tuberculosis AND (mycobacterium w OR immunotherapy OR immunoadjuvant OR vaccine) for experimental and quasi-experimental studies. Active group included cases inoculated with heat-killed *Mycobacterium w*, control group included cases who got placebo or no *Mycobacterium w*. Two studies were eligible to be considered in the review.

Results | *Mycobacterium w* immunotherapy used as adjuvant therapy has shown higher cure rates and significant reduction in time to sputum conversion in tuberculosis patients with high bacterial load. *Mycobacterium w* immunotherapy has shown potential in tuberculin conversion in HIV-infected people.

Discussion | Future research should seek to further evaluate the effect of *Mycobacterium w* immunotherapy as adjunctive treatment in tuberculosis in large clinical trials.

TE 012

Validation of bleach treated smears for the diagnosis of pulmonary tuberculosis

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Introduction | Diagnosis of pulmonary tuberculosis (TB) is dependent on direct sputum smear microscopy, which detects only about half of culture-confirmed cases in most settings. As smear microscopy is likely to continue to be the main TB diagnostic tool in resource-constrained settings, techniques that improve its performance are urgently needed.

Methods | Consecutive patients visiting health centre laboratories in Awassa, southern Ethiopia, submitted spot, morning and spot sputum samples between June and September 2006. The sputum samples were pooled for each patient. Direct smears were stained with hot Ziehl-Neelsen (ZN) technique and aliquots cultured for mycobacteria on Löwenstein-Jensen media. The remaining sputum was treated with household bleach, aliquoted and processed with short-term digestion, centrifugation and sedimentation techniques, and stained with ZN.

Results | Acid-fast bacilli were detected in respectively 126 (25%), 141 (28%), 169 (34%) and 198 (40%) of the 497 pooled sputum samples processed by the direct, short term, sedimentation and centrifugation techniques ($P < 0.001$). The sensitivity of the direct, short-term, sedimentation and centrifugation techniques was respectively 51.1%, 53.2%, 57.6% and 63.6%. The difference between the direct smear and centrifugation ($P < 0.001$) or sedimentation ($P < 0.005$) methods was significant. The specificity of the direct, short-term digestion, sedimentation and centrifugation techniques was respectively 97%, 93%, 86.5% and 80.8%.

Discussion | Bleach treatment of sputum and centrifugation significantly improves the sensitivity of smear microscopy for the diagnosis of TB in a health centre in a high TB burden area, but the operational advantages need to be evaluated under program conditions.

CE 017

Strategies for developing staff capacity to conduct GCP compliant clinical research in resource constrained settings

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Introduction | Conducting clinical research poses many challenges in resource-constrained settings including lack of skilled staff. The Professional Development Program (PDP) is an Aeras-SATVI model developed to address this challenge through targeted training interventions. The programme is implemented as part of the site development TB vaccine preparation activities in Uganda. The programme trains both staff and trainers in the essentials of clinical research such as Good Clinical Practice (GCP) and informed consent.

Methods | Through a learner-centred train-the-trainer approach, the PDP builds capacity of a team of 3 locally sourced trainers who form part of the clinical research team to train study staff. Staff are trained according to the specific roles they perform using a role-based training strategy. The programme also offers avenues for individual self-paced learning through a resource centre. Strategies to assess performance following training are in place in order to address errors that may require timely response or retraining.

Results | Since April 2008, 52 of 56 core staff have been trained on at least one clinical research course and up to 18 foundational or role-specific courses while 40 have obtained GCP certificates. Initial assessment of staff performance 3 to 6 months after training on informed consent indicates a high level of conformity to what was taught.

Discussion | The programme has made significant strides in cost-effectively training staff conducting clinical research. However, more effort is needed in following up on trainings to ensure participants' rights are protected even with limited resources.

CE 018

Capacities and capabilities of Research Ethics Review Committees (RECs) in Africa

Joyce Kemilembe Ikingura • Tanzania Commission for Science & Technology, Dar es Salaam, Tanzania

Introduction | Good health research stewardship demands that countries have functional research ethics review systems to provide an independent third-party review aimed at protecting the dignity, integrity and safety of bio-medical research participants. The independence of Research Ethical Review Committees (REC) to effectively and efficiently fulfil its tasks depends very much on both human and financial resources availability.

Methods | We undertook an electronic information collection from 15 Institutional Review Boards (IRBs) and RECs in African countries on financing of their activities and human resources available. We also undertook reviews of publications on the subject matter.

Results | Very little financial support is given to the functioning of the IRBs/RECs. The host institution is left to provide for the IRBs/RECs mostly in-kind through provision of space, materials and facilities. Some committees have no operational budgets in place. Revenue sources included external contributions, grants, in-kind donations and review fees. A few REC members have received formal training on research ethics. Some have received short-term basic training on research ethics through seminars and workshops.

Discussion | IRB and REC activities in Africa are limited by human capacities and financial resources. Inadequate funding of REC is orchestrated by poverty and threatens the independence of the IRBs/REC processes, which sometimes may lead to blinded decisions in favour of material and status benefits that the project being reviewed would bring to the institutions, researchers, community members and participants.



CE 019

Regional information and advocacy support model for health research utilisation

James Watiti • East, Central and Southern African Health Community (ECSA-HC), Tanzania

Introduction | The link between health research to policy and programme improvement in countries of the East and Southern African region is weak. Diverse institutions, partners and other stakeholders undertake research in various thematic areas, but there exist few mechanisms for harnessing the research output to inform transformative improvement.

Methods | The ECSA Health Community can link various research processes to its regional high-level policy advocacy cycle which includes the Thematic Technical Networks, the ECSA Best practices Forum, the Directors Joint Consultative Committee and the ECSA Health Ministers Conference. This regional advocacy support model has been developed through identifying synergistic links between these annual forums which were previously independently planned. This has resulted in a complete cycle that allows continuous sharing and feedback which is essential for utilisation.

Results | Health research processes that link with the regional information and advocacy cycle are more likely to gain and sustain political buy-in, policy and technical support by a larger group of key stakeholders, thus ensuring higher likelihood of utilisation of findings for policy and programme planning in countries. The ECSA Information and Advocacy support model has been effectively applied to various thematic areas in maternal health, and human resources for health.

Discussion | A regional Information and Advocacy support mechanism for health research can strengthen generation and utilisation of research for improved policies and programmes. Strengthening such a mechanism can provide regional stakeholders with an effective avenue for catalysing utilisation of research findings for improved policies and programmes.

CE 020

Framework for health research regulation in Zimbabwe: Involvement of communities in promotion of ethics compliance

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Introduction | All health research falls under the jurisdiction of the Medical Research Council of Zimbabwe (MRCZ), a statutory body set up in 1974 under the Research Act of 1959. MRCZ hosts the National Ethics Committee responsible for ethical review, oversight, popularising good ethical conduct, issues of informed consent and human protection through training and raising awareness. Community Advisory Boards (CABs) serve as a tool for facilitating acceptances of research and compliance in the community.

Methods | Through an EDCTP capacity building grant MRCZ was able to facilitate the training of 10 CABs to facilitate the implementation of the DetectTB project- a study evaluating case-finding strategies for the detection of TB in households in 10 high density residential suburbs of Harare. Baseline survey for HIV infection and active TB disease in all adults was conducted, followed by an HIV prevalence survey and bacteriological assessment in routinely diagnosed TB patients registering for treatment from the same suburbs.

Results | Participation rates (with written informed consent) were high in a study with neighbourhoods with 107,980 adults in 41,263 households. A total of 12,426 adults (82%) completed questionnaires, 81% provided sputum and 73% provided HIV specimens, mainly (91.2%) venous blood. Successful implementation and response to the research by community attributed to the support received from the CABs.

Discussion | Active engagement and social mobilisation of the community affected by the problem under investigation is key to successful implementation of the research and compliance with ethical issues governing research. This contributes to outcomes that allow coordinated planning, avoidance of wasting the limited resources, facilitating translating the research into action.



CE 021

Are ethical clinical trials possible without formal ethics instruction in medical schools?

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Introduction | The paper highlights the critical role ethics education could play in promoting ethical clinical trials in Africa – with particular reference to Zambia. The paper starts by acknowledging that ethics education is now firmly integrated in medical curricula in most of the developed world, including many countries in Asia, the Middle-East, and South America. However, in spite of these global developments, at present (with the exception of Algeria, Kenya, Nigeria, South Africa, and Tunisia, a.o.) the majority of sub-Saharan African countries are way behind as far as incorporating formal ethics education in medical schools is concerned. It is with this background that the paper questions whether medical graduates could undertake ethically prudent clinical trials when they have not been exposed to formal ethics training in undergraduate and residence training.

Methods | Extensive review of literature was done. Then structured in-depth interviews were conducted with 11 out of 16 government nursing schools and the medical school at the University of Zambia.

Results | In spite of the widespread acceptance of ethics education, in practice formal ethics instruction does not feature much in pre- and post-basic education of medical students in Zambia. Further, knowledge of ethics among students and physicians was largely lacking. Even those who exhibited a reasonable grasp of medical ethics problems, their knowledge was deficient in several areas.

Discussion | While ethics education does not necessarily translate into ethical clinicians and researchers, it is critical if medical professionals are to have the required capacity to negotiate their way through a myriad of ethical challenges in medical research. Medical researchers cannot appropriately handle many ethical issues that arise in medical research without the knowledge and skills necessary for ethical decision-making.

CE 022

Establishment of an HIV vaccine cohort among clandestine female sex workers in Ouagadougou, Burkina Faso: Situation analysis of sexual and reproductive health and HIV needs

Isidore Tiandigo Traore • Centre Muraz, Ouagadougou, Burkina Faso

Introduction | An EDCTP-funded multi-centre study aims to establish and follow cohorts of women at high-risk of HIV infection in Burkina Faso and Tanzania in preparation for future HIV vaccine trials. A multicomponent situation analysis of the sexual & reproductive health (SRH) and HIV/AIDS needs of overt and clandestine female sex workers (FSW) was undertaken in Ouagadougou.

Methods | Geomapping of sex work venues was done throughout the city. Social science methods were applied in recruiting key informants and eliciting information on sex work experience and on past and current access to SRH services and HIV prevention and care among these high-risk women. Four focus groups discussions and 37 in-depth interviews were conducted.

Results | Since 1990, more than 17 HIV/AIDS interventions have targeted FSWs in Ouagadougou. They have generally focussed on education on safer sex, provision of condoms, and access to treatment for sexually transmitted infections. Little emphasis has been placed on access to antiretroviral therapy or on other SRH issues. Over 65% of these interventions were discontinued when funding ceased, legal repression of prostitution significantly limits the impact of the remaining interventions. The target population expressed the desire to have dedicated, accessible and integrated SRH and HIV/AIDS prevention and care services offered in a confidential and non-stigmatising manner, particularly for the clandestine FSWs.

Discussion | The EDCTP project, by providing integrated SRH and HIV/AIDS services, will address the SRH and HIV care needs of this highly vulnerable population. From its high patronage depends the success of future HIV vaccine studies.





HP 021

Sexually transmitted infections among Mozambican women enrolled in a microbicides development programme (MDP) feasibility study and comparison between rural and urban areas

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Introduction | Despite the implementation of several prevention strategies, the HIV pandemic has increased in Mozambique, particularly in women, with estimated HIV prevalence rising from 20.7 % in 2005 to nearly 30% in 2008 in pregnant women attending antenatal clinic ANC. Vaginal microbicides, if proved effective, would complement the current interventions to prevent HIV as they could be initiated by women, and would permit pregnancy unlike barrier methods. We have completed enrolment of the participants of the first microbicide feasibility study in Mozambique to evaluate the site's preparedness to conduct a randomised controlled trial of a candidate microbicide. Objectives of the study are to describe the prevalence of selected sexually transmitted infections (STIs) and bacterial vaginosis among women from urban and rural areas in Mozambique enrolled in the study.

Methods | From August 2007 to October 2008, sexually active women aged 18 to 60 years were screened, and considered eligible if HIV negative, not pregnant, and able to provide contact details. Women were recruited from urban (Maputo) and rural (Manhiça) locations and the target enrolment was 500. At screening RPR and HIV serology were performed and at enrolment endocervical samples were collected for *Neisseria gonorrhoeae* (NG) and *Chlamydia Trachomatis* (CT) through PCR; a high vaginal swab for *Trichomona Vaginalis* (TV) using In-Pouch; and a vaginal swab for Bacterial Vaginosis (BV) according to the Ison-Hay score on Gram stain. Bacterial vaginosis was considered to be present if the Ison-Hay was >7. Women were followed for 52 weeks and have 12-weekly HIV rapid

tests, and gynaecological samples collected at 24 weeks.

Results | In total 790 women were screened and 505 were enrolled. Between 393 and 424 of the enrolment samples have been processed. The preliminary results show that in general, the prevalence of HIV and other STI was higher in Manhiça compared to the Maputo cohort: HIV (22.6% vs 10.1%); RPR (6.8% vs 3%); NG (0.4% vs 3.4%); CT (4.8% vs 4%); TV (8.9% vs 5.2%) and BV (50.9% vs 41.8%).

Discussion | Although the prevalence of the majority of infections was higher in the rural cohort in Manhiça, the figures do not adjust for age. Of note, the one infection more prevalent in Maputo is NG, an infection associated with partner change and unprotected sex.

HP 022

CCR5 genotypes in Ghanaian couples discordant for HIV-1 infection

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Introduction | The prevalence of HIV among heterosexual couples is high. In spite of this, there are instances in which one partner is HIV sero-positive and the other HIV sero-negative (discordant couples) despite being at risk for HIV infection. A number of factors are responsible among which is a deletion in the major coreceptor, chemokine co-receptor CCR5, for entry of HIV-1 into CD4+ T lymphocyte cells. Individuals homozygote for a 32 base pair deletion (CCR5 Delta32) do not express the CCR5 receptor at their cell-surface and have a natural resistance to HIV-1 infection.

Methods | In order to determine the CCR5 genotypes of Ghanaian serologically discordant couples and the possible role of CCR5 Delta32 mutant allele in the lack of HIV-1 transmission, 32 couples (serologically discordant couples SDC and serologically concordant couples SCC) visiting the Fevers Unit of the Korle-Bu Teaching Hospital were enrolled. Blood samples were taken for HIV-1 antibody screening and confirmation. HIV-1 negative serostatus of discordant partners was confirmed by PCR. The CCR5 genotypes were determined by PCR.

Results | HIV antibody testing with PCR revealed 8 SDC and 24 SCC. One SDC seronegative individual out of 8 SDC seronegatives was heterozygous for the CCR5 Delta32 allele. The rest had wild-type alleles. This finding was important (although possession of one allele cannot be implicated in natural resistance) because the gene mutation is said to be absent in people of African descent due to its linkage with the bubonic plague.

Discussion | CCR5 Delta32 allele is unlikely to explain discordance in this cohort.

HP 023

Evaluation of the HDB p24 antigen assay for early diagnosis of HIV-1 infection in infants and for monitoring viral load in HIV-1 positive women

Zahra Theilgaard • Institute for Medical Research, Tanga Centre, Tanzania

Introduction | Nucleic acid based tests are the golden standard for monitoring antiretroviral therapy and for early diagnosis of HIV infection in infants. We have established the optimised HDB p24 antigen assay at the AMBRELA Lab of the National Institute for Medical Research, Tanga Centre, in Tanzania to assess its applicability in the current setting for early diagnosis of infants and for monitoring viral load.

Methods | Plasma samples for quantification of p24 antigen and HIV RNA from HIV-positive mothers are collected at delivery, 7 and 42 days post-partum. Samples from their babies are collected at 42 days and 9 months post-partum.

Results | The study is ongoing and the results are therefore preliminary. Monitoring viral load in mothers: Complete sets of results for delivery, day 7 and day 42 were thus far available from 35 mothers. After administration of ART for PMTCT significant decreases in p24 ($P=0.001$) and HIV RNA ($P\leq 0.001$) were seen. A subsequent increase following cessation of treatment was seen from day 7 to day 42 in both p24 ($P=0.136$) and HIV RNA ($P\leq 0.001$). Diagnosis of children: 44 samples from children of HIV-positive mothers were HIV-negative (cut-off=10000 cp/ml) and 4 samples were HIV-positive by both assays. One sample was HIV-negative by p24, but HIV RNA result was 84117 cp/ml.

Discussion | The p24 antigen analysis shows promise for early diagnosis of children in this setting and for monitoring changes in viral load.



HP 024

Modulation of HIV-1 replication in human primary cells by macrophage migration inhibitory factor: A concept for potential antiretroviral compounds/vaccines

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Introduction | Cytokines play a critical role in the pathogenesis of HIV-1 infection. However, the involvement of macrophage migratory inhibitory factor (MIF) in HIV-1 infection has not been well documented. The objective was to investigate if MIF modulates HIV-1 replication in monocyte-derived macrophages (MDC) and phytohaemagglutinin-activated peripheral blood mononuclear cells (PBMC)

Methods | PBMC was obtained from 12 healthy donors by density gradient centrifugation and MDC by plastic adherence of PBMC. These cells were infected with HIV-1 and latter exposed to human MIF or anti-MIF antibodies. Flow cytometry was used to analyse cellular expression of CD4 and ELISA to measure levels of MIF and p24 Ag in cell culture supernatants

Results | HIV-1 infected PBMC induced a significant increase in MIF secretion in 8 (66.7%) of donors. MIF also increased viral replication in PBMC ($P=0.002$). In PBMC treated with anti-MIF antibodies, HIV-1 replication was inhibited by 64% ($P=0.0001$). MIF did not enhance cellular expression of CD4 cells suggesting that MIF-induced enhanced HIV-1 replication was not as a result of increased expression of HIV-1 receptors

Discussion | Thus, MIF enhances HIV-1 replication in peripheral human cells. There is need for further studies to unravel the mechanisms of MIF-enhanced HIV-1 replication and to develop an MIF-inhibitory concept that can result into potential vaccines and/or antiretroviral compounds.

HP 025

Evaluation of the QuantiFlexx TB ELISA in University College Hospital, Ibadan, Nigeria

Samuel A Fayemiwo • University of Ibadan, Nigeria

Introduction | Tuberculosis (TB) is the second most common infectious cause of death in adults worldwide after HIV/AIDS. In recent years, serum tests for the diagnosis of active TB have become available. This study was aimed at finding the information on the sensitivity and specificity of QuantiFlexx TB ELISA test in University College Hospital (UCH), Ibadan, Nigeria.

Methods | This was a prospective cross-sectional study involving one hundred and eighty-three subjects from UCH and Oyo state Chest Hospital, Jericho, Ibadan. Serum/plasma was collected from these subjects after informed consent. Sputum of each of these patients was tested for alcohol and acid-fast bacilli (Aafb). 183 sera/plasma from subjects who were high risk for tuberculosis and negative controls were referred for testing. The methods described in the insert of the manufacturer were carefully followed and results were interpreted.

Results | Overall, 60 subjects were positive each for Aafb and TB ELISA tests respectively using high standards. The sensitivity and specificity for the TB ELISA tests were found to be 73.2% and 78.2% respectively using high standards. However, with the low standards (specificity standard) the specificity was found to be 97.0%. No immediate problem was noticed with the kit interpretation except the high room temperature during the evaluation.

Discussion | QuantiFlexx TB ELISA test was found to be simple and highly specific for the detection of IgG in the sera/plasma of patients with susceptible TB when compared with acid-fast smears. It is more convenient as it only requires one patient visit and improved turnaround time.



HP 026

Using community participatory approach in BCC/IEC material development for TB control awareness

Abdullrahman Orosanya • Concern Conscience International, Nigeria

Introduction | Behavioural change communication (BCC) tools and information, education and communication (IEC) materials are vital in creating awareness about TB control services in rural communities and hard to reach areas.

Methods | We developed a BCC/IEC workshop to develop appropriate and user-friendly BCC tools and IEC materials suitable for different target groups and communities. Cultural sensitive BCC tools and IEC materials were developed for the programme. Outcome from high TB prevalence communities and the brainstorming sessions were used to develop the BCC tools and messages on the IEC materials. Four focus group discussions were conducted to pre-test the developed materials to ascertain their level of understanding of the messages in the IEC materials, while in-depth interviews were used for testing the BCC tools.

Results | The process enabled target specific programmes and materials to be developed to educate and sensitise the communities on TB infection, prevention and treatment.

Discussion | The use of community participatory learning assessment (CPLA) tool to identify and develop BCC and IEC messages would assist to enhance programmes acceptance and sustainability

HP 027

Adherence to ART in PLWHA at Yirgalem Hospital, South Ethiopia

Endrias Markos • Hawassa University, Awassa, Ethiopia

Introduction | Non-adherence to antiretroviral therapy (ART) is a major challenge to AIDS care, and the risks associated with it are extensive.

Methods | A comparative cross-sectional survey was carried out at Yirgalem Hospital between 10 July and 30 August 2006. The two-proportion formula for unmatched case control study with 1:3 ratio was used to calculate the sample size. Systematic sampling was used to recruit patients. Using a structured and pre-tested questionnaire, data on drug adherence were collected through interview and pill count. Non-adherent patients were compared with adherent patients and associations with key risk factors were determined.

Results | Two hundred and ninety-one AIDS patients were involved in the survey. Prevalence of adherence in the week before the interview was 74.2%. The main reasons of non-adherence cited by the patients were: being busy or simply forgetting (51%), change in daily routine (9.4%), and being away from home (8.3%). Non-adherence was commoner among patients reporting symptoms in the past four weeks (Adj. OR=6.41, 95%CI: 2.41 to 17.08), who lived more than 47 km away (Adj. OR= 2.48, 95%CI: 1.24 to 4.98), or who had dependents (Adj. OR=1.95, 95%CI: 1.06 to 3.57).

Discussion | Efforts must be made to make the service accessible by commencement of ART service in more health centres, to improve patients' awareness of ARV adverse effects, and to provide social support to all People Living with HIV, particularly those who have dependents.

HP 028

Challenges to recruitment/sampling in a fishing population

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Introduction | People engaged in fishing (fishermen/traders/processors) are often mobile, going to where fish/trade can be found. One of the objectives of the EDCTP-funded fishing community cohort study is to establish whether the fishing population is a suitable group for HIV prevention clinical trials. With high HIV prevalence (~30%) in these communities, establishing means to reach such individuals is essential.

Methods | The project is being conducted in six fishing villages in two lake shore districts in Uganda. Through community mapping and a demographic census the target is to recruit 1000 consenting/assenting HIV-negative volunteers (aged 13–49 years) for the main cohort study, and 250 HIV-positive volunteers for the virology sub-study. Socio-behavioural research, to build-up a greater understanding of these communities is being undertaken utilising mostly qualitative methods.

Results | While mapping the physical structures in the communities allowed residents to be censused, people who camp at the landing site, or regularly sleep in bars/lodges were left out. We allocated 'house numbers' to regular non-house dwelling places, thus including people in the census and cohort recruitment and follow-up. Availability during irregular hours and seasonality affect the ability of some cohort members to attend during regular working hours. Flexibility in work schedules, routine mobilisation and call-backs are feasible strategies to overcome the challenges.

Discussion | Establishing a cohort among a mobile population is a challenge, but research teams adapting working practices to the realities of participants' working lives is possible and enables recruitment of the target group.

HP 029

Preparation of a youths clinic at the Infectious Disease Centre (IDC), Dar es Salaam, Tanzania for the recruitment of youths in HIV prevention clinical trials

Guerino Chalamilla • Dar es Salaam City Council IDC Clinic, Tanzania

Introductions | HIV preferentially affects youths. Their participation in ethically sound and socially acceptable HIV preventive trials is important. IDC is a specialised sexual and reproductive health clinic in Dar es Salaam, Tanzania, that provides youth-friendly services.

Methods | A description of experiences from the past and ongoing studies as well as ongoing preparations aimed at preparing the site for youth's participation into HIV vaccine and possibly microbicide preventive trials.

Results | Previous studies showed that youths have high prevalence of sexually transmitted infections (STIs), including HIV, as a result of risky sexual behaviours and inter-generational sex. The study on feasibility and acceptability of female youths to microbicide and HIV vaccine trials in 2006 revealed a high level of acceptability (98.2%). In an effort to form a larger cohort, the site has so far registered 1,213 youths of whom 49.8% are females. Their mean age is 21 years. The established core group of 10 Peer-Educators promoting HIV prevention activity have been trained to serve as the primary recruiting ground. Since January 2009, 7 workshops and 3 sessions of larger groups have been conducted. Issues discussed included sexual reproductive health, contraceptives, HIV/AIDS, life skills and participation in preventive trials. Through funding from EDCTP and other partners, the clinic's capacity has been further improved through renovations, staff recruitment, laboratory strengthening, GCP & GCLP training of staff, and strengthening of data management. A link with the Maputo youth clinic has been established.

Discussions | The improved capacity at IDC clinic will enable the site to actively engage in HIV preventive trials.



HP 030

Alcohol and illicit drug use in a cohort of female sex workers in Kampala, Uganda

Judith Vandepitte • MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda

Introduction | The Good Health for Women Project (GHWP) in Kampala is recruiting a cohort of 1000 sex workers. A microbicide feasibility study is being conducted among the enrolled HIV-negative participants of this cohort with support from EDCTP. Other studies from sub-Saharan Africa have reported that high levels of alcohol abuse may be associated with risky sexual behaviour and HIV and other sexually transmitted infections (STIs). We report preliminary findings on alcohol and illicit drug use in our study population.

Methods | Baseline information on alcohol and illicit drug use was collected using structured questionnaires including CAGE indicators (Ever felt like Cutting down on drinking/ Ever felt Annoyed by being criticised about drinking/ Ever felt Guilty about drinking/ Ever needed a drink in the morning as an Eye-opener). A CAGE score of ≥ 2 (2 or more affirmative answers) has been reported as indicative of alcohol abuse.

Results | By 28 February 2009, 802 sex workers were enrolled in the cohort. The HIV-prevalence was 36.7%. Alcohol use was reported by 248 (84.3%) HIV-positive and 381 (75.0%) HIV-negative women ($P=0.02$). A CAGE score of ≥ 2 , indicating alcohol abuse, was found in 72.4% of the study population (72.6% among HIV-positives and 72.4% among HIV-negatives; $P=0.91$). Illicit drug use (marijuana, khat or cocaine) was less frequent (8.6%) and not significantly different in HIV-positive and HIV-negative women (respectively 7.9% and 9.0%, $P=0.58$).

Discussion | The use of alcohol in this vulnerable population group is high which may further endanger the women's health and may compromise adherence to HIV prevention and treatment interventions.

HP 031

Evaluation of survival and lessons from patients on highly active antiretroviral therapy

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Introduction | Highly active antiretroviral therapy has been shown to improve survival worldwide. Its goal in Nigeria is to improve quality of life and survival of patients living with HIV/AIDS. However, limited information is available on survival of patients in Nigeria. This study evaluates survival of patients on treatment.

Methods | A retrospective medical record review of 324 patients based in Lagos from January 2005–March 2008 was undertaken. Demographic variables, CD4 count, opportunistic infections, weight, clinical staging, and laboratory parameters were obtained. Cox proportional hazards regression models were used to evaluate survival.

Results | Mean age: 34.5 years; male 156 (48%); female 168 (52%); 1053 person-years of follow-up; median survival time was 29.5 months. 18% of the patients were co-infected with tuberculosis. The variables that were independently associated with mortality were age ≥ 40 (HR=1.3, 95%CI 1.2–1.5); CD4 <100 cells/mm³ (HR=2.4, 95%CI 1.7–3.1); weight <50 kg (HR=1.4, 95%CI 1.1–1.9) and tuberculosis (HR=4.2, 95%CI 3.3–6.7). Mortality was modified by gender with female more likely to die compared to male (HR=1.4, 95%CI 1.1–1.8). Efavirenz-containing regimen had better survival compared to nevirapine-containing regimen ($P<0.001$).

Discussion | Evaluation of patient survival in HIV treatment programmes is necessary for future scale-up of HIV treatment in our resource-limited settings. Patients on efavirenz-containing regimen did better than nevirapine-containing regimen. Likewise, there is a need to give prevention of tuberculosis priority in HIV treatment programmes as tuberculosis was significantly associated with mortality.



MP 017

Assessment of rational use of artemisinin-based combination therapies (ACT) in Kinshasa, Democratic Republic of Congo

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Introduction | The spread of resistance to common antimalarials in sub-Saharan Africa is a concern. Irrational use of these drugs enhances incorrect dosage, inappropriate treatment and drug interactions. More than 15 African countries including the Democratic Republic of Congo (DRC) have adopted artesunate plus amodiaquine as first-line treatment policy of uncomplicated malaria. Two years after the adoption of this combination in DRC, this study aims to assess the rational use of this combination in Kinshasa.

Methods | A transversal study has been conducted in 457 health centres and 524 pharmacies.

Results | 20.6% of Kinshasa's health workers claimed to give rationally the combination artesunate plus amodiaquine (that means in accordance to the directives of national programme of fighting against malaria (PNLP) in adults). 17.1% of drug sellers in pharmacies recommended a rational use of this combination to patients. 74% of Kinshasa's health workers that prescribed the combination artesunate plus amodiaquine in treatment of uncomplicated malaria claimed to use it for children under 6 months in contrast to the directives of national programme of fighting against malaria (PNLP).

Discussion | The use of artesunate plus amodiaquine in Kinshasa is largely irrational and may contribute to the spread of resistance to this combination.

MP 018

Mothers' use and perceptions of artemisinin-based combination therapy for treating malaria among under-five children in Ibarapa central local government area, Nigeria

King Odor • National Malaria Control Programme (NMCP), Federal Ministry of Health Abuja, Nigeria

Introduction | The adoption and promotion of artemisinin-based combination therapy (ACT) in Nigeria is influenced by the increasing prevalence of chloroquine resistant malaria. However, little is known about the adoption and perceptions of nursing mothers regarding ACT. The study therefore assessed the perceptions and pattern of use of ACT among mothers of under-five children in Ibarapa Central Local Government Area, Oyo State.

Methods | The study was a cross-sectional survey involving the use of a 5-stage random sampling technique to select 720 participants from households. A validated questionnaire with a 6-point knowledge scale was used for data collection. Descriptive and Chi-square statistics were used to analyse the data using Epidemiology Package Information software.

Results | The participants' mean age was 29 ± 5.3 years. Their levels of education were as follows: No formal education (26.0%), Primary (50.7%), Secondary (18.2%) and Higher Institution (4.9%). Thirty percent (30%) of participants had ever heard of ACT and their main sources of information include health facility (69.0%), physician (11.0%), nurses (11.0%) and pharmacy (4.0%). Participants' mean knowledge score relating to ACT related drugs was 1.2 ± 2.0 .

Discussion | Despite the positive attitude of the population that are aware of ACT and its effectiveness, the awareness and accessibility as well as its use for the management of malaria in under-five children are still low among nursing mothers. Advocacy, social marketing and subsidisation of ACT drugs especially in the private sector are needed to address the problem.

MP 019

The effect of training on use of ITN and integrated community network system for control of malaria in vulnerable groups: A randomised cluster trial

Amare Deribew Taddege • Jimma University, Ethiopia

Introduction | There is paucity of researches on human behaviour regarding the proper use of insecticide-treated mosquito nets (ITNs) to prevent malaria in vulnerable groups (children <5 and pregnant mothers). This study assesses the effect of training heads of the households and subsequent follow-up for use of ITN and integrated community network system on the burden of malaria.

Methods | The study employed a randomised community trial in Gilgel Gibe Field Research Center, Southwest Ethiopia. 22 villages (11 intervention, 11 control) are included. The intervention consists of training the heads of the households about the proper use of ITNs and establishing a community network system that makes the training sustainable. Community leaders will give tailored training and demonstration about the use of ITNs to the heads of the households using local language. After this, ITN use and occurrence of malaria will be monitored in each household in the intervention village.

Results | 3750 households were included in the baseline survey. Only 10% of the households had functional ITNs. A total of 2924 children <5 and 254 pregnant women were included in the study. About 16% of children <5 were positive for malaria by microscopic examination. 55% and 43% of cases were *Plasmodium vivax* and *P. falciparum* respectively. 14% of pregnant women were positive for malaria. Malaria and fever were more common in the intervention villages than in control villages ($P < 0.05$). Anaemia was observed in 18% of pregnant women and 15% of children.

Discussion | The prevalence of malaria in the dry season in Gilgel Gibe is very high compared to other literatures. This unusual high burden of malaria might be due to the effect of the Gilgel Gibe hydroelectric dam.

MP 020

Implementation of the national treatment guideline in the management of children with severe and uncomplicated malaria in Douala, Cameroon

Joel Bertrand Pankoui Mfonkeu • University of Douala, Cameroon

Introduction | The public health burden of malaria in Cameroon is worsened by the spread of resistance. Several lines of treatment recommended throughout the years by the ministry of public health revealed some failures.

Methods | In order to test the efficiency of the latest treatment guideline, we implemented it during an enrolment of 225 children in 4 hospital centres in Douala. They were classified as uncomplicated malaria, severe malaria anaemia, and cerebral malaria patients according to the WHO 2000 criteria. The uncomplicated and severe malaria anaemia groups received quinine, while the cerebral malaria groups received the combination of quinine and an artemisinin therapy. Their clinical data and outcome was recorded. Some pathophysiological parameters were also investigated.

Results | Means fever resolution and prostration resolution times were the longest in the cerebral malaria group (66 ± 37.44 hours and 56.25 ± 26.55 hours, respectively). Their hospital stay was also longer. It is the only group in which fatalities were recorded (6 cases), however, no neurological sequelae were noticed at discharge. Furthermore, at discharge, an improvement was noticed in their mean level of some pathophysiological parameters of interest like creatinin, urea, bilirubin, lactic acid and nitric oxide as in the severe malaria anaemia group.

Discussion | Overall, the national treatment policy for malaria was effective in our cohort, and the poor prognosis associated with cerebral malaria was just the reflection of the severity of this form of the disease rather than a failure in the treatment.



MP 021

The role of immunoglobulin E antibodies in protection against *Plasmodium falciparum*

Reem Bairam • University of Khartoum, Sudan

Introduction | In endemic malaria areas, there is an increase of serum levels of IgE during *Plasmodium falciparum* infections. It is well known that IgE mediates activation of various effectors cells such as monocytes/macrophages), this may suggest that IgE may also play a role in protection against malaria. The main objective of my research is to determine the role of IgE in protection against acute *P. falciparum* malaria in an area characterised by highly seasonal but stable malaria transmission in Sudan.

Methods | Blood sample were collected from malaria patients with different clinical presentations, severe cases, asymptomatic, mild and controls. Total and specific IgE levels were determined by ELISA. IL10, IL4 and TNF expressions were determined with Real Time PCR.

Results | There was a significant increase in both total and specific IgE in mild and asymptomatic infectious compared to other groups severe and control. This may suggests that IgE antibodies contribute to protection against severe malaria. No association between TNF and IgE levels were found. However, a significant positive correlation was found between the total IgE and IL-10 in the mild group and a significant negative correlation with the asymptomatic group. IL10, TNF α and IL4 were confirmed to increase upon infection.

Discussion | Infection with malaria leads to a significant elevation of both total and malaria specific malaria IgE antibodies. Furthermore this study suggested that IgE may contribute to protection against severe malaria in area characterised by meso-endemic malaria transmission.

MP 022

Detection of malaria parasites by nested PCR in an area of seasonal malaria transmission in Eastern Sudan

Limya Elyamani • Institute of Endemic Diseases, Khartoum, Sudan

Introduction | Malaria in Sudan is considered to be the major health problem in the country, yet our knowledge of the epidemiology of malaria in term of morbidity and mortality in most part of the country is still unclear.

Methods | In the course of epidemiological and immunological baseline studies, a parasitological cross sectional survey was after the transmission season, in two villages (Koka and Umsalal) situated on the bank of the Rahad river, eastern Sudan. The area is characterised by seasonal but stable malaria transmission, using both blood stained Giemsa slide and PCR techniques, parasitological were used to determine the prevalence of malaria parasites in the area.

Results | Blood film parasite point prevalence of the two surveys were (26%), and (10%), after the rainy season and (1.2% and 1.1%) before the rainy season, in Koka and Umsalal villages respectively. Eight percent of the reported malaria cases during these surveys were due to *Plasmodium falciparum*, the rest were due to *Plasmodium malariae*. No other malaria species were detected during the survey. The prevalence of both *P. falciparum* and *P. malariae* is markedly increased when nested PCR method where employed for detection of DNA of malaria parasites in samples collected from the study subjects. The results showed that the PCR point prevalence were 43% and 13% of *P. falciparum* and *P. malariae* respectively in Koka village, and PCR point prevalence of 10% and 4.4% for *P. falciparum* and *P. malariae* in Umsalal village respectively.

Discussion | This data indicated the sensitivity of nested PCR for detection of other *Plasmodium* species which are characterised by low asymptomatic infection.



MP 023

Changes in antioxidant status in malaria patients treated with artemisinin combination therapy

George Ademowo • University of Ibadan, Nigeria

Introduction | Reactive oxygen species (ROS) are mediators of tissue injury and are believed to be involved in pathophysiology of malaria. We studied the effect of malaria on the antioxidant defence system in patients treated with artemisinin combination therapy.

Method | Twenty-seven patients with *falciparum* malaria were administered standard doses of dihydroartemisinin-sulphadoxine/pyrimethamine (DHA-SP) or artesunate-amodiaquine-chlorpheniramine (AAQC) combinations and monitored for clinical and parasitological responses up to day 28. Thick and thin blood films were made for malaria parasite screening. Two millilitres of blood was withdrawn from each patient at days 0, 7 and 28 for the determination of PCV and levels of malondialdehyde MDA (an indicator of lipid peroxidation) and glutathione (GSH). Activities of glutathione-S-transferase (GST), superoxide dismutase (SOD) and catalase (CAT) were also measured.

Results | Parasitaemia cleared in all patients by day 7 except in two patients on DHA-SP group in whom parasite reappeared by day 28. As parasitaemia decreased, MDA and SOD also decreased progressively while GSH, GST and CAT increased above baseline by day 28. Changes in MDA, GSH, GST, SOD and CAT between baseline and day 28 in the DHA-SP group were not significant. However, in the AAQC group, the increase in PCV, GSH, GST and CAT and reduction in MDA level and SOD activity by day 28 were significant.

Discussion | Malaria infection induced oxidative stress in the host. Treatment with DHA-SP and AAQC cleared parasitaemia, alleviated the oxidative stress and caused considerable alteration in the antioxidant defence system in the host.

MP 024

Linking social science and clinical research networks in the development of new clinical tools against malaria in sub-Saharan Africa

Alexander Nartey • Partnership for Social Sciences in Malaria Control, Ghana

Introduction | Effective new clinical tools against malaria must be tools that can be effectively applied in malaria control in the sub-Saharan African context. Effective new clinical tools against this disease therefore require not only clinical research but also social science research to provide understanding the complex interplay of factors (socio-cultural, economic, political and environmental) that influence the behaviours of both those who suffer from them as well as those who provide health care for the disease and therefore the design and application of new clinical interventions. The contributions that social science and social scientist can make to EDCTP programmes are critical.

Methods | A visible network would be created to link social scientist and clinicians. A capacity training course to improve the knowledge about malaria among social scientists and clinicians will offer experience in applying social science methods and knowledge to malaria control situations, strengthening their capacity to contribute effectively to malaria control and research.

Results | The network will contribute towards a reduction in malaria-related morbidity and mortality in sub-Saharan Africa by enhancing the socially appropriate and effective design as well as effective translation from research into practical clinical and public health application of new clinical interventions against malaria.

Discussion | A visible network would help link social science to clinical research in the development of new clinical tools against malaria.



MP 025

An assessment of the dusting effect of the biological larvicide Bti on the occurrence of malarial sickness in a district of Cotonou



Dorothee Kindé-Gazard • University of Abomey-Calavi-Bénin, Cotonou, Benin

Introduction | The present study seeks to assess the effectiveness of the biological larvicide Bti in reducing morbidity linked to malaria.

Method | An experimental study carried out in six districts involved spraying Bti over a period of one year followed by a clinical and biological evaluation conducted in households and at health centres. Three of the districts, the control districts, were not sprayed. 401 children in the control zone and 401 children in the sprayed zone, all aged under 5. Blood samples were taken from all children and blood smears done for malaria microscopy. Their mothers as well as 128 pregnant women in the two district groups were interviewed.

Results | The presence of clinical malaria was found to be 17% in the sprayed zone and 28% in the non-sprayed zone and that of malarial infestation 13.8% against 31.4% respectively. The biological findings were 1.2% against 1.5%. The rate of uncomplicated malaria infection dropped from 35% in 2006 to 31% in 2008 in the sprayed zone. In the pregnant subjects, the occurrence rate of malaria was 23.4% in the sprayed zone against 51.4% in the control zone. The larval density in households was reduced by 99% and the aggressiveness of adult mosquitoes was reduced by 62%. The Bti remained effective for 9 days.

Discussion | An anti-vectorial strategy involving the use of a biological larvicide such as Bti can result in a significant reduction in the occurrence of malarial morbidity.



TP 06

Landscaping the bridge between the bench and the bush*Shreemanta K Parida • Max Planck Institute for Infection Biology, Berlin, Germany*

This is a thought-provoking presentation to raise awareness among a young enthusiastic budding scientific community in the resource-constrained settings in Africa. The presentation will cite issues faced in the real world mirroring the progress in the laboratories and the gaps between the two polarised worlds of basic science and clinical medicine. Using the examples of progress made in the Grand Challenge in Global Health Consortium on Biomarkers of Protective Immunity against Tuberculosis in the context of HIV/AIDS in Africa in an early attempt to connect these two worlds, the landscape of the wishful effective bridge of translational research will be addressed.

Increasing efforts in educating youngsters in resource-poor settings to build capacity in the regions should be a major global agenda. By helping those to acquire competence and developing credible infrastructures (centres of excellence) in the high prevalent settings would make them self-sustainable to take charge of their problems as well as to contribute to the global health research and development efforts as equal partners.

TP 07

Participant cohort retention in a rural setting - experiences and lessons learnt*Daniel Mwanja Mumphe • Makerere University Iganga Mayuge Demographic Surveillance Site, Uganda*

Introduction | The Uganda TB infant cohort study to prepare for a vaccine trial is based in a rural demographic surveillance site. Demonstrating the ability to retain a participant cohort is one of the requirements to qualify for a vaccine trial. This presentation shares early experiences and lessons learnt in this setting with respect to follow-up of participants.

Methods | All BCG-vaccinated infants under the age of 2 months are eligible to participate. They are followed up regularly either at designated centres or at home. Strategies used to enhance follow-up include reminders, use of village scouts and incentives.

Results | Between November 2008 and April 2009, 905 participants were enrolled. 1306 follow-up visits were scheduled, of which 1248 (95.6%) were attended. About 90% were done timely while 5.2% were done late. Reasons for non-attendance included emigration (12), travel out of study area (26), failure to trace home (24), scheduling errors (5) and death (10). Occasionally, attendance at follow-up centres was low due to failure of village scouts or staff to send reminders to participants with no phones. Some village scouts were reluctant to help locate the participants to do home based follow-ups due to lack of motivation resulting from delays in paying their incentives. These led to both non-attendance and late attendance of the follow-up visits.

Discussion | In rural-based research, taking advantage of opportunities in the community structures is important to enhance contact with participants. Careful planning, execution and continued assessments of implementation strategies are crucial. Incentive commitments to a community should be honoured timely.



CP 08

The challenges in enrolment and retention of African women in clinical trials: A pilot study in Nigeria

Felix N Chukwuneke • University of Nigeria
Teaching Hospital, Enugu, Nigeria

Introduction | The difficulties of recruiting and retaining African women in biomedical research cannot be underestimated. Despite the epidemiologic realities of the trends and burden of diseases in Africa, women have had minimal participation in biomedical research, especially in clinical trials. The purpose of this paper is to critically examine and identify the challenges involved in recruiting and retaining African women in clinical trials using a pilot study in Nigeria.

Methods | A semi-structured questionnaire on knowledge, constraints and willingness to participate in clinical trials were randomly distributed among females attending outpatient obstetrics and gynaecology clinics in Nigeria. The data collected were converted to numerical values for generation of statistic analysis.

Results | Out of the 200 questionnaires distributed, 172 were returned unanimously representing a 86% response rate, which were used in the data analysis. Eighty-two (47.7%) were willing to participate depending on the type of trials while 60 (35%) were concerned about monetary compensation. Most of the respondents ($P < 0.05$) are of the opinion that their husbands and families must be in support before they could participate.

Discussion | This study shows that knowledge and education play an important role in motivating women to participate in clinical trials in Africa while family attachments and cultural barriers are an impediment to their participation. This calls for an awareness campaign to emphasise not only the necessity for women participating in clinical trials, but also the establishment of adequate protective measures for those willing to participate in a male-dominated society like ours.

CP 09

Effect of maternal socio-economic status on neonatal mortality in rural Tanzania

Justice Ajaari • Kintampo Health Research Centre,
Kintampo, Ghana

Introduction | Poverty is considered to be an underlying cause of many neonatal deaths, either through increasing the prevalence of maternal risk factors or through reducing access to effective care. It is therefore of importance to make available the epidemiological information on the effect of maternal socio-economic status on neonatal deaths. This will help to quantify the toll of low socio-economic status in neonatal deaths.

Methods | Data from the Rufiji Health and Demographic Surveillance System (RHDSS), Tanzania, was used for the analysis. A total of 5124 live births and 166 neonatal deaths were recorded from 1.1.2005–31.12.2006. The household characteristics and assets ownership of the mothers of the neonates were used for a principal component analysis (PCA) with Stata v.10 software. The PCA was used to construct a Wealth Index which was used to determine maternal socio-economic status. Univariate and Multivariate Logistic Regression models were used to assess the association between neonatal mortality and maternal socioeconomic status while adjusting for potential confounders.

Results | In the univariate analysis, maternal socio-economic status was significantly associated with neonatal mortality. The least poor mothers were 95% less likely to have experienced neonatal mortality (unadjusted $OR = 0.5$, $P = 0.003$; 95%CI (0.3–0.8)) compared to the poorest mothers and this was statistically significant. However, after adjusting for other maternal risk factors such as age, parity, education occupation and marital status, the association was found to be borderline statistically significant (adjusted $OR = 0.6$, $P = 0.046$, 95%CI (0.4–1.1)).

Discussion | Maternal socio-economic status appears to have an impact on neonatal survival. Interventions aimed at reducing neonatal mortality must incorporate micro-financing, programmes to improve the socio-economic status of pregnant women



14:00–14:05
Brief introduction
from the Chairs

14:05–14:15
The AAVP and UVRI model: Building research capacity
through partnerships in synergy with EDCTP

*Dr Pontiano Kaleebu • MRC-UVRI Uganda Research Unit on
AIDS and UVRI-IAVI HIV Vaccine Program, Entebbe, Uganda*

In the past few years there has been an emphasis for collaborations and networking in order to maximise resources and strengths but also to avoid duplication. In addition, this allows sustaining support for the core capacity required for research and future clinical trials. Two organisations, MRC-UK and IAVI, have built clinical trial and basic research capacity in Uganda through their collaborations with the Uganda Virus Research Institute (UVRI). Due to this backbone, two other organisations namely the African AIDS Vaccine Programme (AAVP) and EDCTP have provided additional resources enabling the creation of a Centre of Excellence in HIV prevention research.

Through these synergies, activities such as the establishment of high-risk cohorts in the fishing communities and among sex workers have been initiated for future intervention trials. Additional assays to measure immune responses have been introduced such as multi-colour flow cytometry, neutralisation assays and microarray assays. Training in GCP and GCLP for clinical and laboratory personnel has been conducted, as well as establishment of GCLP accredited laboratories. The infrastructure at UVRI has been expanded and the administrative and financial management capacity improved. Important data produced so far include the prevalence of HIV infection and the distribution of HIV-1 subtypes in the above high-risk groups, sexual networks and other preparatory studies for future vaccine and microbicide trials.

The UVRI model is a clear example of how different networks can complement one another to build capacity and generate useful information required for future interventions studies.



14:15–14:25

Developing HIV prevention options for women worldwide

Dr Zeda F. Rosenberg • International Partnership for Microbicides, USA

Prevention is an important part of the global strategy to combat HIV and AIDS, but existing HIV prevention strategies are not enough. We urgently need new prevention options, especially those that enable women – who are at the epicenter of the epidemic – to protect their own health and well-being. That's where microbicides can play a vital role. Vaginal microbicides are products being developed to prevent HIV transmission during sex. Because they are initiated by women, microbicides would offer a powerful new method to prevent infection.

The International Partnership for Microbicides (IPM) is a non-profit organisation that is committed to developing safe and effective microbicides, specifically for use in developing countries where women are at greatest risk for infection. Microbicide development is a complex process that requires collaboration with scientists, policymakers and advocates across the globe, and participation by thousands of clinical trial volunteers in communities where HIV/AIDS is most prevalent. As a product development partnership, IPM brings together private sector technologies and public sector resources to fulfil its mission.

Using a 'best practices' approach, IPM evaluates promising compounds, designs optimal formulations, conducts clinical trials, identifies regulatory pathways for microbicide products, and is establishing manufacturing and distribution capacity to ensure ready access to microbicides when one becomes available. IPM has also engaged major pharmaceutical companies in the global microbicide effort. Through royalty-free licensing agreements with pharmaceutical partners, IPM is working to develop a variety of compounds as microbicides, with full rights to distribute its products at low cost in resource-limited settings.

14:25–14:35

Research capacity strengthening: The Wellcome Trust perspective

Dr Val Snewin • Wellcome Trust, London, United Kingdom

The Wellcome Trust, founded in 1936, is the largest charity in the UK. Its mission is to foster and promote research with the aim of improving human and animal health. A significant and growing proportion of grant funding supports global health research outside the UK, in countries with developing economies where our aim is to broaden the base for scientific endeavour by investing in excellent scientists who have the greatest potential to advance knowledge. Furthermore we aim to ensure that these scientists have the resources and institutional infrastructure they need to carry out their work.

Our funding portfolio ranges from individual fellowships to our major overseas programmes, and from institutional strengthening (eg. the African Institutions Initiative) to country-level research system strengthening (eg. the Health Research Capacity Strengthening Initiative in Kenya and Malawi). Within our current portfolio we fund several clinical trials in developing countries either through our Science Funding Stream or Technology Transfer Division.

Here we will present an overview of our international activities and describe the ways in which these complement the aspirations of the EDCTP programme in sub-Saharan Africa. We will further discuss the need for multi-level initiatives in order to successfully improve research capability in developing countries.



14:35–14:45

The Bill & Melinda Gates Foundation's partnerships with EDCTP

Siobhan Malone • Bill & Melinda Gates Foundation

The Bill & Melinda Gates Foundation and EDCTP share a common interest in ensuring the development and delivery of new and affordable prophylactics and therapeutics for HIV, TB, and Malaria for those most affected in developing countries.

The Gates Foundation and EDCTP first partnered in October 2006 with a joint call to provide research consortia with an opportunity to apply for necessary funding to build capacity in preparation for the conduct of preventive HIV vaccine trials. A call for proposals was made in December 2006 and 6 applicants were funded.

More recently, in October 2008, the Gates Foundation again partnered with EDCTP to fund a consortium to conduct clinical trials on new drugs to shorten and simplify the treatment of TB. The consortium formed around this programme, PanACEA, creates a series of interdependent clinical studies with decision criteria after each study, rather than a single study.

Finally the Gates Foundation and EDCTP are both members of the Malaria Vaccine Initiative's funders group. These are concrete examples of important ways that funders with common strategies and goals can work together to ensure that funding gaps and priorities are addressed in collaboration.

14:45–14:55

ESSENCE on health research

*Prof. Hannah Akuffo • Swedish International Development
Cooperation Agency (Sida), Stockholm, Sweden*

The Enhancing Support for Strengthening the Effectiveness of National Capacity Efforts (ESSENCE) initiative seeks to create efficient mechanisms used by funding agencies for implementing the Paris Declaration principles of coordination and alignment for sustained systems for research for health in Africa.

The overall goal of ESSENCE is to increase and improve the impact of investments into structures and institutions in low-income African countries to ensure that conditions for research and utilisation of knowledge are built on a sustained basis. The initiative will foster analytical capacity and scientific knowledge in low-income African countries through sustainable national research systems in the pursuit of national development.

The strategic objective of ESSENCE is increased coordination, harmonisation and aligned funding with African countries' agendas for developing human, institutional, environmental resources and conditions for advancing scientific activities to find and apply solutions to public health problems.

Expected outcomes of ESSENCE are: (1) Mechanisms for collaboration between funders themselves as well as between funders and recipient countries for: learning from each other, sharing strategies and methodologies for research, and collaborating on research needs associated with health with the aim of coordinating, harmonising and aligning funding and activities with the countries' agendas; (2) Procedures for harmonisation and optimisation of resources, taking into account earlier successes and failures, to promote the development and implementation of national strategies for research and related country-based pilot models of collaboration between programmes; (3) Methodologies including monitoring and evaluation indicators to track the input, process, outcome and impact of investment in capacity development at individual/ institution/ health systems level, and in research environment and political instruments.



14:55–15:05

AMANET: Africa takes up stewardship of appropriate malaria interventional trials

*Prof. Wen Kilama • African Malaria Network Trust,
Dar es Salaam, Tanzania*

The African Malaria Network Trust (AMANET) promotes strong African leadership and stewardship to search for solutions to the malaria problem in sub-Saharan Africa (SSA). The search for effective and affordable interventions for SSA depends on available capacities and active participation of African malaria research institutions. The reality of malaria is intimately appreciated by African health researchers and scientists, and this special intimacy and experience is necessary in developing effective tools against malaria.

AMANET engages a holistic approach in capacity strengthening for malaria R&D. Efforts required to upgrade infrastructure and facilities for critical research, for long-term investments to develop African capacity through short- and long-term training of personnel, and strengthening institutional review boards (IRBs) for sound ethics as integral part of clinical trials.

AMANET provides support to CNRFP (Burkina Faso, NIMR, Tanga Tanzania, TDRC, Ndola Zambia and Makerere University Uganda) for all-round capacity strengthening. AMANET became the first and only African organisation to sponsor malaria vaccine trials. To date, six Phase Ib trials have been successfully sponsored. In 2008 AMANET launched a Phase IIb trial of MSP3-LSP at MRTC Bamako Mali, drawing closer to real pivotal studies. Twenty institutional Ethics Committees are being strengthened, as are 8 in the Afro-immuno-assay network.

Effective networking is essential creating infrastructure and shared competencies for complex interventional trials in SSA. Holistic approaches are a most appropriate option for effective capacity strengthening efforts

15:05–15:15

European Malaria Vaccine Initiative (EMVI): Portfolio and perspectives for the future

Dr Egeruan Babatunde Imoukhuede • European Malaria Vaccine Initiative (EMVI)

Over the past ten years, EMVI has continually strived to maintain its main goal of accelerating the development of candidate malaria vaccines by facilitating the translational gap between promising experimental malaria vaccines and subsequent clinical trials in Europe and in Africa.

To date, EMVI has funded approximately ten vaccine formulations (antigen-adjuvant combination) by developing GMP materials and sponsoring subsequent human clinical trials. In recent years EMVI's role has expanded into harmonisation of activities relevant to malaria vaccine development as well as making contributions to global coordination efforts in the field of malaria vaccine research and development (R&D).

In the next five years, EMVI will be coordinating the European Network of Vaccine Research and Development, a European Commission-supported action implementing a vaccine development infrastructure for Europe. EMVI is currently participating in two EDCTP-funded multinational consortia, which aim to conduct multi-centre clinical trials by integrating project management, capacity building and networking.

Looking into the immediate future, EMVI is in the process of transforming into an EEIG, thereby expanding its current scope of operations. By stimulating collaboration, cooperation, networking and joint integrated activities across various fields of research and diseases, and by facilitating the federation of research infrastructures, EMVI is acting today as a catalyst for tomorrow's vaccines.



15:25–15:35
Discussion

15:15–15:25

MMV: Partnering to develop the next generation of medicines to combat malaria

Stephan Duparc • Medicines for Malaria Venture, Geneva, Switzerland

Over the last few years we have seen a major change in the development of new fixed-dose artemisinin combination therapies (ACTs). After the decision by the WHO to ban artemisinin monotherapy, the challenge has been to produce affordable new combination therapies.

Medicines for Malaria Venture (MMV) has pioneered three new ACTs:

- Coartem-D (artemether-lumefantrine), with Novartis, which was approved at the end of 2008 by the stringent authority Swissmedic, and by WHO prequalification
- Eurartesim (DHA-piperaquine), with Sigma-Tau, which was submitted to the EMEA in July 2009
- Pyramax (pyronaridine-artesunate), with Shin Poong, which will be submitted in 2010.

In addition, Drugs for Neglected Disease Initiative (DNDi) and Sanofi-Aventis achieved WHO prequalification with Coarsucam (artesunate-amodiaquine) in 2008, and have launched artesunate-mefloquine with Farmanguinhos in Brazil.

We will briefly discuss the advantages and challenges of each medicine. For the future, MMV and its partners have a pipeline of over 50 projects in development. The major medium-term issues are the emergence of artemisinin resistance – in the Thai-Cambodia border regions. We are profiling the next generation of synthetic peroxides both *in vitro*, and eventually in patients with a view to identifying suitable next generation medicines. Our hope here is to simplify the ACT regimens eventually to a single dose. In addition, with our partners we are pioneering the next generation of therapies for the eradication agenda including transmission blocking medicines, and medicines targeting the hypnozoite of *P. vivax* – the cause of relapsing malaria.

CLOSING SESSION

EDCTP Future Perspectives

16:00–17:30
Victoria Hall

CHAIRS

Prof. David Ofori-Adjei
Dr Christian Burri

16:00–16:45

One World, One Partnership: Forum recommendations and EDCTP future direction

Dr Sodiomon Sirima, Prof. Charles Mgone • EDCTP

16:45–17:00

Award giving ceremony for outstanding African scientists

17:00–17:30

Future of EDCTP: EC perspective and concluding remarks

*Dr Ruxandra Draghia-Akli • EC Director for Health and
Research*



Notes

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