

## **AIDS International Training Program**

Dr. Moses Kamywa, the Master of Ceremonies welcomed Ms. Jayne Byakika Tusiime the Chairperson of Uganda Society for Health Scientists. In her opening remarks, she welcomed all participants present and she thanked them for honouring USHS' invitation to the Research Meeting. This meeting is sponsored by the AIDS International Training Program and membership is open to whoever is interested in health research even those with a non science background can join the society. She hoped that the deliberations would make a positive contribution to the fight against this scourge through sharing of information. She then invited the guest of honor, Prof. John Ssebuwufu to address members.

Prof John Ssebuwufu in his official remarks said, “ It is a pleasure for me to be here. When the society was starting I was approached by a group of scientists who asked me to be patron to the society. They told me there was a gap in the area of research that needed to be addressed. I therefore accepted to be patron to the society. It is a pleasure to be here. I am sorry that I have not attended all the meetings because of my busy schedule but I hope to have more time for the society when I retire.

It is a pleasure to see the people at the forefront of the fight against a very important problem. At one time people all over the world thought Uganda was the epicenter of HIV/AIDS, little did they know that this was not only confined to Uganda but was spread to many parts of the world. I thank the people at the forefront of the fight. We hope that a cure or vaccine for this disease will be found one day. It is through your, work, health scientists that the prevalence of the disease has come down. Also through your work we have learnt that some people live with HIV infected partners but do not get the disease. As I speak I think we have done well so far so congratulations ladies and gentlemen for that achievement. The war is not yet over but a few battles have been won. You have done a great piece of work to attract funding from international sources.

The health scientists have done a tremendous piece of work and should be able to share the experiences learned. Nevirapine, which is doing wonderful work, is an effort of people in Uganda; Prof Miiri and others, so I want to thank you all.

I want to thank the founders of the Academic Alliance who worked very hard and attracted Pfizer that has given us a state of the art facility at the IDI. This was the first time Makerere University had a turnkey project. Thank you very much colleagues of Academic Alliance for facilitating that kind of facility to be here.

There is hope, it is not an easy battle but like all previous battles for example small pox and TB, human kind has a way particularly through advances in medical sciences to overcome these battles. I must also thank our president who has worked hard to ensure that everybody knows about the disease.

Every problem has a silver lining and one of the things that has come out of this AIDS problem is the collaboration between medical scientists and the non medical people particularly social sciences or behavioral sciences. That kind of interdisciplinary and multidisciplinary approach to problem solving is good.

Uganda Society for Health Scientists, I wish you to continue because the functions of a learned society is to bring people together to share information in research and other areas. I wish to thank the Society chairperson Madam Byakika for the calls you keep giving me. As long as I am available I will be with you. Thank you very much and with those remarks I want to declare this meeting open.

## **Presentations at the Research Meeting - Day One**

*Session I      Chairperson   Prof. Florence Mirembe*

### **1. MU- Case Western Reserve University Collaboration By Prof. Harriet Mayanja Kizza**

This collaboration was started about 15 years ago and is based in Upper Mulago at the TB unit above ward 5 and 6. It was started in collaboration with Case Western Reserve Unit in Cleveland Ohio and the purpose was to do research in areas of TB, HIV and STDs both in adults and children. Later on HIV vaccines were included.

The emphasis was to establish long term collaboration, build infrastructure, technology transfer, and training and conduct relevant research.

The research was integrated research between various disciplines as outline below;

- Preventive research studies and treatment studies - prevention of TB in HIV.
- Intervention studies; drugs to intervene in the TB and HIV interaction and the prednisolone study.
- Ongoing studies include; the Punctuated Antiretroviral therapy study to try to ameliorate the effect of TB on HIV and HIV on TB.
- Short studies looking at shortening TB treatment from 6 months to 4 months among people with non-cavitary TB disease.
- Other studies; Immunotherapy study of Mvac vaccine as an adjuvant to anti TB drugs especially with drug resistance TB and studies to look at the role of new drugs like the quinolones in TB treatment especially with TB drug resistance.
- Epidemiological studies: Kawempe community study looking at the transmission of TB in the community and household and protective immunity in early TB. This will give new insight in looking at new strategies of getting surrogate markers for TB vaccines. New techniques to diagnose TB.

Prof. Mayanja encouraged young researchers to present at both local and international meetings and called upon two young researchers from the collaboration to give a detailed description of one of their research projects.

#### **a) Tuberculosis Treatment shortening Study (TX) by Dr Barret Sewali**

Comparing the efficacy of 4 months to 6 months of anti TB treatment.

Study question: Can TB treatment in HIV negative patients with minimal disease (non-cavitary) be efficaciously shortened to 2ERHZ/2RH?

The study design used is 2 study arms.

Inclusion Criteria

- HIV Negative adults with PTB
- Newly diagnosed culture +ve PTB (Smear+ve/-ve)
- Drug susceptible MTB to ERHZ.
- CXR: minimal disease. Cavities none or up to < 1cm in diameter.

### Primary Endpoints

- Relapse: Bacteriologic or clinical relapse at 30 months after the onset of initial anti-TB treatment.
- Cure: Patient does not relapse before the end of the follow-up phase (30 months).

### Study Ongoing - analysis of screened patients

- Screened 699 suspected PTB adults to date.
- Presented by CXR non cavitory PTB.
- Did HIV test, LFTs, FBC, CXR Review, and Pregnancy Test.
- Pre-enrolled 164 patients- who met the eligibility criteria of HIV –ve, non cavitory PTBHIV –ve, non cavitory PTB
- Enrolled 82 patients.
- Who have completed 4months Rx.
  1. Culture +ve at baseline.
  2. Culture –ve at 2months.
- Randomized to 4 or 6months arm.
- 41 in the 4 month arm
- 41 in the 6 month arm

### **b) Integration of TB and HIV – experience of Mulago TB clinic by *Dr Henry Luzze***

HIV epidemic contribute substantially to the increased numbers of TB cases. Overlap between the AIDS and TB epidemics continues to result in increases in TB morbidity. 4000 patients are treated yearly in the TB clinic of Mulago hospital.

- 50% of are co-infected with HIV
- 50% of TB/HIV infected persons have CD4 cells <200 cell/ml and need ART

### Patients eligible for ARVs.

- Patient on anti-TB treatment who are:
- Positive HIV test
- WHO Clinical Stage III or IV
- CD4 counts < 200/mm<sup>3</sup> available

Challenge: 50% of TB patients are co-infected with HIV thus the need to treat TB and HIV concurrently.

### **2. HIV/AIDS Prevention in the Era of increased treatment Access: A Case Study of the Prevention Program of Gates Grant by *Dr. Stella Neema PHD PI Behavioral Surveillance.***

#### Prevention Grant Summary

- Title: HIV Prevention Interventions in the Context of Antiretroviral Therapy.
- Implementing Institution: Academic Alliance for AIDS Care and Prevention in Africa (AAAC&P) in collaboration with MU IPH.
- Funding Agency: Bill and Melinda Gates Foundation.
- Nature of Grant: Pilot.

- Duration of Grant: from July 1, 2003 to June 30, 2005.

#### Focus of the Gates Grant

- HIV Prevention Messages and Information
  - HIV/AIDS information and education campaign.
  - AIDS treatment information centre for physicians and other health care providers.
- Interventions in the Clinical Setting
  - VCT for medical in-patients.
  - ARV adherence in maternal-to-child transmission.
  - ARV related laboratory monitoring.
  - Consistent therapies for opportunistic infection and ARV delivery through care algorithms.
- Evaluative Measures
  - Behavioural surveillance in the context of ARV delivery.
  - Serial cross sectional knowledge, attitude and behaviour surveys.
  - Rationale for Integrating Prevention into the Care and Treatment.
- High quality HIV/AIDS care may lead to:
  - Complacency and dis-inhibition.
  - Return of physical strength and sexual prowess.
- With increasing access to ARVs new prevention initiatives are essential.
- New initiatives based on premise that care and treatment are integral parts of HIV prevention.
- ARVs can reduce infectivity and thus, contribute to HIV prevention.

#### Prevention Agenda

- To enhance training in HIV prevention through workshops, the CDC/IPH HIV Fellowship Program, student internships and the one month comprehensive HIV/AIDS care and prevention course.
- To conduct repeated HIV/AIDS knowledge, attitude, beliefs and practices cross-sectional surveys.
- To develop HIV/AIDS messages and information campaigns in relation to increasing access of ARVs.
- To establish and implement a behavioral surveillance system.
- To monitor and evaluate HIV/AIDS prevention initiatives

#### Rationale for the Prevention Grant

Improved access to ARVs and HIV/AIDS related treatments will lead to:

- Increases in health care seeking behaviours;
- Increased demand for HIV testing and appropriate counselling;
- Increased demand for information on ARVs and other treatments by the general public;
- Increased demand for information on ARVs and other treatments by health care providers.

Introduction of new therapies requires a period of learning and adaptation will lead to:

- Variable drug adherence;
- Rapid development of drug resistance
- Fluctuations in viral load;
- Challenges in clinical monitoring.

Programs in the Prevention Grant

1. Program I: Messages and Information Campaigns
2. Program II: AIDS Treatment Information Centre
3. Program III: In-Patient Voluntary Counselling & Testing
4. Program IV: Adherence Measurements
5. Program V: Innovative ARV Care Delivery
  - *Care and treatment algorithms*
  - *Laboratory monitoring in ARV therapy in a resource limited setting*
6. Program VI: Behavioural Surveillance
7. Program VII: Serial Cross-Sectional Surveys

Progress on the Prevention Grant

- A new generation of HIV messages were developed and disseminated based on.
  - Baseline KABP
  - Target Audience Analysis
  - Stakeholder involvement
- ATIC has provided information to HCWs on the availability of ARVs, pricing, management, drug interactions and storage through telephone, fax, contact visits, talk shows, newsletter and the internet.
- 2 studies on VCT:
  - a cross-sectional study to describe HIV testing practices in Mulago Hospital.
  - a randomized trial to compare free, in-pt RCT with ambulatory VCT.
- 2 studies to assess adherence measurement approaches in MTCT-Plus Program:
  - Unannounced home pill counts.
  - Structured interviews, to assess cultural acceptability, feasibility and validity.
- 7 study protocols for dementia, headache, CNS, vision, liver, adolescents and cryptococcal meningitis developed. Testing of algorithms underway.
- Developed protocols for parallel testing of standard vs cheaper methods of testing for CD4 counts and viral load.
- A plan for prospectively monitoring behavioral indicators among IDC clients, their spouses and the community is being implemented.
- Baseline KABP survey conducted in early 2003 and a repeat survey was scheduled for early 2005.
- Outputs
  - Several abstracts presented at International Conferences (CROI, IAC, IDSA)
  - ATIC Newsletter
  - Papers

- Reports (Baseline Survey, Surveillance indicators, Target Audience Analysis etc)
- Messages

#### Lessons learnt

##### i) Grants Management

- It is possible to establish a grants and contracts office within Makerere University to manage a large grant.
  - A system of structures and functions.
  - Human resource, procurement and financial management guidelines.
- It is possible to set up sub-contracts within the Makerere University – UCSF, JHU
- Working with University bureaucracies can be challenging and requires patience.

##### ii) Program Implementation

- Program implementation requires proper planning and budgeting.
- Adherence to HR and financial management guidelines requires a learning curve.
- Important to include a start up phase for recruitment, training, procurements and planning.
- Integration of 7 independent but linked programs desirable to avoid duplication and foster complimentarily.

##### iii) Program Outputs

- HIV messages must be based on detailed assessment of gaps and must involve key stakeholders.
- Demand for information on HIV/AIDS care is high and requires a technical clearing house.
- RCT is a very imp strategy in patient mgmt while traditional methods may not be applicable with large numbers of patients

##### iv) Program Outputs

- Adherence near perfect in those on ARVs. Challenge is to pick out those likely not to adhere and intervene.
- Simple clinical tests and approaches can be used to guide effective mgmt of patients.
- Alternative lab monitoring (to CD4s & viral load need to be id to cut costs.
- Behavior change interventions need to be based on a firm theoretical framework and must be monitored by a behavioral surveillance system.

##### v) Monitoring and Reporting

- Challenging to design a monitoring system for multiple programs with multiple objectives and outcomes.
- Important to define monitoring indicators early before program implementation begins.
- Program milestones are dynamic and may need to be revised periodically.
- Reporting to multiple levels of authority and needs must be harmonized to avoid duplication.

### **3. The National Strategic Framework for HIV/AIDS Activities in Uganda 2000/01-2005/06. A Guide for all HIV/AIDS Stakeholders, Revised, February 2004 by Uganda Aids Commission by Ms. Rose Kindyomunda**

This presentation cover:

- Goals, objectives and strategies in the revised National Strategic framework (NSF) and its relationship between the National aids Program (NAP).
- 6 thematic areas identified in the NSF and to identify how participants, as stakeholders, contribute to the achievement of the NSF goals.

National Strategic Framework

Uganda has one: agreed HIV/AIDS Action Framework, national AIDS authority, and country-level monitoring and evaluation system.

The purpose of NSF is to:

- Provide basis and benchmark to measure progress and impact of HIV/AIDS interventions
- Serve as a tool for resource mobilization
- A hub for strategic information and relate to development goals.

Thematic Areas of the NSF are:

- HIV/AIDS prevention, care and treatment, behavior change, advocacy, psychosocial support, ensuring rights and protection of people living with HIV/AIDS, coordinating HIV/AIDS institutions, resource planning, management, monitoring and evaluation.

The goals of the revised NSF are:

i) To reduce national HIV prevalence by 25% (set in the 2000).

Target activities:

- Promotion of safe sexual behavior especially among 15-24yrs
- Reduce risk of blood born HIV transmission by 50%
- Reduce prevalence of STIs other than HIV by 25%
- Reduce MTCT of HIV by 30%.

ii) Mitigate the HIV/AIDS health, psychosocial, economic effects and the macro-economic development impact.

Target activities:

- Strengthen district level infrastructure, expand and sustain human resources, increase access to quality prevention and 100% to opportunistic infection (OI) care, Support approaches for alternative / complementary treatment Increase equitable access to ART, Promote and expand specialized pediatric and adolescent, Support and expand provision of home-based care, Support and provision of palliative care, ensure a functional continuum of care through referral, promote improved care-seeking behavior through IEC, Improve quality of PHAs through

counseling, nutritional support, and 50% access to antiretroviral therapy (ART) .

- To reduce psychosocial and economic effects we need to prevent and protect human rights violation of PHAs, incorporation HIV/AIDS concerns in HR management.

We need to promote psychosocial and economic support of PHA, and affected families to at least 50% of those in need. Strategies involve expand psychosocial support, promote psychosocial and spiritual support for those in and out of school OVCs.

To mitigate the effects of HIV/AIDS the country hopes to;

- To strengthen national capacity to coordinate and manage the Multisectoral response to HIV/AIDS, the country hopes to strengthen coordination at national, district and lower levels, strengthen capacity to coordinate and under-take HIV/AIDS research, To promote and strengthen capacity to manage strategic information for HIV/AIDS.

The necessary information with relevant key indicators will be collected and shared with stakeholders.

## *Session II*

*Chairperson Dr. Fred Nuwaha*

### **4. Centers for Disease Control and Prevention (CDC) by Donna Kabatesi and Dr. Rebecca Bunnell**

CDC employs about 200 staff; about half are in Entebbe and half in Tororo.

The major focus in Uganda is to provide funding and technical assistance under PEPFAR.

Activities include

1. Programme evaluation, operational and applied research.
2. Training opportunities; CDC sponsors a Fellowship Program under IPH, and offers sponsorship for short courses.

What has CDC done so far?

- Blood Safety Research
- Cotrimoxazole Prophylaxis
- Laboratory
- Prevention with Positives
- Home-based AIDS Care Programme (HBAC)

i). Blood Safety Research.

- Transmissibility of Human Herpes Virus 8 (HHV-8) by Blood Transfusion.  
Background
- HHV-8 is causative agent for Kaposi's sarcoma (KS).
- KS most frequent malignancy in Uganda.
- Risk of HHV-8 transmission by blood transfusion unknown.

- No blood bank screens for HHV8.

#### Methods

- Prospective cohort study
- Transfusion recipients from Mulago Hospital
- HHV-8 testing:
  - Transfusion recipients (N=991)
  - Pre-transfusion
  - Post-transfusion (repeatedly over 6 months)
  - Linked blood donations
- Compared HHV-8 incidence in 2 groups:
  - Transfused with HHV-8-seropositive blood

#### Results

- Blood donor HHV-8 prevalence: 36%
- HHV-8 transmissible by blood transfusion
- Risk: 2.3% per HHV-8-seropositive unit
- Higher risk seen for older recipients
- HHV-8-pos units of shorter storage time

Mortality was 1.5 times higher among exposed vs. unexposed (p=. 04)

#### ii) Basic care and prevention package.

- Goal to prevent morbidity, mortality, and HIV transmission
- Cotrimoxazole Prophylaxis.
- Safe drinking water.
- Insecticide-treated bed nets.
- Family VCT efficacy of cotrimoxazole prophylaxis.

#### iii) Laboratory National Program for Infant HIV Diagnosis.

- Pilot program to test infants born to HIV-infected mothers
- HIV-infected mothers/infants identified at post-natal immunization clinics
- Whole blood collected in Vacutainers or as DBS; tested on Roche Amplicor DNA PCR assay
- DBS protocol to be validated

#### Other validations:

- Total HIV Nucleic Acid assay on DBS
- Ultra-sensitive HIV p24 antigen assay on plasma
- Stat-Pak on finger-stick blood

#### iv). Prevention with Positives (PWP) Formative Evaluation.

##### Methods:

- Cross-sectional study
- 1092 TASO Jinja clients
- Pre-ART
- HIV Transmission Prevention:
  - Sexual Transmission
  - PMTCT and Family Planning

v). Prevention of Sexual Transmission

- 58% of people living with HIV abstaining
- 48% of men
- 66% of women

Of these:

- 51% had decided to abstain permanently
- 49% had “temporary” reasons for abstaining:
- No interest in sex
- Poor health
- No current partner
- On-going counseling and peer support needed for those choosing to abstain

vi). Prevention of Vertical Transmission.

- Provision of family planning to people living with HIV is primary prevention for PMTCT.
- Integration of family planning in AIDS service organizations not universal.

Desire for children& pregnancy Risk Behavior.

- 64% of PLWHAs had experienced the death of at least 1 biological child.
- 7% of women and 27% of men desired more children.
- 33% of HIV-positive men and women were practicing pregnancy risk behavior - no condoms or family planning.

Sexual Behavior Among People on ART (N=992) behavioral interventions for people initiating ART.

- Group education during enrollment
- Family and partner VCT
- 30 minute sexual behavior plan done with counsellor prior to ART initiation
  - Assess current transmission risk
  - Reinforce personal motivation to avoid transmission
- Altruistic approach
- Follow-up counselling and condoms if requested
- Sexual behavior and transmission risk after 6 months on ART
- >85% of risky sex took place in married couples
- 70% reduction in unprotected sex with partners of unknown or known negative HIV status.
- Median viral load of those reporting risky sex declined from 122,500 copies/ml to 49 copies/ml.
- 98% reduction in transmission risk to partners of unknown or known negative status.

Conclusions

- Research findings critical for:
  - Ensuring evidence-based programmes.
  - Informing MOH policies

### Challenge for researchers

- Are we conducting research that applies directly to Uganda's most important problems?
- If our studies were completed today, what is the chance that the findings would be implemented and make a difference for people in Uganda?

### Acknowledgements

- MOH
- UVRI
- TASO
- AIC
- Mulago Hospital
- CDC-Uganda staff
- HBAC and other study participants

## **5. Medical Research Council Research unit on AIDS by *Dr. Paula Munderi***

### Mission Statement

- To investigate determinants of HIV transmission and HIV disease progression.
- To develop and evaluate new interventions through clinical and population based intervention trials.
- To inform health policy in Uganda and elsewhere in Africa.
- To contribute to capacity building in HIV research in Uganda

### Funding

- MRC
- DFID
- Wellcome Trust
- European Commission
- IAVI
- CDC
- soon: Int. Partnership on Microbicides

### Research sites and Partners

- Entebbe MRC/UVRI laboratories
- MRC/UVRI field stations: Masaka, Kyamulibwa
- St Francis Hospital, Kampala
- Mulago Hospital
- Entebbe Hospital; TASO Entebbe
- Masaka Hospital; TASO Masaka
- Jinja Hospital; TASO Jinja

### Main areas of ongoing studies

- Studies of the epidemiology of HIV infection and of the determinants of transmission and disease manifestation
- Intervention studies aiming to prevent HIV transmission
- Intervention studies aiming to improve the health of HIV infected patients

Studies of the epidemiology of HIV infection and of the determinants of transmission and disease manifestation.

- General Population Cohort - Kyamulibwa
- Rural Clinical Cohort
- Paediatric Cohort
- HIV epidemiology, behavioural determinants, impact of ART on the epidemic
- Clinical, behavioral, viral and immunological determinants of disease progression

Intervention studies aiming to prevent HIV transmission

- Microbicide safety trials - St Francis Hospital, Nsambya.
- Microbicide efficacy trial, to start in October 2005, 6 African sites (incl. rural Masaka), Pro2000 (a naphthalene polymer).
- HIV vaccine preparedness studies: prevalence, incidence, and normal values.
- Social science studies on acceptance, intervention uptake and barriers to microbicides and vaccine.

Intervention studies aiming to improve the health of HIV infected patients

- Prevention of OIs:
  - Cryptococcal disease prevention trial
- Major focus on ART; e.g.
  - DART trial
  - Jinja ART rollout trial
    - Behavioural studies on adherence
    - Virological studies on response to treatment

Other major work

- The effect of maternal helminths on infant response to immunisation and on the susceptibility to diseases in childhood ('Mother-and-Baby Study')
- Support for a study on multidrug-resistant tuberculosis

Priorities for 2006 – 2011

- Microbicides
- Basic science research to inform vaccine development e.g. immunology of acute HIV infection and exposed uninfected
- Intervention research on high risk behaviour groups: e.g. bar workers
- Research on STI / HIV interaction and control: e.g. STI cofactor effects; oral treatment of syphilis
- Strategies for ART delivery in the African context.

DART Trial – Preliminary Results

- Occurrence of anemia
- Virological Efficacy of CBV/TDF
- Impact of ART on Mortality

## 6. MU-JHU Research Collaboration by *Prof. Francis Miro*

The Makerere University – Johns Hopkins University (MU-JHU) Research Collaboration has conducted HIV research in Uganda since 1988. MU-JHU Research Collaboration is committed to increasing access to ARV therapy for participants and providing basic comprehensive HIV/AIDS services. Over 6000 families have participated in our research activities and programmes since 1988.

### Mission

To improve the health status of families infected and affected by HIV/AIDS through Research, Training, Prevention and Care.

### Objectives

- To conduct relevant HIV/AIDS research for primary and secondary HIV prevention
- To build capacity of Health care providers and allied professionals in research and care
- To facilitate community involvement in HIV/AIDS research and Prevention
- To disseminate research findings in care, treatment and prevention of HIV/AIDS

### Research Activities Completed Studies

#### i) HIVNET 012

##### Study Objective

- To compare the use of oral NVP versus oral AZT given to the mother in labour and to the infant after delivery to prevent HIV MTCT in pregnant HIV infected women.

##### Study Population

##### Infant Results

- Infant HIV results at 145 wks (HIV RNA-PCR)
- NVP arm: 13% transmission
- AZT arm: 26% transmission
- 50% reduction of HIV MTCT in NVP arm
- Drugs were safe and well tolerated
- No side effects related to drugs

Infants: 18 months HIV ELISA; 60 months safety data

- The study of NVP has formed the scientific basis for the rapid expansion of PMTCT throughout the developing world.

##### HIVNET 012 Re-monitoring

- The thorough re-monitoring of the HIVNET 012 study engaged all levels of core study staff in an intensive data review process and hands-on orientation to the requirements of Good Clinical Practice in research.
- The final reports from all re-monitoring activities (including the recent Institute of Medicine report) showed that the findings of the study were valid, that the trial

was conducted ethically and with proper Institutional Review Board approval, and that the Investigators maintained careful safety review and reporting procedures for adverse events.

## **Ongoing Studies**

### **ii). HIVIGLOB**

A phase III randomized clinical trial of the standard two dose Nevirapine (NVP) regimen with the addition of HIV immunoglobulin (HIVIGLOB) or extended infant NVP dosing compared with the standard NVP regimen alone for the prevention of maternal-infant HIV transmission in Uganda.

## **Objectives**

### **Primary**

- To determine rate of HIV infection among infants in each arm of the study.
- Determined at birth, 2wks, 6wks, 14wks, 6mos, 12mos, and 18mos
- Safety and tolerance of HIVIGLOB given to pregnant women and neonates in combination with NVP
- Safety and tolerance of NVP alone in short and extended dosing regimens

### **Secondary**

- To determine rates of HIV disease progression in infected infants in each arm by assessment of CD4 cell count and viral load.
- Rates of virologic progression in each arm through assessment of quantitative HIV-1 RNA.
- Infant survival in each arm (mortality, regardless of HIV infection).
- Relationship of immunologic, virologic, and pharmacologic factors to the risk of perinatal transmission.
- Potentially including but not limited to NVP levels, HIV subtype, NVP resistance, HIV antibody levels, maternal RNA at delivery.

## **Methods**

- A prospective, three arm randomized partially blind controlled study.
- Study population: A sample size of 660 - 800 eligible HIV-1 infected Ugandan pregnant women between 28 and 36 weeks gestation and their neonates.
- Study duration: 3yrs
- Enrollment period: 18months.
- Follow-up: Neonates - 18 months post birth and Mothers - 6 weeks postpartum.

## **Study Population**

- HIV infected women identified through the PMTCT program, who are 18 years and older and intend to breastfeed
- Screened at 28-35 weeks
- Meet necessary laboratory criteria for study enrollment – positive western blot, HB level  $\geq 7.5$  g/dl, serum creatinine  $> 1.5$  mg/dl, ALT levels  $< 135$  IU/L
- Enrollment is between 32-36 weeks gestation. Effectively randomized at enrollment to one of the three arms
- Those mothers randomized to the HIVIGLOB arm will be scheduled for infusion visit at the 36-37 weeks gestation.

- Mothers are followed through ANC, labor and delivery, and for 6 weeks postpartum
- Infants in the HIVIGLOB arm receive HIVIGLOB infusion within 18 hrs of birth
- Infants are followed up weekly for first 6 weeks, 10 weeks, 14 weeks, 6, 12, and 18 months
- Randomization into the 3 Treatment ARMS

## **Study Progress to date**

### **i) HIVIGLOB**

This is an experimental HIV immunoglobulin therapy preparation containing antibodies against HIV.

- Was prepared by collecting HIV-1 antibody positive plasma from donors at Nakasero Blood Bank - Uganda starting in 1993
- 300ml of plasma was collected from units with CD4 cells  $>500 \times 10^6/l$ . These units tested negative for Hepatitis B surface antigen, hepatitis C virus antibody and HIV-1 p24 antigen.
- The plasma was shipped to the Swedish Institute for Infectious Disease Control for fractionation into intravenous HIV-1 hyperimmune globulin.
- The fractionation process involved multiple steps, which included multiple ion exchange, precipitation and extraction procedures of antibodies (HIV and others) and treated to destroy HIV and other infectious agents.
- The fractionation procedure yields a pure monomeric unfragmented and undenatured human immunoglobulin. The final product was then formulated as a 5% IgG isotonic solution for intravenous injection.
- HIVIGLOB does not contain HIV.
- Was tested here in Uganda in a phase I/II study between June 1996 and April 1997 on 31 HIV infected pregnant women and their infants and was found to be safe.

### **ii) Nevirapine Resistance Study**

Prospective and Retrospective assessment of transmission rates and resistance patterns with repeat Nevirapine (NVP) use in second pregnancies in Uganda.

### **Background**

Single-dose nevirapine (sdNVP) is widely used to prevent mother-to-child HIV transmission (PMTCT) in resource limited settings. Given early detection of resistant mutants in a subset of mothers who receive sdNVP for PMTCT, concerns have arisen over potential reduced efficacy of sdNVP in subsequent pregnancies.

The aim of this case-control study was to assess infant infection rates among women with prior sdNVP exposure (cases) compared to infants of NVP naïve pregnant women (controls) who receive sdNVP using a combined retrospective and prospective study design.

### **Objectives**

#### **Primary**

- To determine HIV transmission rates in infants born to HIV-infected women who receive single dose Nevirapine in a repeat pregnancy (NVP- experienced) and to

compare these transmission rates in infants born to HIV-infected women who have not received prior single dose NVP (NVP-naïve) This will be assessed using both retrospective and prospective data.

### **Secondary**

- To prospectively determine the rate of genotypic Nevirapine resistance among HIV-positive women who receive single dose NVP prophylaxis for a repeat pregnancy after single dose NVP prophylaxis in a prior pregnancy vs NVP naïve women.
- To prospectively describe the type of NVP resistance mutations that emerge following SD NVP prophylaxis in SD NVP-experienced vs NVP-naïve women; to describe the type of NVP resistance mutations that emerge in the HIV-infected infants born to SD NVP-experienced vs NVP-naïve women.
- To prospectively examine fading of detectable NVP-resistant HIV for 12 months following SD NVP in SD NVP-experienced vs. NVP-naïve women and in the HIV infected infants born to these women.
- To compare the proportion of women with subtype A vs. D infection with the presence of detectable NVP-resistant HIV, prior to and following SD NVP prophylaxis.

### **Study Design**

- The NVP-RP study is both a prospective and retrospective on-going observational study at MU-JHU Research Collaboration located at Upper Mulago Hill, Kampala – Uganda since June 2004.
- In both the prospective and retrospective arms of this study, women were identified through the HIVNET 012 follow up and PMTCT program at Mulago Hospital.
- Prospective study participants were enrolled at  $\geq 28$  weeks of gestation and closely followed up to 1 year post-delivery. Enrollment into the prospective arm ended in June 2005.
- Enrollment into the retrospective arm remains open and so far 99 participants have been enrolled. Participants in the retrospective arm are not followed up except babies who stopped breast feeding less than 2 months ago who are given one more appointment 3 months post breast feeding for DNA PCR.

### **Clinical Variables**

- Maternal age.
- Maternal gravity and parity.
- Maternal HIV signs and symptoms: based on WHO clinical classification system.
- History of NVP prophylaxis, including date of prior SD NVP dose.
- Birth outcome: live birth, miscarriage, and stillbirth.
- Gestational age at delivery, birth weight of the infant.
- Mode of delivery, including: labour (hours), rupture of membranes (hours), laceration, episiotomy, caesarean section or vaginal delivery.
- Mode of feeding: breast or formula.

### **Laboratory Variables**

- Viral load (infected infant and mother).
- CD4 count (infected mother).
- NVP resistance mutations (presence or absence) using standard genotypic assays.

- NVP resistance mutations (quantifiable levels) using real-time PCR for K103N and Y181C mutations.
- DNA PCR (all infants).

### **Study Progress**

A total of 110 mothers were enrolled but 105 mother baby pairs are being followed up. 1 died, 2 did not swallow the SD NVP pill, 1 was lost to Follow-up and 1 withdrew consent.

### **Planned Studies**

#### **i). HPTN 046**

This is a phase III trial to determine the efficacy and safety of an extended regimen of Nevirapine in infants born to HIV + infected women to prevent mother to child transmission of HIV through breastfeeding.

#### **Purpose**

- To evaluate the efficacy and safety on extended Nevirapine for 6 months or through the end of breastfeeding whichever is earliest compared to placebo for prevention of mother to child transmission of HIV-1.

#### **Study Population**

- HIV-1 infected mothers and their breastfeeding infants. All participants will be offered single dose Nevirapine – the standard treatment.

**Study size:** ~ 1600 mother infant pairs

**Study Duration:** 3.5 years

#### **Treatment**

- Eligible infants will be randomized on the 3<sup>rd</sup> or 4<sup>th</sup> day to one of the two ARMS.

**Group I:** Infant in the ARM will receive extended Nevirapine for 6 months or to the end of breastfeeding whichever is earliest.

**Group II:** This group will be on placebo for a similar period.

### **Study Objectives**

#### **Primary**

- To compare the rate of HIV infection at 6 months in infants determined to be HIV uninfected at birth in each arm
- To evaluate and compare the safety and tolerance in infants in each arm.

#### **Secondary**

- To compare the proportions of infants who are alive and free of HIV at 6 months and 18 months of age in the two arms
- To compare the relative rates of HIV infection in infants over 18 months in the two arms
- To compare the infant survival rates (mortality regardless of HIV infection) over 18 months in the two arms
- To determine the frequency and duration of NVP-resistant HIV strains in maternal plasma and breast milk and the relationship with MTCT

#### **Maternal Eligibility Criteria**

- 18 years of age or older
- Willing to provide study informed consent
- HIV infection confirmation

- No serious current or past complication of this pregnancy
- Free of other opportunistic infection
- Intend to breastfeed
- Intend to deliver at Mulago hospital.

### **Infant Randomization**

The infants who have received their single dose NVP at delivery will be randomized.

- **ARM I:** Receive NVP suspension. Once daily with increasing dose from 0.6ml (6mg) at birth to 2.8 ml (28mg) at 6 months
- **ARM II:** Will receive a non NVP syrup (Placebo) with ranging dose from 0.6 to 2.8ml at 6 months.
- Randomization will take place at or before day 3 from birth

### **Infant Randomization Criteria**

- Born to HIV infected eligible mother
- Breastfeeding
- Birth weight of at least 2000gm
- Blood sample taken for HIV-1 DNA PCR. CBC with differential and Liver Function Test
- Is health as judged by study clinician

### **Study Endpoints**

Primary endpoints:

- HIV infection at 6 months in infants determined to be HIV – uninfected at birth s determined by HIV DNA PCR.
- Frequency and severity of adverse reactions among participating infants.

Secondary endpoints:

- Proportion of infants who are alive and free from HIV at 6 and 18 months of age in the two arms.
- Relative rates of HIV infection at 18 months in the 2 ARMS.

## **ii) HPTN 027**

A phase I study to evaluate the safety and immunogenicity of ALVAC-HIV CP1521) vaccine in Infants born to HIV infected women in Uganda.

### **Background**

The study of HIV vaccines in breastfeeding infants born to HIV+ mothers has the potential to provide signification benefits not only to the population being studied, but to the advancement of HIV vaccine development as well.

- Data in these Ugandan neonates will compliment data from phase I/II and phase III trial of this clade E/B vaccine in adults in Thailand, a trial of the clade B in Uganda Alvac-HIV vC205 in Uganda adults, and similar clade B HIV v CP 205. and ALVACHIV v CP1452 vaccine in infants conducted in USA by National Institute of Health (PACTG 326).
- ALVAC HIV C1521 is currently undergoing efficacy testing for prevention of HIV infection in adults in Thailand

### **ALVAC HIV Vaccine**

- Alvac-HIV (vCP1521) is a preparation of live recombinant canary poxvirus expressing gene products from HIV-1 env (clade E) gag (clade B) and protease (clade B) coding sequences, cultured in chick embryo fibroblast cells.

- It is formulated as a lyophilized vaccine for injection and is reconstituted with 1.0ml sterile sodium chloride solution (0.4%) for single dose. It is stored at 2-8°C- and is freshly prepared and administered within 2 hours of its reconstitution

#### **Study Design**

- The study will be a phase I randomized double blind placebo controlled trial of ALVAC-HIV CP1521 in infants born to HIV –1 infected women in Uganda.

#### **Study Procedure & Population**

- Infants born to HIV –1 infected women with CD4 count >500 cells/ul attending ANC Mulago hospital.

#### **Study size**

- 50 (Vaccine 40, Placebo 10)

#### **Study Duration**

- Enrollment: Approximately 3 –6 months  
Follow-up: 24 months

#### **Study Treatment Regimen**

- The eligible infants will be enrolled and randomized after birth to one of the 2 immunization ARMS – as shown below. The initial dose will be given on or before day after birth.

#### **Study Objectives**

##### **Primary**

- To evaluate the safety and tolerance of ALVAC-HIV Vcp1521 in infants
- To evaluate the immunogenicity (cell-mediated and humoral response responses) of ALVAC\_HIV vCP1521 in infants born to HIV-1 infected Ugandan women with CD4 counts > 500 cells/μL

##### **Sexual Behavior among People on ART (N=992)**

- People initiating ART were taught behavioral interventions, which include group education during enrollment and family plus partner VCT.
- Each client made a 30 minute sexual behavior plan with the counselor prior to ART initiation and during this time assessment of current transmission risk was made as well as reinforcement of personal motivation to avoid transmission. Follow-up counseling and condoms were given if requested.

#### **Results**

- After 6 months on ART, Sexual behavior and transmission risk was assessed. More than 85% of risky sex took place amongst married couples. There was a 70% reduction in unprotected sex with partners of unknown or known negative HIV status. The median viral load of those reporting risky sex declined from 122,500 copies/ml to 49 copies/ml. There was a 98% reduction in transmission risk to partners of unknown or known negative status.

#### **Conclusions**

- These research findings are critical for ensuring evidence-based programs and informing MOH policies.

#### **Challenge for researchers:**

Are we conducting research that applies directly to Uganda's most important problems?

If our studies were completed today, what is the chance that the findings would be implemented and make a difference for people in Uganda?

**7. The Joint Clinical Research Centre .Key Recent and on going research in the last year and the current issues in ART scale up by Dr. Francis Ssali.**

Phase I

i). Study of the Safety and Immunogenicity of Live Recombinant ALVAC –HIV v CP205 in HIV-1 Uninfected Adult Volunteers in Uganda.

- Double-blinded 3-arm placebo controlled phase 1 trial of safety/immunogenicity of a recombinant HIV-1 canary pox vector vaccine (ALVAC vCP250).
- Primary end points were cytotoxic T lymphocyte responses, neutralizing and binding antibodies and safety.

Stopping Infection from mother to child through breastfeeding in Africa (SIMBA)

- This was a phase III, randomized, open label multi-centre study to investigate the efficacy of postnatal prophylaxis of lamivudine (3TC) or nevirapine (NVP) in HIV negative children during breastfeeding.
- Pregnant women (300 in Uganda, 100 in Rwanda) received a short term course of zidovudine and didanosine from gestational age of 36 weeks onwards to one week postpartum.
- Prophylactic treatment was administered for a period of 6 months during the breastfeeding period.

ii) Cohort program to evaluate access to anti-Retroviral therapy and Education (CARE-STUDY).

A single arm, 96-week, open-label cohort program. 50 eligible patients were recruited from each site (JCRC in Uganda) provided with free ARVs for a period of 2 years and monitored for response toxicity and quality of life.

- Regimen used was CBV+SQV/RTV.
- Study dates Dec 2000 – Dec 2004.

A randomized, controlled trial of short cycle intermittent versus continuous HAART for the treatment of chronic HIV infection.

This is an intent-to-treat, randomized, controlled trial of continuous versus 2 approaches to short cycle intermittent HAART.

- 57 Patients randomized in each of 3 study arms and response measured by viral load.
- Started April 2002.

iii). Global Initiative to characterize Differences in Antiretroviral Pharmacokinetics in HIV-Infected Populations.

Primary objective

This study is to characterize the PK of the NNRTI Nevirapine in a Ugandan HIV-Infected population and in a similar cohort of HIV-infected individuals in the US.

- Study dates Nov 2004- April 2005

A link between the genotype and the plasma  $t_{1/2}$

Effect of 7-valent Pneumococcal conjugate vaccine and 23-valent-pneumococcal-polysaccharide vaccine among HIV-infected adults in Uganda.

- To determine whether immunization with CV followed by PV induces type-specific IgG in sera and the serum opsonic activity against *S. pneumoniae*.
- To determine whether type-specific IgG induced by pneumococcal vaccine correlates with the serum opsonic activity against *S. pneumoniae* and viral load.
- To determine whether the levels of type-specific IgG in sera and the serum opsonic activity remains for at least one year among HIV-1 infected adults with the peripheral CD4 higher than 200/ $\mu$ l who are not receiving antiretroviral drugs.

iv). Clinical Protocol A0661134.

- A phase 11/111 randomised, double blind, comparative trial of azithromycin Plus Chloroquine Versus Mefloquine for the treatment of uncomplicated plasmodium falciparum malaria in Africa.
- Jun 2004- Jun 2005
- Cell function in HIV Sero-positive Ugandan adults.

Purpose of study.

To investigate the effects of viral antigen exposure on CD8 and CD4 immune responses to gain insight into mechanisms by which this immune dysfunction might be reversed.

- Particular emphasis is placed on immunopheno-typing distinct T cell populations, which actively suppress HIV-specific responses.
- HIV Vaccine feasibility study at Kakira.
- A cross sectional, observation feasibility study to assess recruitment and determine HIV prevalence among potential Volunteers for an efficacy trial of a vaccine to prevent HIV (Protocol A).
- Study participants were enrolled from sugar plantation workers and also from the population neighbouring the plantation (Jun2004-Dec 2004)

### **Tuberculosis studies**

i) Multidrug Resistance (MDR) TB study

- To determine resistance to first line and second line Tb therapy.
- Transmission of Tb on the Mulago TB ward.
- Identify host and microbial factors that predict transmission.
- To evaluate new interventions including rapid diagnostic methods and monitoring response to therapy.

ii). Treatment shortening study

- HIV negative, Non-cavitary, smear negative at 2/12.

iii). PART STUDY (Delaying HIV disease progression with Punctuated Anti-Retroviral Therapy in TB patients).

- Effect of punctuated 6/12 ART during TB therapy on HIV disease progression.

iv). TBTC NAA STUDY

- A pilot study to evaluate the utility of molecular tests to predict TB relapse and monitoring treatment).

DART trial: Uganda & Zimbabwe

Haemoglobin at scheduled assessments after initiation of ART.

Hormonal Contraception and the Risk of HIV Acquisition, HIVNET Protocol 021.

### **Major Clinical Studies to start 2006**

1. OCTANE 5208

2. PROTOCOL 5207

3. THE ARROW STUDY

- 5 year randomised trial with a factorial design
- 1300 children will be enrolled in Uganda and Zimbabwe.

The study will investigate:

- The monitoring practice of ART among children.
- The ART strategy among children.
- The role of Induction and maintenance regimen.

### **HIV TREATMENT**

Challenges of the ART scale up

- Timely delivery of supplies
  - Developed a logistics management system.
- Countrywide knowledge and experience in ART was limited.
  - Embarked on staff training in ART.
- Data collection
  - Developed Data collection tools and a database.
- Infrastructure
- Adherence
  - Developed an adherence strategy.
- Maintaining a quality service
  - Monitoring & Evaluation
  - Mentorship
  - Regional Centres of excellence
  - Operational research
- Stigma
  - Communications strategy

### ***Session III***

***Chairperson Dr. Israel Kalyesubula***

### **8. Makerere University-Walter Reed Project Update on HIV Vaccines, *Dr Hannah Kibuuka, Director, Clinical Programs.***

- Project overview
- Vaccine trials
- Cohort development activities
- Local institutional normal reference ranges

Purpose

- HIV vaccine development and establishing vaccine testing capability in Uganda

## Objectives;

- Conducting vaccine trials
- Monitoring of HIV trends

## HIV vaccine trials:

- Developed phase I/II vaccine testing capability
- Vaccine research clinic
- CAP certified laboratory
- HIV, Hep B, C and syphilis diagnostics,
- Safety monitoring
- Immunogenicity testing
- ELISPOT
- Intracellular cytokine staining
- Chromium release assay
- Data management center
- Trained staff

## Phase I trial:

To evaluate the safety and Immunogenicity of a multiclade HIV I plasmid vaccine in adult uninfected Ugandans.

- Started in late November 2004.
- First vaccination in January 2005 and all vaccinations completed by June 2005.
- Enrolled 30 volunteers aged 18-40 years.
- Fully enrolled within 4 1/2 months.
- Volunteers will be followed up for 1 year subsequent to enrollment.
- So far vaccine has been safe.
- Vaccine provided by VRC and trial sponsored by DAIDS.

## Upcoming trial

### Phase I/II trial

- To evaluate the safety and immunogenicity of a multiclade HIV I DNA plasmid vaccine as a prime boosted by a multiclade HIV I recombinant adenovirus 5 vectored vaccine.
- A multicenter study with sites in Uganda, Kenya and Tanzania.
- Will enroll a total of 324 volunteers (108 per site).
- Protocol has completed IRB review in the US and currently under review in the 3 East African countries.

## Monitoring HIV trends

### Previous studies.

- Done in collaboration with Rakai Health Sciences Program
- Cohort activity to determine willingness to participate in HIV vaccine trials
- 75% willing to participate in vaccine trials
- MER: HIV subtypes circulating in Rakai and early viral and immunological markers during HIV infection.
- Subtype D (55%), Recombinants (30%) and Subtype A (15%)

#### Planned studies

- Cohort development for phase III vaccine testing in Kayunga district.
- Enroll 2000 volunteers who will be followed up at 6 monthly intervals.

#### Objectives.

- Determine HIV prevalence and incidence and risk factors.
- Determine circulating HIV subtypes.
- Evaluate population stability and willingness to participate in vaccine trials.
- Protocol under review.

#### Normal Reference Range Study

##### Rationale.

- Important to have local institutional normal reference laboratory values.
- To establish eligibility criteria that is not too restrictive.
- Accurately assess adverse reactions during trials.

#### Current trial

- Screened 222 volunteers to obtain 30 who were vaccinated.
- Common reasons for screen outs were eosinophilia and neutropenia.

#### Reference range study

- Study done in collaboration with Nakasero blood bank.
- Blood from 2000 blood donors will be analysed for haematology, chemistry and lymphocyte immunotyping after screening for HIV, Hep B & C, Pregnancy and syphilis.

#### Acknowledgement

- MUWRP
- VRC
- DAIDS
- USMHRP
- KAYUNGA DISTRICT ADMINISTRATION
- NAKASERO BLOOD BANK
- VOLUNTEERS

### **9. Makerere University of Medical & Dentistry New Jersey Collaboration Strategies for the Management of Multi-Drug Resistant Tuberculosis in Kampala, Uganda” by Dr. William Worodria.**

#### AIM 1

- To determine the prevalence of acquired MDRTB at the Mulago Tuberculosis clinic.  
*Study population:* 500 consecutive re-treatment TB cases attending Mulago
- Study measurements:
  - Clinical questionnaire
  - Sputum
  - HIV serology

#### AIM 2

- To measure the rate of nosocomial transmission at the Mulago Hospital TB ward and to elucidate host, bacterial and environmental factors involved

*Study population:* All patients admitted to Mulago TB ward for 2 consecutive years (700 subjects)

- Study measurements:
  - Clinical questionnaire
  - Hospital epidemiology
  - Baseline and incident sputum smear/cultures
  - CxR, HIV, CD4
  - CASS, WBKA, RFLP
  
- Deciphering Transmission

i) Environmental Factors

- Hospital epidemiology
- Cough Aerosol Sampling System (CASS)

ii) Host Factors

- Clinical
- HIV status

iii) Bactercterial Factors

- Baseline
- Incident isolates
- WBKA

Aim 3: Interventions to Improve Diagnosis and Management

Diagnostics

- Rapid methods
  - Indirect phage
  - Direct LJ
  - Quadrant
- Ultra-rapi methods
  - Direct phage
  - Direct Bactec
  - INNO LiPA
  - Gene X-pert
  - E-test
  
- Cost analysis (LSHTM student)

Direct BACTEC (Rifampicin)

- 34 isolates tested
  - 30 susceptible
  - 4 resistant
- 100% correlation
- All rifampin-R were MDR isolates
- \$15.00 per test

Current Efforts

- Complete enrollment into Aim 2

- Initiate MDRTB treatment program
  - Clinical training
  - Laboratory expertise
  - DOT program
  - Purchase and storage of drugs (GLC)
  - Drug toxicity monitoring

- National Drug Susceptibility Survey
- Presentations and publications

#### Presentations

- CASS feasibility
  - American Thoracic Society, Orlando 2004
- CASS reproducibility
  - American Thoracic Society, San Diego, 2005
  - Tuberculosis Keystone Symposium, Whistler, April 2005
- Indirect phage
  - Rapid Drug resistance Testing, Cape Town, December 2004
  - European Society for Mycobacteriology, Sardinia, June 2004
- Gene X-pert
  - American Society of Microbiology, Atlanta, June 2005
  - Tuberculosis Keystone Symposium, Whistler, April 2005

#### Final Package (Affordable MDRTB Program)

##### Data

- Prevalence of drug resistance
- Quantify nosocomial transmission

##### Interventions

- Rapid drug resistance testing
- MDRTB treatment delivery
- Interrupt transmission

##### Education

- Dissemination of results
- New proposal of MDRTB in households

### **10. Programs and Research at the Infectious Diseases Institute (IDI) by *Dr Andrew D. Kambugu Head, Clinical Services-IDI***

The Infectious Diseases Institute (IDI) is a state-of-the-art clinical, training and research facility at Makerere University. It is strategically situated adjacent to Makerere University Medical School and Mulago National Referral and Teaching Hospital.

The IDI mission statement is to “To build capacity in Africa for the delivery of sustainable high quality HIV/AIDS care and prevention through training and research.”

#### **Background to the IDI**

IDI was borne out of a public-private partnership spearheaded by North American and Ugandan clinicians and scientists called, The Academic Alliance for Aids Care and

Prevention in Africa (AAACPA). The Buildings and programs were enabled through a grant by Pfizer Inc and IDI was inaugurated one year ago (Sept 2005).

### **Programs within the IDI**

#### **i) Clinical**

The adult clinic began as a one-day-a week clinic in 1987. Under the AAACP this clinic was restructured and facilitated in 2002. The first free ART program was initiated in June 2004 using MAP drugs. The clinic moved to IDI in September 2004 and currently over 13,000 patients are registered in IDI with 3000 patients on Anti-retroviral drugs. IDI gets 275-325 patient visits with 30-35 new patients per day. Nurses are involved in ART delivery.

The staff at IDI are involved in weekly meetings including journal clubs on Monday, ART switching meeting on Tuesday and case presentations on Friday.

The IDI houses the MU-JHU collaboration Lab that is an accredited laboratory and certified by the College of America Pathologists (CAP).

The Data System used at the IDI is IDIL Clinical Enterprise Application (ICEA) V 1.3 which includes basic clinical data capture and medical record functionality, anti-Retroviral therapy Monitoring and evaluation module, stores & Pharmacy Modules.

#### **ii). Training Program**

The Mission Statement for the training program:

“To be the center of excellence in Africa for training in HIV/AIDS and other infectious diseases by building capacity among health care workers for the provision of high quality, comprehensive care and prevention, including antiretroviral therapy.”

The focus of the training is equipping health care workers in Africa to become leaders in the provision of quality HIV/AIDS care and prevention, contributing to the enhancement of health care infrastructure in Africa and building a platform for multinational ARV delivery programs.

IDI offers three training programs:

- The HIV/AIDS Training Program for Medical Doctors in Africa, which is a comprehensive program in HIV/AIDS care and prevention for physicians based on a train-the-trainer model. It is a one month program which uses didactic, interactive, and practical training methods of instruction. The training is offered through a special collaboration with trainers from the Infectious Diseases Society of America (IDSA). A total of 300 medical doctors have been trained between May 2002 to May 2005 from Uganda and 13 other African countries.
- The Multi-disciplinary topical training program.
- The Nurses & Clinical Officer Training program

### **3. Research at the IDI**

The Mission Statement for research is

“To conduct clinical research that will contribute towards improving the health of Ugandans” and specifically, to answer questions pertaining to prevention and treatment of HIV/AIDS and other infectious diseases.

Research studies at the IDI include:

- The DART trial, which is a multi-site study that is designed to give insights to monitoring ART and STI in resource-limited settings.
- The Gates program (5A/5B) which looked at clinical algorithms and lab monitoring in resource-limited settings.
- The Observational Cohort, which was developed to characterize the natural history of HIV in a clinical setting. Initially included patients on ART and patients not on ART and due to cost, a subset of patients would be enrolled into cohort (n=600). Systematic data collection using a custom application purpose built for the study was used.

#### **4. Prevention**

In summary, IDI is a private-public partnership (University/Public hospital/Industry) built on a model for integration of clinical care, research and training. The observational cohort is an opportunity to answer questions relating to ART delivery in resource-limited settings.

#### **11. Makerere University of California San Francisco Research Collaboration by Ms. Jayne Byakika-Tusiime, Project Director.**

##### Project Overview

- Started in September 2002 under the name Adherence Monitoring Uganda.
- A pilot study to Evaluate Measures of Adherence to Antiretroviral Therapy in Uganda.
- Observational Prospective Cohort Study
- 96 enrolled
- Follow up of 6 months

##### Objectives

- To investigate 3 adherence measures to determine
  - Acceptability of each adherence measure using qualitative interviews.
  - Feasibility of each measure as defined by the proportion of achievable data points over a six-month period.

Validity of each adherence measure as defined by their association with HIV viral load.

Measures were:

- Electronic medication monitoring (EMM)
- Unannounced home visit pill count
- Interviewer administered structured patient self report

AMU Adherence

AMU Correspondence of Adherence Measures.

AMU Virologic Treatment Outcomes by Adherence 24 weeks.

Reasons for Non-adherence to ART.

- Lack of money
- Drug Inaccessibility
- Forgetfulness
- Travel away from home
- Drug adverse effects
- Busy

- Complex regimen
- Co-morbidity
- Taking alcohol

#### AMU Qualitative Study Findings

##### Three salient themes

- Cost of treatment as primary barrier to adherence
- Adherence requires considerable resourcefulness and financial sacrifice
- Concern over the future family welfare as a principal motivator to adherence

##### Follow up of AMU Cohort

- Patients are visited every 3 months to assess their adherence and barriers to treatment MTCT+ Adherence Study.

##### Overview

- Started in April 2004
- Observational Prospective Cohort Study
- 75 enrolled
- Receiving free therapy

##### Objectives

- To measure adherence
- Qualitative Study to assess adherence barriers

#### MTCT+ Adherence

##### MTCT+ Qualitative Study Findings

- Strong commitment to adherence
- Primary motivator
  - Desire to stay alive in order to continue to care for one's children
- Spouses reminded their partners to take their pills
- Type of medication packaging promoted adherence (blister packs)

##### Acknowledgement

- Dr David Bangsberg
- Dr Philippa Musoke
- Dr Jessica Oyugi

##### Funding

- Doris Duke Charitable Foundation
- NIMH
- NIAAA
- UCSF Center for AIDS Research
- Bill and Melinda Gates Foundation

## DAY TWO

### 12. Roll out of ART by *Dr. Elizabeth Namagala ART Programme, STD/AIDS Control Program –MoH*

#### Background

- HIV prevalence: 7% (2004), Average 6.2% Antenatal prevalence (2003)
- Lowest in 15-19 yr olds: 2.2% (F:3.2%, M:1.2%)
- Highest in 30-34 yr olds: 10.7% (F:12%, M: 9.1%)
- About 1.2 million infected, 120,000 need ARVs
- Urban: 10.7%, Rural: 6.5%
- Lowest in W. Nile: 2.2%, highest in Kampala 10.7% (F: 12.5%, M:9.1%)

#### HIV/AIDS Care and Support Services

- Counseling for HIV, including HCT & Psychosocial support)
- Prevention of further spread of HIV (PMTCT, condom promotion, Information, Education, Communication - IEC)□
- Clinical management:
  - Prevention of opportunistic infections (Cotrimoxazole use etc)
  - Treatment of opportunistic infections
  - Antiretroviral treatment (ART)
  - Home-based care / Palliative care
  - Paediatric AIDS care
  - Appropriate Nutrition in HIV/AIDS
- Available ART documents
  - National ART policy
  - National Antiretroviral Treatment guidelines for adults and children
  - National training guidelines for ART
  - Implementation guidelines for ART
  - ART costing report
  - Advocacy strategy for ART
  - ART Communication Strategy
  - Logistics considerations for ART

#### Situation of access to ART

- Scaling-up of all basic HIV care programmes: HIV counseling and testing ART, PMTCT, HBC, Cotrimoxazole prophylaxis etc.
- Uganda has achieved its National 3x5 target: At least 60,000 on ART by end 2005
- 67,583 people on ART from 150 sites (Sept. 2005)
- 1,663 health workers trained in ART mg
- Public sector ART Programme
  - expanded from 26 to 150 health facilities
  - targeting 18,000 people (14,000 patients recruited by end of Sept. 2005)

The National Scale-up Plan for ART services in Uganda.

#### Expansion of ARVs is in 4 Phases

- Phase I: Regional Referral Hospitals – Complete by Dec 2003 (completed)
- Phase II: District and other Hospitals – Complete by Dec 2004 (in progress)
- Phase III: HC IVs - Complete by Dec 2006 (in progress)
- Phase IV: Lower level facilities/community

#### Accreditation Criteria for ART centers

- Adequate staffing level (Drs, Counselors, Lab workers, Nurses, Pharmacists/Dispensers, etc)
- Laboratory capability for basic tests (Hb, CBC, HIV test)
- Drug storage facilities that ensure drug security
- Availability of counseling and patient's support services for PLWHA
- Record keeping facilities to allow M&E

#### Accredited ART sites (Oct 2005)

- 175 health facilities have been accredited for.
- 99 of these are public facilities which include;
  - 2 national hospitals
  - 11 regional hospitals
  - 42 district level hospitals
  - 44 Health center IVs.
  - 44 Private-not-for profit
  - 25 private for profit medical centers/hospitals
  - 7 centers of excellence/research based facilities

#### Training for ART scale-up

- Strengthening regional referral hospitals capacity to train and supervise lower health facilities.
- Training and establishment of clinical teams in each facility: (1663 Health workers trained).
  - 1 medical
  - 1 clinical officer
  - 2-3 Nurses, 2-3 Counselors
  - pharmacist/ dispenser
  - lab person
- Strengthening referral network across a continuum
- Improving coordination of stakeholders

#### Coordination of the ART activities

- MoH is responsible for overall coordination with the STD/ACP as the secretariat
- National ART Committee responsible for:
  - Guiding policy and guidelines development
  - Evaluation of the ART programme
- At district level: A coordination team for ART is recommended
- At ART centre level: The health unit-based care team provides and coordinates ART services.

#### Available resources

- Available funds for public sector (50m USD) can support 35,000-40,000 pts for 3 years
  - World Bank MAP Project: 3000 pts for 2 yrs
  - Global Fund for AIDS, TB and Malaria: 30,000 pts in 3yrs
- Presidential Emergency Plan for AIDS Relief (PEPFAR): Targeting 70,000 over 5 years.

#### Other free treatment programmes

- AIDS Health Care Foundation in Masaka, Rakai, Mpigi and Soroti, Kampala
- CDC Tororo Home-based Care Project treating 1200 TASO clients
- MSF - France in Arua (about 2,200 pts recruited)
- GTZ in Fort Portal
- Clinical trials at JCRC, Mulago hospital, Nsambya hospital & MRC in TASO Entebbe and Kyamulibwa

#### Recommendations for starting ART

- Adults and Adolescents with documented HIV infection with:
  - WHO Stage IV disease with any CD4 cell count
  - Advanced WHO Stage III disease with any CD4 count or total TLC. (persistent or recurrent oral thrush and invasive bacterial infections)
  - WHO stage I, II or III with CD4 cell counts  $\leq 200/\text{mm}^3$ .

#### Factors that enabled Uganda achieve its 3 by 5 target

- Strong political will and support
- Substantial support from partners: PEPFAR, World Bank, Global Fund, MSF, AHF, and GTZ etc
- Technical and financial support from WHO
- Large pool of HIV patients who were already accessing care (TASO and other HIV care clinics)
- Commitment by the Ministry of Health and health workers

#### Challenges

- Human resource constraints: increased workload, long lines
- Monitoring of adherence, resistance and toxicity to ART
- Low public knowledge on ART
- Stigma affecting partner disclosure and male enrollment
- Coordination of health care providers and stakeholders
- Sustainability

#### Next steps

- Prepare more health facilities for ART
- Continue to lobby for staff recruitment
- Scale-up community mobilization and sensitization
- Strengthen M&E: establish system for monitoring adherence, resistance and toxicity to ART
- Strengthen coordination within facilities/districts

### **13. The President's Emergency Plan for AIDS Relief by Mr. Bill Fitzgerald US Deputy Chief of Mission.**

#### **Vision**

The Emergency Plan for AIDS Relief will contribute to strengthening national capacity to address the HIV/AIDS epidemic, achieving improved quality of life, equitable access to services, and sustainable systems, within the framework of Uganda's multi-sectoral response.

#### **Objectives**

- Strengthen family and community response for prevention, care and treatment.
- Strengthen national systems and institutions.
- Develop a broad portfolio of quality activities, both proven to be effective and innovative new programs.

#### **Focus on Outcomes and Results**

##### Strategy

- Consult and coordinate with host government, civil society and development partners.
- Ensure consistency with national strategies and guidelines.
- Work with a broad array of partners.
- Seek out new partnerships.

#### **Emergency Plan Country Team**

- Led by Ambassador Jimmy Kolker
- Team Members from:
  - Dept. of State
  - USAID
  - CDC
  - Peace Corps
  - Dept. of Defense
  - National Institute of Health
- Weekly meetings chaired by DCM Bill Fitzgerald to discuss GOU policies affecting HIV/AIDS, identify areas for funding, and collaborate on Country.

#### **Operational Plan and Annual Report**

Funding by Agency, Funding by Program Area

#### **Strategic Approaches: Prevention**

- Abstinence for youth, e.g. PIASCY program, YEAH campaign.
- Improve blood safety/medical injections practices: expand VCT for blood donors, support safe medical waste management.

#### **Strategic Approaches: Treatment**

- Support MOH to develop widespread access to high quality ART care within a sustainable and cost-effective system.
- Work with the MOH and partners to develop quality assurance system for ART

➤ Support a network approach for scaling up in districts; develop links to CBOs & FBOs to deliver elements of care and support adherence.

### **Strategic Approaches: Care**

➤ Expand access to counseling and testing through stand alone centers, outreach, and routine approaches; evaluate and apply innovative approaches such as routine and door-to-door.

➤ Support a network model approach through multiple channels.

➤ Draw on Uganda's network of CBOs/FBOs linked to facilities providing clinical care.

➤ Expand access to basic preventive care.

➤ Cotrimoxazole, safe drinking water, long lasting insecticide treated bed nets, family VCT, links to supplemental nutrition and psychosocial support.

### **Strategic Approaches: Orphans & Vulnerable Children.**

➤ Strengthen national system for technical oversight and grants making under MOGLSD.

➤ Support communities to meet the needs of orphans and vulnerable children – and helping adolescents meet their own needs.

### **2004 Key Results**

➤ Over 26,000 people on ART in 53 sites (30 government, 10 NGO, 13 Faith-based).

➤ Over 300,000 people counseled and tested (tripled from 2003) at 300 sites.

➤ 95,000 women counseled and tested through PMTCT at 147 sites.

➤ Over 300,000 HIV+ individuals receiving non-ART palliative and TB care.

➤ 7,000,000 youth reached with PIASCY prevention programs in school.

➤ 70,000 orphans reached with support.

### **14. Roll Out of ART Reach Out – Mbuya Parish HIV/AIDS Initiative by *Dr. Margrethe Juncker.***

Reach out-Mbuya Parish started in May 2001 with 12 clients and has steadily grown to 1834 active clients as per Aug 2005.

#### **Basic program Statistics:**

About 250 persons per month receive VCT with an initial HIV prevalence of 61% but has declined to 51 %. Their average CD4 count is less than 250 of whom 22 % have less than 100. 50% of the clients need ARVs.

Presently 741 are on ART (70% females): 90 clients on w. DART Study, 90 self sponsored, 465 by PEPFAR/CDC (March 04) and 189 by the Global fund.

The reach out offer a holistic care approach to management of HIV/AIDS in consideration of body, mind (spiritual support), family and community support.

#### Case study

#### History

Ojuk is 32 years old illiterate Christian male from Banda Kampala, initially married with 3 wives of whom two had divorced him. He has 9 Children and caretaker of 2 orphans. They stay 10 people in the house. No history of TB disease or contact. He had been attending an up country hospital where he was diagnosed with HIV and CD4 count of 1, Lumbar test: +++ fungus, normal LFTs. He was started on TDF, 3TC,EFV but discharged 26.1.05 from up-country hospital with 1 month's ARVs plus a request to return when he has funds for chemotherapy (probably for his Kaposi Sarcoma).

*He was enrolled in the program on 11.2.05 and caretaker was his brother.*

He presented at Mbuya with pain, difficult with swallowing, headache, fevers especially at night, cough, chest pain and a big muco-cutaneous KS with hard woody edema of left side of face and a bad smell. Investigations: Sputum: AFB++ , CxR: Indicative of PTB and CrAg: Pos.

Diagnosis: HIV + person previously on ARVs with cryptococcal Meningitis, pulmonary TB and Kaposi Sarcoma. He was enrolled in the program on 11.2.05 and was being looked after by a brother.

**Management:**

Started on Codeine, Fluconazole, anti TB drugs, and continued on ARVs. He was referred to Hospice for Morphine and Mulago Cancer Institute for treatment of Kaposi Sarcoma (he was started on anti cancer drugs). The program visited him in hospital, gave milk and later WFP food (Food was given to his family too). When discharged a Community ARV &TB Treatment Supporter assigned.

The program met costs of transport (including that of care taker), testing, and treatment at Mulago, House rent, some clothes and blankets in close collaboration with his brother.

After about 4 months, the patient significantly improved. His smelling ulcerating ulcer resolved to a small nodule. When he improved, he disappeared but his brother informed us that he went back to the village and is on ARV and TB therapy from nearby local hospital. A transfer letter was written and delivered to him.

Study findings by Reach out.

Summary: A 556 clients were started on ARVs, 46.9 % had CD4<100 at beginning of treatment of whom 75% had CD4 cell counts below 50 cells/mm<sup>3</sup>. Overall cohort survival rate was 85%. Of the 405 clients enrolled between October 2003 and January 2005, adherence was 99.4%. Adherence improved with time over the period the patients were on ARVs.

Challenges faced by reach out program

- Clients are poor, move to get care and have little support away from family.
- Uncertainty of access to ARV providing centers in their home area.
- Most funding is limited to drugs and tests.

**15. Updates on HIV/AIDS Programmes in Arua Regional Referral Hospital.**

PROFILE:

- Arua Regional Referral

- Hospital serves;
- West Nile region and
  - Parts of Democratic Republic of Congo (DRC) and the Sudan.
- Located 504 km from Kampala.
  - The hospital has 399 beds:
    - 270 beds as official bed capacity

#### INTRODUCTION:

Arua Hospital AIDS/HIV Programme (AHAP)  
 Started in 1994 as a branch of The Aids Support Programme (TASO).

It was established with the aim to carry out preventive activities, which include among others Voluntary Counseling & Testing (VCT) and Health Education. The Programme has expanded in activity and geographical coverage to benefit not only the rest of West Nile but also the neighboring countries of Democratic Republic of Congo (DRC) and the Sudan.

#### THE ACTIVITIES INCLUDE:

- 1) Routine Counseling and Testing (RTC)
- 2) Management of OI's
- 3) ART.
- 4) Palliative care and home visiting.
- 5) Human resource development of staff and communities in HIV/AIDS.
- 6) Social support for orphan children.
- 7) PMTCT and MTCT plus.
- 8) Desirable laboratory test including CD4 count.
- 9) Food supplements through World Food Programme (WFP).
- 10) Support supervision in the region.

#### Other Activities:

Peer support by PLWHA groups such as;

- Women groups (NACWOLA, PMTCT, Moslem)
- Men groups (ADMACA – Arua Men Association with AIDS)
- Youth groups

The strategy has been through collaboration and networking with partners such as:

- MSF- France  
 Provision of ARVs, Human Resource, Training, Drugs for treatment of OI's, Infrastructure development, Infection Control.
- AIC  
 VCT Technical Support and Testing Kits
- TASO  
 Funds for social support, home visit, VCT out reaches
- WFP  
 Nutritional support to patients on ARV, TB and PMTCT
- AIM

- Laboratory support and training
- WHO
- Human Resource Development
- Arua Local Government
- Advisory and Supervisory Role
- MOH
- Development of guidelines and policy, Human and Infrastructure Development

Patients according to geographical location attending HIV/AIDS clinic.

- 6,033 HIV+ patients were registered in the HIV/AIDS clinic.
- The majority of patients 4,433 (73.5%) were from Arua district followed by Nebbi 504 (8.4%) and Yumbe had 203 (3.4%) .
- DRC 268 (4.4%)
- Others 625 (10.3%)

Results for VCT Adults

- In 2002, 971 male tested negative and 180 tested positive, 1102 women tested negative and 350 tested positive.
- 2003, 984 male tested negative and 357 tested positive, 1,153 tested negative and 587 tested positive.
- 2004, 2,495 male tested negative and 674 tested negative, 3,370 tested negative and 1,292 tested positive.
- 2005, 1,972 male tested negative and 356 tested positive, 3,039 female tested negative and 671 tested positive.

VCT results for children below 13 years.

- 2002, 26 male tested positive and 95 tested negative, 27 female tested positive and 92 tested negative.
- 2003, 39 male tested positive and 111 tested negative, 31 female tested positive and 114 tested negative.
- 2004, 47 male tested positive and 296 tested negative, 47 female tested positive and 310 tested negative.
- 2005, 38 male tested positive and 223 tested negative, 39 female tested positive and 233 tested negative.

PMCT from July 2002 to Aug 2005.

- 2002, 6,413 new patients enrolled for ANC of these 4,181 were tested and 206 tested positive while 99 negative patients were post counseled.
- 2003, 6,451 new patients enrolled for ANC of these 5,534 were tested and 306 tested positive while 218 negative were post counseled.
- 2004, 6,662 new patients enrolled for ANC of these 5,575 were tested and 287 tested positive while 205 negative were post counseled.
- 2005, 4,902 new patients enrolled for ANC of these 4,061 were tested and 160 tested positive while 154 negative were post counseled.

Adult patients initiated on VCT

- Between 2002 to 2005, a total of 2,497 patients were initiated on ART. Females were 1,498 and 999 were males. Of these 235 patients died.

#### Children initiated on VCT

- Between 2002 to 2005, a total of 112 children have been initiated on ART. Female are 64 and 48 are male.

#### Strengths

- Comprehensive approach has created confidence in HIV/AIDS management.
- Human resource development for the region. (Training of other facilities including Sudan and DRC).
- Strong collaboration and networking with partners
- Free access to ARV's
- Involvement of peer psycho-social groups
- Use of clients as expert patients during training.
- Availability of nutrition support has enhanced adherence to treatment of HIV/AIDS.
- Good community and family link/NACWOLA, ADMACHA, PMTCT support group and increased awareness.

#### Challenges

- Limited manpower
- Poor male involvement
- Limited space
- Inefficiencies in logistics (inadequate HIV testing kits, Reagents for CD4 count)
- Loss to follow up like in DRC & Sudan
- Over dependence on Donors.
- Lack of transport for follow up.
- Burn out (health personnel and careers).

#### CONCLUSION

- Between 2002 to end of August 2005 about 21,372 have attended VCT with HIV seroprevalence of 22% (4,490) positive of those testing with seroprevalence higher in females 25% of (above 13 years) while in PMTCT 5.1% of ANC Clinic mothers were found HIV positive.
- Only 1% of partners tested for HIV, 61 children have been tested since onset of PMTCT in Arua Regional Referral Hospital (above 18 months) of which 59 are negative and 2 positive.
- 68% of patients attending to HIV clinic presented at late stage (Stage III & IV). 63% of patients presented CD4 cell count of  $\leq 200$ .
- 2,497 patients have been initiated on ARVs, 1,940 remain active of this. 1,824 are Ugandans, 104 from DRC while 12 are from the Sudan.
- Monthly enrolment on ART in 2005 has been of 102 person/month. The number of children enrolment on ART is still low (only 4.5%).

The Cumulative Deaths on ART update 9.4% (235) while 274 (11%) have been lost follow up or defaulted and 48 have been transferred to other centers.

#### Recommendation

- Decentralization of ART services to ease the life and improve the quality of care of PLWA by facilitating their access to HIV care in their area of living.
- Equipping other health facilities.
- Advocacy for male involvement.
- Continuity research on ART compliance and resistance studies
- A need for training in Child counseling.
- Enhance information sharing among the stakeholders.
- Improve referrals
- Strengthen the Home base care component
- Training more service providers
- Improving IEC to strengthen the preventive aspect of HIV transmission.
- Establish database for HIV/AIDs activities
- Encourage collaboration and networking and information sharing among stakeholders

#### Acknowledgement

- All staff of Arua Regional Referral Hospital
- MSF- France,
- MOH
- MFP
- WHO and Other Partners who work with us

#### **Session 1V Chairperson Prof. Harriet Mayanja - Kizza**

#### **16. Mulago-Mbarara Teaching Hospitals' Joint AIDS Program (MJAP)**

*By Dr Doris Mwesigire and Dr Cecilia Nawavvu*

#### Introduction

MJAP is joint collaboration of Mulago and Mbarara Teaching hospitals funded by PEPFAR/CDC. Other key partners include MOH, AIDS Control Program, Mulago Hospital, Infectious Diseases Institute (IDI) and satellite clinics.

MJAP provides comprehensive HIV/AIDS care such as RTC, ART, Family based HIV counseling and testing for index ART patients, OI management, TB screening and treatment for TB-HIV co-infected patients, post-exposure prophylaxis, and Training in HIV prevention, care and treatment

#### **Implementation sites**

These include: Mulago and Mbarara teaching hospitals, Infectious Diseases Clinic (IDC) and Kawempe, Naguru, Bwizibwera and Mbarara municipality health centers, HIV/AIDS clinic at Mulago Hospital (Mulago ISS clinic) and Mulago TB-HIV clinic.

Patients identified through HIV testing programs are referred to the above clinics where they are counseled, offered psychosocial support, screened and those eligible are offered ART, OIs treatment and or prophylaxis.

#### **ART and basic care statistics update**

1,413 patients are receiving ART, 900 (64%) at Mulago IDC and 513 at Mbarara ISS clinic. 20 patients have died and three lost to follow-up. 26 patients reported pregnant of whom 9 got pregnant while on therapy. 93% have an adherence score of > 95%. 50% of the patients have reported side effects to ART, although the majority did not warrant therapy switch. Over 400 patients have registered in the satellite clinics and 26 health care workers received post exposure prophylaxis. 2,816 patients in Mulago and Mbarara hospitals have had sputum smears with 17% sputum positive. 7,988 patients are receiving cotrimoxazole prophylaxis.

### **Training Updates**

1,602 health care workers in Mulago and Mbarara hospitals trained in ART, RCT, and HIV basic care. 23,776 patients received health education in Mbarara ISS and Mulago IDC.

### **RTC Rollout: Mulago & Mbarara Hospitals**

RTC was integrated with other hospital activities and has been expanded to 20 units now (12 at Mulago & 8 at Mbarara). All patients including family members of index patients with undocumented HIV status are offered testing with an opportunity to opt out. Rapid testing with same day results is performed. Over 28,000 individuals have been tested since November with an Acceptance rate of greater than > 95% and HIV prevalence of 32%.

HIV prevalence in hospital units ranges from 14%(surgical inpatients) to 37% (Diagnostic testing outpatient). HIV prevalence among paediatric inpatients was 22% but 36% for their mothers. Overall Prevalence Among index Patients and family members are 33% and 29% respectively.

### **Challenges**

- There is Overwhelming unmet demand for HIV testing and the current program covers limited wards (20%). Over 9,000 HIV +ve individuals were identified within 10 months and it is projected that about 10,000 HIV+ will be identified per year. The existing HIV clinics are overwhelmed and ART, basic care supplies, OI drugs and laboratory support and human resources are still limited to handle.

### **Conclusion.**

- MJAP augments HIV/AIDS care & prevention in Mulago & Mbarara hospitals and the satellite clinics. Successful implementation will require continued joint effort between MJAP and its partners.

## **17. Response to HAART Among Children and Adolescents at PIDC, Mulago Hospital, Dr. Addy Kekitiinwa, Clinic Director**

### **Paediatric HIV treatment**

- As usual, paediatrics lags behind adult care and gets much less publicity.
- Most Paediatric data on HIV Treatment is from the industrialised world.
- Paucity of data in the RLS.

- HAART has dramatically improved prognosis in the industrialised world.
- Optimal time to initiate HAART remains unclear.
- No randomised controlled trials.
- Hence use immunological and virological response to HAART according to CD4 and HIV –RNA levels.

### **Current situation**

- 20,000 new infections thru MTCT per year
- 30% require ARV's in 1<sup>st</sup> year (6,000)
- National Children with HIV: 100,000
- National Adult with AIDS: 150,000
- Approx. 10% of these are children

### **Research Setting**

- The PIDC Mulago started operations in 1988
- Runs both screening clinics and clinical care
- Average clinic attendance: 150 patients
- Screening clinic: 300 patients per month
- Average positive for the 0-12 yrs=45% while for the adols =60%)
- Offers comprehensive care: TEN POINT PROGRAM
- Lab services offered include HIV testing for all age groups, CBC, CD4 etc
- Viral loads
- Strict pre ART adherence criteria tool
- Spot on home visits for adherence
- Follow-up of admitted patients

### **Objectives**

- To evaluate the periodic CD4% response to HAART among ART naïve patients (0-15yrs) at PIDC.
- To evaluate the effect of Age, ART regimen, WHO staging and Baseline CD4% to CD4% response to HAART
- To determine the proportion of patients who would have attained a CD4% of at least 25% by 6 and 12 months

### **Methodology**

- Retrospective review of all HAART patients' charts attending PIDC-Mulago
- Data abstracted from the ART naïve patients included:
- Patients age, gender, WHO staging, weight and type of ARV at recruitment on HAART
- CD4 count, CD4%age at baseline, month 6 and 12 months

### **Patient Enrollment**

Patient Enrollment (by 31<sup>st</sup> August 2005)

General Baseline statistics (n=650)

- Average age of children: 8.1 years
- Median age: 7.8 years, range (1 – 15 yrs)
- Female composition: 50.9%

Baseline Immunological and Virologic statistics (n=650)

- CD4%: Median 7.2% (0 –35.2%)
- CD4 Count: Median 234 (1 – 3150)
- Viral Load (n=206): Median 5.5 (2.8 – 5.9) Log10
- Age and Sex Distribution (N=650)
- WHO Stage at Baseline (N=531)

#### Distribution of Patient by ARV Regimen

- 6 Months Cohort (379 Children) CD4% Trend (n=379)

#### Multivariate Analysis

- 12 Months Cohort (128 Children) CD4% Trend (n=128)
- Percentage of Children achieving 25% CD4%
- At 6 and 12 months children had higher CD4% than at baseline, median increase of 4.7 and 2.5 percent respectively.
- 14.7% of the children had achieved a CD4% of  $\geq 25\%$  after 12 months of follow-up.
- Age, baseline CD4% and type of regimen are significant factors associated with response to HAART.

#### Acknowledgements

- All our patients and their caretakers
- All our partners
- Organisers of this meeting

### 18. The Mildmay Centre Uganda by *Ms. Irene Kambonesa*

#### History

Mildmay Hospital was founded in 1866 to fight the cholera epidemic in London, England. The hospital was re opened in 1988 as Europe's first AIDS hospice. In 1993, Mildmay received an invitation from the GOU to visit and subsequently to establish an HIV/AIDS care and training centre that was opened in 1998 as a MOH establishment. Mildmay operates Uganda, Zimbabwe, Kenya, Tanzania and United Kingdom. In Tanzania it works with Elton John Foundation, offers modular training in Kenya and pediatric care in Zimbabwe and Uganda. A needs assessment is planned for Belarus, Ukraine and Russia.

#### The Center's Vision.

Children, women and men living with HIV/AIDS resource limited settings will have access to good quality, holistic and comprehensive care so as to substantially improve their quality of life.

#### Mission

Mildmay will deliver education, training, consultancy and model clinical best practice, which will empower local health care providers to develop primary HIV/AIDS care throughout Uganda, and in the sub Saharan region.

As a Christian organization, the center operative to high ethical standards in all it does and is committed, within the resources available to excellence, innovation, culturally appropriate holistic models of care.

### **Clinical services**

Mildmay is one of the main centres in Uganda providing ART especially to children. In addition to ART, it offers treatment of opportunistic infections, palliative symptom control and rehabilitation.

It uses inter-disciplinary team to address patients' spiritual, physical, social and psychological dimensions. Counseling services, spiritual counseling, physiotherapy, Nutritional advice, occupational therapy, client briefing and Pefar workshops are offered.

The center accesses drugs through Pefar (from March 2004), MOH (from Feb 2005) and some drugs are given free of charge and remainder are purchased via local suppliers.

### **Training**

Objective:

- To use training and education as a means to increase access to quality care adults, children and families infected with or affected by HIV/AIDS here in Uganda, and other parts of sub Saharan Africa.

Training programmes include: short courses (for doctors/clinical officers/Nurses, counsellors, Lab technicians, Religious leaders), clinical placements, and diploma and soon degree in HIV/AIDS care and management. Some local training is done by mobile teams. Key trainees are health care professionals in Africa, MOH, Uganda people defense forces, prison service personnel, and faith based organizations, schools, private companies and other NGOs operating in Uganda.

Other activities include Jajja's Home, Client support (MISCA/LAD) and adolescents' club.

The center has a resources directorate that deals with human resources, finance and accounting and site management. The other directorate is the Quality assurance that does the monitoring and evaluation, IT, data management and public relations.

Partners:

CDC, WHO, Academic alliance, and regional AIDS Training Network (RATN).

### **Success of the center.**

We have excelled because of building on AIDS- related experiences since 1988, recruiting high quality staff, updating staff, functional 5 year strategic plan, reliable funders, working within a structure that allows expansion and growth, setting high standards of operation based on Christian principles of fairness, respect and putting God as first.

The big issues for the year 2004-05 are to increase access to those who cannot pay for treatment, cater for the special needs of orphans and youth growing up with HIV and to scale up expertise throughout the country/region.

## **19. Protocol for the Selection and Evaluation of Herbal Medicines for the Treatment of Opportunistic Infections in HIV/AIDS & other diseases THETA EXPERIENCE by *Dr Alex Opio Chono***

### **THETA's Premise**

To improve access to quality health care for most vulnerable communities through mobilising traditional herbalists (THs) to provide basic HIV/AIDS prevention care and support services in partnership with biomedical health workers.

#### **Key definitions**

1. Traditional Medicine (TM) is indigenous knowledge (IK) used to alleviate all forms of human suffering. This includes various practices like; use of plant products, animal products, minerals, cowry shells, spiritual media etc.
2. A Traditional healer (TH) is a person recognized & respected by his/her community and uses IK handed down from generation to generation to alleviate human suffering.

### **Situational Analysis**

WHO estimates 60-80% of the population in Sub-Saharan Africa consult traditional healers for health and personal reasons independent of socioeconomic or educational status (WHO – Afro report 2001). According to MOH report 2001, TH practices are (not mutually exclusive): Spiritualists (44.9%), Herbalists (42.2%) Bone Setters (33%), Traditional Birth Attendants (12%) and False Teeth" Extractors".

**Common qualities TH and TM:** Accessible and available, their beliefs and attitudes are culturally acceptable, offer affordable and flexible terms of payment, maintain confidentiality.

In Uganda, TH: patient ratio is 1:450 compared to patient: Doctor of 1:20000 (MOH 2001). The community sometimes attributes that some Diseases/conditions can only be managed by TH/TM while some are dissatisfied with the modern health care system.

### **Identification of herbal remedies by THETA**

Theta follows strategic format in identifying herbal medicines. It generates information about potential herbs from their clients such as THs, TMs, community Biomedical health practitioners (BHPs) from the different geographic locations. Ethnographic data is generated through focal discussions, reports, surveys and Key informant interviews (KII). The information is cross matched and initial candidate preparations are identified. Literature review is done about the initial candidate preparations and those with no safety data or low toxicity are subjected to biosafety assays. Those that are reasonable undergo a small clinical observation study involving about 10-15 participants. Any preparation that elicit greater than 70% response or significant p-value undergo a randomized trial, those with 30-70% response get their results documented and may undergo further research using a different criteria and those of less than 30% are documented and shelved.

## **Example of studies done by THETA.**

**A study objectives:** To determine the clinical safety and efficacy of locally available herbs commonly used by healers in the management of pruritic dermatitis in HIV/AIDS.

**Collaborators:** Traditional health practitioners, biomedical health workers from Nakifuma health centre 3, Naggalama hospital, Makerere University Department of Pharmacy and THETA.

### **Methodology**

Stage 1: involved Information gathering in 5 districts that included 68 persons living with HIV/AIDS (PHAs), 164 THs and 30 BHPs . Information was gathered through 22 Focus group discussions (FGDs), 30 KII about skin rash, oral candidiasis, chronic cough and immune boosting.

Stage 2: Cross matching of information and selection of common herbs with reported effectiveness was done. 25 different herbs were reported to be used for pruritic dermatitis of which 4 were selected based because they were more than one location.

Step 3: Composition, dosage and preservation was agreed with THP and batched.

Step 4: Non-randomised, non-placebo controlled, prospective clinical observational study was conducted at Nakifuma Health centre III and Nagalama Hospital in Mukono district. The Study outcome variables were resolution of skin lesions and skin itch. Treatment was initiated at week 0 and stopped at week 4. Participants were followed for 12 weeks.

### **Results**

The study involved 6 and 9 HIV positive men and women aged 25-29yr(2) 30-34yr (6), 35-39yrs (6), and 40-44 yr (1). Most of the skin rashes (54%) were of a mixed picture (bacterial and fungal dermatitis), 38% fungal rash and 7% bacterial.

Progress of the rash over the study period was as in table below:

RASH	Week 0	Week 4	Week 12
Severe	2	0	0
Moderate	9	1	1
Mild	2	11	8
Absent	0	1	4

There was one lost to followed and one death. At week 4, >50% of the patients experienced significant relief of both the skin lesions and itch that was maintained up to 12 weeks. There was remarkable improvement of moderate and severe rashes unlike those with mild/absent baseline rash/pruritus.

### **Challenges**

Lack of Intellectual Property Rights and Traditional Medicine bills. Limited capacity to process and avail standardized herbal preparations and difficulty raising resources for research. Need to adopt credible and affordable research protocols.

### **Conclusions**

Traditional and modern health practitioners can collaborate in conducting clinical observations studies. The preparations can offer an affordable, accessible alternative for

the management of various forms of pruritic dermatitis in PLHAs in Africa. Further research is needed to confirm this finding.

## **20. UGANDA CARES “Program update” by Mr. Bernard Okongo Chief Africa Bureau AIDS Healthcare Foundation**

Uganda Cares is collaboration between the MOH and AIDS Healthcare Foundation (AHF). AHF has activities in other countries like Zambia, Republic of South Africa, Rwanda, Swaziland, India, China, Mexico, Haiti, Honduras, and Ukraine. In Uganda it operates in Masaka, Rakai, Soroti, Mpigi, Mbale, Kampala, with the MOH, local NGOs and Community based organisations.

### Objectives

- Provide standard ARV treatment to socio-economically disadvantaged people living with advanced AIDS.
- Scale up ART in collaboration with national program.
- Identify determinants for treatment success.

### Strategies

- Collaboration with the different partners.
- Location within Regional Referral Hospital/District Hospital.
- Training and logistical support from AHF-GI.
- Strong CBO involvement for referral, psycho-social support and follow-up
- Support from the Ministry of Health.

### **Basic statistics**

#### Demographics of clients:

- Recruitment is randomly done at the different facilities for ARV naïve or experienced patients. The program has 4012 patients. 935 are on TVD, NVP, 315 on TVD, EFV and others on Triomune 30 or 40. In the age group of 19-48 yrs 650 are on TVD+NVP/EFV. Overall the majority of participants are female (81%).

#### Common Monitoring parameters/tools:

- Weight gain average by Karnofsky Performance Score, CD4 counts at initiation (56) and at 80 weeks (308), CBC, Hb, LFTs & RFTs are done on case by case while Viral Load is not usually done. Infections and ART side effects: The most prevalent infection in the cohort is malaria followed by pulmonary tuberculosis, Eosinophilic folliculitis, giardiasis, oral thrush, diarrhoea, Herpes simplex and others.

#### Side effects:

- The most commonly observed side effects are gastro intestinal effects such as nausea, abdominal pain, indigestion, anorexia and vomiting. Others include Headache, insomnia, dizziness, rash, hypnosis, fatigue, lipodystrophy and peripheral neuropathy. The major causes of missing pills for less than 30 days are forgetfulness, lack of transport, travel problems, and being sick. A few (3) that missed for more than 30 days had been imprisoned/ transferred.

ART providing sites:

- Masaka regional referral (RR) Hospital, Rakai District Hospital, Kalisizo Hospital, Lyantonde Hospital, St. Balikkudembe Market clinic, Nkozi hospital, Mbale RR Hospital, Kakuuto Health Centre (HC) IV, Soroti HC Center, AID Child homes, Gombe hospital and Maddu HC IV.

Operational activities include:

- Health care provider HIV training, interviews, ART workshops, patient marches, rallies, patient treatment education sessions, routine counseling and testing, outreach voluntary counseling and testing, training of unemployed health care professional and lay people in HIV management, bicycle distribution, and physical infrastructure development like at Masaka Hospital.

Conclusion

- The Pilot program at Masaka was successful and the collaboration has extended to other districts in Uganda. The experience and expertise is also being shared with other countries in the African region.

## **21. TRAINING OPPORTUNITIES IN AITRP AND ICOHRTA by *Dr. Ezekiel Mupere***

AIDS International Training and Research Program (AITRP) was started in 1988. Following the late Dr. Frederick Robbins visit to Uganda in 1987, International Collaboration for AIDS Research was established between Uganda and CWRU in 1988. Training of Ugandan started in 1989.

### **AITRP mission:**

To train international health professionals in research on prevention of HIV infection.

### **Goals:**

- To train foreign scientists in disciplines necessary for the control of the HIV/AIDS epidemic in developing countries.
- To advance knowledge about HIV/AIDS and related diseases such as STDs, TB, and opportunistic infections.
- To promote international exchange of research findings.
- To enhance technology transfer of essential information and technologies.

The philosophy of AITRP Program based at Case Western Reserve University is to build capacity to deal with HIV/AIDS, operate with institutional support, address substantive problems, train in the context of research or program projects, provide continuity of support to trainees, demonstrate productivity and select motivated candidates.

The program fosters training and research in HIV/AIDS areas such as HIV Vaccine development, natural history of HIV infection, HIV transmission and prevention. Initiative has been undertaken in the fields of HIV virology and vaccine, HIV-TB Interaction, Natural History of HIV infection, STDs diagnosis and surveillance, AIDS Malignancies, Biomedical Ethics, Nursing, Medical Informatics, and pediatrics.

To achieve its goals, the program offers short courses, advanced degrees and PHD in health related areas and Laboratory development. Courses are done US, Uganda and other countries At least 2 Advanced/postdoctoral degrees are offered in some of the following fields Immunology, Biostatistics, Anthropology, Immunology, Health Services Research, Microbiology, Virology and Nursing. Averages of 2 fellows are trained per year and are hoped to be able to train others.

Short courses in the US include Data management, laboratory training, writing sabbatical and other extra-mural courses. In Uganda coherent series of courses on HIV epidemiology, computer (basic and advanced), laboratory training, data management, didactic sessions on HIV/AIDS related topics and international meetings are conducted.

The program collaborates with various Uganda institutions such Ministry of Health, Makerere University Medical School, Mulago Hospital Complex, Joint Clinical Research Center, National Tuberculosis and Leprosy Control Program, National Sexual Transmitted Disease Control Program and Uganda Cancer Institute.

### **International Clinical Operational and Health Services Research on TB and AIDS (ICOHRTA)**

Fogarty International Center (FIC) is building capacity for clinical, operational, and health services research in developing countries.

ICOHRTA program was developed to meet this need in partnership with and developing countries. Training will be offered to scientists from developing countries for 5 years then they would do the training in their countries.

Collaborating institutions are Joint Clinical Research Center (JCRC), Makerere University Medical School, Mbarara University of Science and Technology, Kampala City Council, Institute of Public Health, Case Western Reserve University and University of Medicine and Dentistry of New Jersey

### **Goal of ICOHRTA**

To expand national capacity to address the public health and scientific challenges of the evolving HIV and TB epidemic in Uganda through clinical and field research.

### **Objectives**

- Develop and promote scientific leadership in HIV and TB control
- Provide training for Health Scientists in fields of clinical, laboratory, operational and health services research for HIV and TB
- Build capacity to translate research into Public Health policy that can be evaluated critically.

- Develop the infrastructure and critical mass for clinical, operational, and health services research projects among collaborating institutions
- Stimulate collaboration between HIV programs and TB control programs as well as between these programs and academic and research institutions

#### **Some of the Strategic activities**

- Build expertise in supportive services through workshops, seminars, short courses, and scientific meetings.
- Over 5 years, the program hopes to have built sustainable capacity to evaluate new public health interventions and translate successful ones into public policy for Uganda.
- Present and planned advanced courses include; MS and PHD in health service research, master of business administration, masters in public health and master of medicine.

#### **Trainee selection criteria**

- Demonstrated potential to apply acquired knowledge & skills to HIV/TB prevention, care or treatment after completion of the Degree
- Demonstrated interest in HIV/TB activities or involvement in HIV/TB research & prevention programs.
- Potential to enhance research & public health activities either in health institutions or programs in Uganda after completing the Degree.
- Potential to handle rigorous academic requirements of PG degree program.