Effects of BV-Associated Bacteria and Sexual Intercourse on Vaginal Colonization with the Probiotic *Lactobacillus crispatus* CTV-05

Benjamin Ngugi*[1,2], Anke Hemmerling[3], Elizabeth Bukusi[1], Gideon Kikuvi[2], Joseph Gikunju[2], Stephen Shiboski[4], David Fredricks[5,6], Craig R Cohen[3]

[1]Kenya Medical Research Institute (KEMRI), Nairobi, Kenya; [2]Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya; [3]Department of Obstetrics, Gynecology and Reproductive Sciences, and [4]Epidemiology and Biostatistics, University of California, San Francisco, USA; [5]Fred Hutchinson Cancer Research Center, Seattle, Washington, USA; [6]Department of Medicine, University of Washington, Seattle, Washington, USA

Background: Several fastidious bacteria have been associated with bacterial vaginosis (BV), but their role in BV recurrence and lactobacilli recolonization following antibiotic treatment and application of exogenous lactobacilli under development as probiotics is unknown. We studied the effect of seven BV-associated bacterial species and two *Lactobacillus* species on vaginal colonization with *L. crispatus* CTV-05 (LACTIN-V).

Methods: Twenty four women with BV were treated with a 5-day course of metronidazole vaginal gel then randomized 3:1 to receive either LACTIN-V or placebo applied vaginally once daily for 5 initial consecutive days, followed by a weekly application for 2 weeks. Vaginal swabs for *L. crispatus* CTV-05 culture and 9-bacterium specific 16S rRNA gene quantitative PCR assays were collected at screening, enrollment (2 days after antibiotic treatment) and 28 days after randomization for the 18 women who received LACTIN-V.

Results: Vaginal colonization with CTV-05 was achieved in 44% of the participants at the day 28 visit. Participants not colonized with CTV-05 generally had higher median concentrations of BV-associated bacteria compared to those who colonized. Between enrolment and day 28, the median concentration of *Gardnerella vaginalis* reduced from $10^{4.5}$ to $10^{4.3}$ 16S rRNA gene copies per swab in women who colonized with CTV-05 but increased from $10^{5.7}$ to $10^{7.3}$ in those who failed to colonize (p=0.19). Similarly, the median concentration of *Atopobium vaginae* reduced from $10^{2.7}$ 16S rRNA gene copies per swab to below limit of detection in women who colonized with CTV-05 but increased from $10^{2.7}$ to $10^{6.6}$ in those who failed to colonize (p=0.04). The presence of endogenous *L. crispatus* at enrollment was found to be significantly associated with a reduced odds of colonization with *L. crispatus* CTV-05 on day 28 (p=0.003). Vaginal intercourse during the study significantly impaired successful *L. crispatus* CTV-05 colonization (p=0.018).

Conclusion: Vaginal concentration of *G. vaginalis* and *A. vaginae*, two BV-associated organisms that produce epithelial biofilms, appeared to inhibit colonization with *L. crispatus* CTV-05. In addition, vaginal intercourse during treatment and presence of endogenous *L. crispatus* at enrolment were associated with failure of CTV-05 to colonize the vagina following treatment for BV. Future research on prevention of bacterial vaginosis needs to include a detailed assessment of fastidious bacteria.

High HIV Incidence And Willingness To Use Rectal Microbicides Among Argentine MSM: Potential For Rectal Microbicide Studies

Alex Carballo-Diéguez[1] (presenting author), Ivan Balan[1], Rubén Marone[2], Marian Pando[3], Curtis Dolezal[1], Cheng-Shiun Leu[1], Victoria Barreda[2], María Avila[3]
[1]HIV Center for Clinical and Behavioral Studies at New York State Psychiatric Institute and Columbia University, New York, NY, US; [2]Nexo Asociación Civil, Buenos Aires, Argentina; [3]Universidad de Buenos Aires, Centro Nacional de Referencia para el SIDA, Facultad de Medicina, Buenos Aires, Argentina

Objective. Studies conducted in Buenos Aires, Argentina, repeatedly show high HIV incidence per 100 person years among MSM. Rates were 6.7 in the Vignoles et al. (2006) cross-sectional study that used STARHS, and 3.9 in the Segura et al. (2007) study of a prospective cohort followed up for 12 months (retention: 97.2% at 6 months and 91.5% at 12 months). With prevention efforts limited to condom promotion and no locally developed, proven effective, behavioral interventions, new strategies are urgently needed. We assessed HIV prevalence and incidence and studied acceptability of microbicides among MSM in Buenos Aires.

Methods. 500 MSM were recruited through Respondent Driven Sampling. They provided blood samples and underwent CASI interviewing on microbicide acceptability. HIV-positive plasma samples were tested using a detuned version of an HIV-1 enzyme immunoassay (Vironostika HIV-1 Microelisa System; bioMerieux Inc, North Carolina, USA) to sort out potential recent infections (less than 6 months) from chronic infections using the STARHS strategy. Microbicide acceptability was measured with questions on willingness to use a gel microbicide for anal sex measured on 10-point Likert scales ranging from 1= completely unwilling to 10 = completely willing.

Results. Sample HIV prevalence was 15.7 % (CI: 11.8-20.2), being higher among gay identified men (30.6 %) than non-gay identified MSM (12.9%, χ^2 $p < .001$). When the 85 HIV-positive plasma samples were tested using a detuned version of the HIV-1 enzyme immunoassay, 23 cases were identified as possible recent infections, this yielding an HIV incidence of 11.4 per 100 persons/year. Incidence was significantly higher among gay men (22.6) than non-gay identified MSM (8.3). Concerning willingness to use a gel microbicide during anal sex, although the mean score was 6.0 (neither willing nor unwilling), gay identified men scored significantly higher (7.1, willing range) than non-gay identified men (5.6) .

Discussion. Gay identified MSM in Buenos Aires have high HIV prevalence and incidence and are willing to use gel rectal microbicides. Furthermore, the research infrastructure (i.e., laboratory facilities, demonstrated participant recruitment and retention success, record of scholarly activity of the University of Buenos Aires/Nexo Asociacion Civil, and effective collaboration with international partners) suggests great potential for successful collaborations in Phase 2 and 3 micro trials.

Acceptability Lessons Learned in a Phase 1 Microbicide Trial Involving Product Use During Vaginal Intercourse

Alex Carballo-Diéguez[1] (presenting author), Rebecca Giguere[1], Beatrice Chen[2], Curtis Dolezal[1], Jessica Kahn[3], Greg Zimet[4], Marina Mabragaña[1], Sonia Lee[5], and Ian McGowan[2]
[1]HIV Center for Clinical and Behavioral Studies at New York State Psychiatric Institute and Columbia University, New York, NY, US; [2]Magee-Womens Research Institute, Pittsburgh, PA, US; [3]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, US; [4]Division of Medicine, Indiana University, Indianapolis, IN, US; ; [5]Pediatric, Adolescent, and Maternal AIDS Branch of NICHD, Bethesda, MD, US

Background: Despite limitations imposed by strict study designs, Phase 1 microbicide trials can shed important light on acceptability issues that need attention before product development can advance. As part of a safety and acceptability trial of SPL7013 Gel, known as VivaGel™, we studied the acceptability of three gel products (VivaGel, SP Placebo, and universal HEC Placebo) by young, ethnically diverse women who used them twice daily, including during vaginal intercourse.

Methods: 61 participants ages 18-24 were randomized to use one of three gels twice a day for 14 days. Acceptability data were collected via Web-based CASI and in-depth video teleconferences. Structured assessments used 10-point Likert scales ranging from negative to positive with a middle, neutral point (e.g., 1= Extremely Unlikely; 5= Neither Likely nor Unlikely; 10= Extremely Likely), and were analyzed using ANOVA and chi-square tests.

Results: Participants' average overall rating in response to how much they liked the gel was 6.21, corresponding to neither liked nor disliked. Concerning intentions to use in the future, average scores were 7.48, indicating a likeliness to use in the future. Although in both cases the VivaGel condition scored lower than the two placebo conditions, the differences did not reach statistical significance (p=.892 and p=.710 respectively). Despite these apparently favorable scores, many participants complained about leakage and related problems. In the qualitative interviews, over half of the participants described the gel as "messy," "gross," "disgusting," "slimy," or "cold," while others did not experience discomfort. Almost all participants had to wear pantiliners during the study and change them often. Concerning use of the gel during sexual intercourse, a third of the participants responded positively to the increased vaginal lubrication, but most complained that the gel was "squishy," "unnatural," and "gooey." Those who complained found the gel to be messy and to leak during sex, soiling the bed sheets, themselves, and their partners. Several women complained about not being able to receive oral sex while using the gel.

Conclusion: Participant concerns about gel leakage and messiness during intercourse pertained not only to VivaGel, but also to the universal HEC placebo. Concerns about gel leakage are not new but remain unaddressed. The potential interference with microbicide use in Phase 2 and 3 trials should not be underestimated.

Introduction of a Quality System to On-Site Laboratories at IPM Research Centres

Andries Engelbrecht; Sandra Abrahamse; Mariette Malherbe; Annalene Nel
International Partnership for Microbicides – Paarl, South Africa

Background: Accurate and reliable on-site laboratory testing is imperative for the successful conduct of HIV prevention trials. On-site HIV rapid testing is an essential tool in establishing participant eligibility and end-points for microbicide trials. HIV rapid tests are performed at screening, during the trial and at the end of the trial.

Methods: To ensure the accuracy of HIV rapid test results, a quality system was introduced at 10 research centres (7 in South Africa and 3 in East Africa) focusing on high quality, reliable testing. All research centre staff responsible for HIV rapid testing (nurses and laboratory technologists/technicians) participated in ongoing training sessions on a variety of relevant topics such as introduction to quality systems in HIV rapid testing, internal quality control and external quality assurance concepts. The success of the quality system at each research centre was measured by the centre's performance on an HIV Serology external proficiency testing program. Eighteen blinded samples were sent in three cycles, February, June and October 2009 (6 samples per cycle), to each research centre. The trained staff performed HIV rapid testing on these samples and submitted the results to the service provider.

Results : Seven of 10 research centres scored 100% on all samples tested in each cycle. Two research centres did not submit results for one cycle, but scored 100% on the 2 cycles that were submitted. One research centre scored 83% on one cycle (5/6 samples correct) and 100% in the other two cycles of samples.

Conclusions: Introduction of a quality system at 10 research centres in Africa resulted in almost 100% accuracy on HIV rapid test results as measured by an external proficiency testing program. Although not a perfect measure of quality and competence, this test provides a practical and objective assessment of quality control procedures at research centres. The quality system will be maintained through ongoing training and competency assessments, as well as quality control processes.

Subliming Solids Matrices as a Novel Delivery System for C5A

Richard Maskiewicz[1], Michael Bobardt[2], Charlene Dezzutti[3], and Philippe Gallay[2]

[1]Loma Linda University School of Pharmacy, Loma Linda, CA; [2]The Scripps Research Institute, La Jolla, CA; [3]University of Pittsburgh, Pittsburgh PA.

Background: C5A represents the prototype for a new generation of HIV microbicides since it i) exhibits a broad range of antiviral activity against primary HIV isolates; iii) prevents transmigration of HIV through genital cells; iii) prevents HIV transfer from dendritic to T cells; iv) is potent at a low pH; and v) offers protection in a humanized mice vaginal transmission model. However, C5A has obstacles to overcome. It must achieve long-term protection and coitus-independent administration if it is to become an accepted prophylactic in real world conditions.

Methods: Subliming solids matrices are chemically inactive and continuously hydrophobic, allowing proteins stored within, and releasing from, such matrices to be more stable than when stored in the solid state in moist air. A subliming solids-based delivery system can provide a broad range of release rates and durations independent of the nature (size, hydrophobicity) of drug, and independent of the environment in which the drug is being released. Such matrices release incorporated proteins at the rate at which they sublime, which in turn is determined by mole fraction composition. We formulated C5A in cyclododecane (CD) solid matrices and tested them for cellular cytotoxicity and sustained C5A release with preserved anti-HIV activities.

Results: Subliming CD solids do not exert any cellular toxicity to PBMC and cervical explants. C5A remains constantly released from CD solids over a period of 30 days. Importantly, C5A released from CD solids from day 9 to 30 completely neutralize HIV. CD solids loaded with C5A were kept at room temperature for 3 weeks before use. A same amount of non-formulated C5A placed under similar culture conditions lost its antiviral activity in less than a week, suggesting that C5A formulation into CD solids preserves its antiviral properties.

Conclusions: By showing that subliming CD solids release C5A with anti-HIV activities for a sustained period of time, these promising data serve as a proof-of-concept that the unique attributes of subliming solids-based drug release could offer an opportunity to overcome unresolved formulation problems intrinsic to a large panel of anti-HIV microbicides.

The HIV/STI Risks, Prevention, Treatment Needs of Men (MSM) who have sex with men.

ESTHER WANJIRU GITHAIGA, ORGANIZATION;-BLISSWOMENANDCHILDRENPROJECT and PAUL MOSES MUTIGA, Ambassadors of Change

BACKGROUND – Despite increasing awareness of the role MSM can play in the dynamics of HIV transmission, research on MSM in Kenya has been limited. Understanding sexual behaviors of MSM as a vulnerable population to HIV is an important component in combating the pandemic.
Practice of men having sex with men is often dismissed as un – African, against local culture , viewed with hostility, violence. Evidence shows in both developed, developing countries MSM are at heightened risk of HIV infection.

DESCRIPTION
Contracted 28 MSMs in Nairobi, 4 in Nakuru, undertaking 75 qualitative interviews, 10 in –depth (IDIs) interviews, 2 focus group discussions participants between 14 – 29 years observing confidentiality. Respondents from diverse social economic backgrounds.

KEY FINDINGS – Respondents reported stigma /discrimination a major challenge, barrier to access health care. Conceal their sexual identities fearing humiliation, aggression in public areas. MSM were found likely to engage in unprotected sex.
MSM are not a negligible population (Institute of African studies/UON, Frontiers in Reproductive Health, Horizon Program)

LESSONS LEARNED – MSM live underground because laws cannot protect them, HIV will continue to infect all walks of life.
Law enforcement , stigma /discrimination from health workers, families fuel the epidemic than lead to behavior change among MSM.
MSM have developed strong personal networks – “hubs” i.e informal social groups .in public parks and bars for social mixing, sharing values

RECOMMENDATIONS – Legal reform to create enabling environment for prevention work, access to treatment.
Peer Education offering social support for MSM to adopt HIV/STI protective behaviors.
Increased funding for research on rectal microbicides for anal sex.

HIV PREVENTION-UNCOVERING NEW GROUND'

ESTHER WANJIRU GITHAIGA
BLISS WOMEN NAKURU, CITY-NAKURU, COUNTRY-KENYA; PAUL MOSES NDEGWA, AMBASSADORS OF CHANGE, CITY-NAKURU, COUNTRY-KENYA

BACKGROUND
DEVELOPING A TEENAGE PREGNANCY AND ABORTION PREVETION STRATEGY
Adolescent girls who give birth have a much higher risk of dying from maternal causes compared to older women. Adolescents growing up in resource – poor settings are at heightened risk for negative behavioral and psychological outcomes. Young women are more likely than young men to be HIV-positive. National programs for Youth often overlook the fact that many youth are not with parents with little understanding of mechanisms of life in dense, dangerous urban populations. Adolescent girls experience sexual violence, molestation, coercion and rape with no legal-medical support services including reproductive health. Girls support, safety networks are extremely thin and gender blind.
DESCRIPTION: Qualitative methods, comparative approaches, policy analysis and literature review. Notable publications providing detailed accounts of the many challenges faced by adolescent girls country wide. Survey conducted in Nakuru Town involving 300 adolescents about their sexual behaviors, knowledge of HIV, and pregnancy prevention. Qualitative data collected through group discussions with 14-24years. In – depth interviews with 12-22years, a group rarely targeted in sexual reproductive research.
KEY FINDINGS: Current programming for adolescents and youth is largely gender-blind.

- Significant proportions of the general populations of young people live on less than US$ 1 a day. 19% of youth of 12-16 years do not live with their biological parents.
- Early marriage increase risks of negative reproductive health outcomes.
- Poverty is associated with some risky sexual behaviors.

LESSONS LEARNED:
Protecting the health of young people is an important priority to reduce rates of unintended pregnancy, unsafe abortions. Young people need access to sexual and reproductive health information / services.
RECOMMENDATIONS:
Comprehensive school-based sex education is an effective, efficient way to educate adolescents on sexual well –being.

- Improving adolescent transition to adult-hood with a focus on major societal institutions that influence their behavior e.g. schools, mass media, families and communities.
- Deepen our understanding of adolescent sexual behavior . Youth participation in decision making processes on health policies, action plans.
- Development of support mechanisms to young women who are victims of domestic violence or survivors of sexual violence.

A Prospective Randomized Double Blind Placebo-Controlled Phase 1 Pharmacokinetic and Safety Study of a Vaginal Microbicide Gel Containing 3 Potent Broadly Neutralizing Monoclonal Antibodies (2F5, 2G12, 4E10) (Mabgel)

Georgina Morris[1], Stanley Chindove [1], Sarah Woodhall[1], Rebecca Wiggins[1],Brigitta Vcelar[2], Charles Lacey[1]
1. Hull York Medical School and Centre for Immunology and Infection, University of York, York, UK;
2. Polymun Scientific, Vienna, Austria

Background: In the light of the recent disappointing results in phase 3 trials with polyanionic compounds, alternative, HIV specific agents are under evaluation as potential microbicides. Monoclonal antibodies offer a valuable alternative to antiretroviral compounds and may avoid problems with potential drug resistance. The antibodies 2F5, 2G12 and 4E10 are human recombinant monoclonal antibodies (MAbs) which potently, broadly and synergistically neutralize divergent HIV-1 subtypes. They have previously been administered intravenously to human subjects in high doses with demonstrated safety. When administered intravenously they have also protected adult female macaques against vaginal challenge with SHIV 89.6PD. Therefore this combination of monoclonal antibodies could potentially represent an extremely promising vaginal microbicide for use in women.

Methods: The primary objective of the study is to assess the pharmacokinetics of the specified monoclonal antibody combination when applied vaginally. Specifically: 1)to assess the retention of the MAbs in the vagina after administration; 2)to investigate whether there is any systemic absorption of the MAbs. The secondary objective of the study is: to assess the safety of the specified monoclonal antibody combination when applied vaginally. Target recruitment n = 30. Healthy volunteers aged 18 to 45 years were enrolled after screening if they fulfilled eligibility criteria. Participants were low risk, HIV seronegative females who were sexually abstinent during the dosing period. They were randomized to receive either high dose Mabgel (20mg/g of each Mab), low dose Mabgel (10mg/g of each Mab) or placebo. 12 doses of gel were self-applied by participants once daily over 12 consecutive days. Cervico-vaginal examination and pharmacokinetic sampling was performed at 1 hour, 8 hours and 24 hours post the first dose and at 12 hours and 36 hours post the 12th dose. Additional safety evaluations took place at day 5 to 7 of dosing and in the subsequent menstrual cycle.

Results: To date (April 15th 2010), 37 volunteers have been screened and 19 have been enrolled in the dosing phase of the study. A scheduled blinded interim analysis of data from the first 11 participants for presentation to the independent Data and Safety Monitoring Board for the study has showed the following: Ten of the 11 participants reported at least 1 adverse event. 3 participants accounted for 50 % of all the adverse events. Overall, 31 individual adverse events have been observed, 29 of these were identified to be at least possibly related to the study gel. Among these 27 were mild and 2 were moderate in severity. Both moderate AEs related to non-menstrual vaginal bleeding. 14 AEs were genitourinary (bleeding, itching, discharge, 1 abrasion < 5mm diameter) 3 were gastrointestinal (nausea, indigestion), 5 were headaches, and 5 were haematological. No serious AEs have been reported to date.
Mab levels in vaginal Weck-Cel samples, cervico-vaginal lavage and serum samples are being analysed currently by Polymun Scientific, Vienna using individual ELISA systems for each antibody with internal purified 2F5, 2G12 and 4E10 monoclonal antibodies as a standard. Growth and decay curves will be estimated for each dose. Doses will be compared by repeated measures analysis with log antibody level as the outcome. Pharmacokinetic data will be

available from all time points for presentation at the conference. Results from vaginal flora and acceptability analyses will be presented elsewhere.
Conclusions: This is the first phase 1 trial assessing the topical application of a microbicide containing a combination of potent, broadly neutralizing monoclonal antibodies against HIV-1. These blinded results from a planned interim analysis of the first 11 participants are encouraging and suggest, thus far, that the product is safe. However we await the completion and final analysis of the trial before drawing any firm conclusions.

Natural humic acids as active components for new microbicides

G.V. Kornilaeva[1], E.V. Karamov*[1], I.V. Perminova[2]

[1]D. I. Ivanovsky Institute of Virology, RAMS; [2]Department of Chemistry, Lomonosov Moscow State University

Background

At present there is a large data set on ability of humic substances to induce non-specific immune response in living organisms. In particular, anitiviral activity of humic substances have been shown. However, the reported effects are mostly obtained for synthetic humic substances. Systematic studies on antiviral activity of natural humic materials are missing. The objective of this study was to assess anti-HIV activity of a broad set of natural humic materials. The set of humic materials tested included samples of coal and peat humic and fulvic acids as well as non-fractionated materials and more narrow fractions. All samples were isolated and purified in laboratory conditions using standard protocols of International Humic Substances Society (IHSS).

Methods

Anti-viral activity of compounds was defined in modeling HIV-infection using laboratory adapted HIV-1 strains and T-lymphoblastoid cell lines. The level of virus reproduction in infected cells at presence of tested compounds was detected with p24 HIV-1 antigen ELISA. The cytotoxicity was defined as the viability of cells cultivated at presence of different doses of tested compounds with MTT-test.

Results

All substances tested in this study showed weak cytotoxicity (10-15%) at concentrations 1,0-1,5 mg/mL. While their anti-HIV activities were high enough. The ED50 values ranged from $3x10^{-3}$ to $4x10^{-2}$ mg/mL. The HIV-activity depended strongly on the source and fraction composition of HS.

Conclusions

Given low cytotoxicity and high efficacy of the humic materials, they can be considered as promising group of compounds suitable for further therapeutic developments. Hence, the performed experiments allowed us to propose new natural humic compounds as active and potent agents for microbicide formulations.

Male circumcision as MICROBICIDES technique -a preventive HIV transmission strategy – acceptability study among parents at Dr.Kutikuppala Surya Rao Hospital Visakhapatnam, India

Dr. Kutikuppala Surya Rao, K. Pavan, R.D. Pilli, Davud, Ritu

Background In India male circumcision is a traditional practice among Muslims alone but its acceptability in other religions in general is not known. There is currently no information on the acceptability of male circumcision in India. In the wake of significant role of male circumcision to decrease the risk of HIV transmission, an attempt is made to study the acceptability of male circumcision among Indian parents of male children.

Methods: A cross-sectional study was conducted among a convenient sample of 1000 parents attending a general health clinic at Dr.Kutikuppala Surya Rao Hospital, Visakhapatnam, India during January 2008 to December 2009 after obtaining their consent and approval of relevant ethical committee. In view of superstitions the educational back ground of the parents also studied.

Results: Out of the 1600 enrolled eligible Hindu couples 1000 couples agreed to participate (response rate = 62.5%). 35% (350) of respondent couples had no schooling, (150)15% couples had primary schooling, 250 (25%)couples had high school education 175 (17.5%) couples are graduates 75 (7.5%) couples are post graduates.. After the couples were informed about the risks and benefits of male circumcision, 810 (81%) couples with uncircumcised children told that they would circumcise their sons if the procedure is offered in a safe hospital setting, free of charge, or nominal charges and130 (13%) said they would consider the procedure in due course and 60 (6%) said that they would not consider male circumcision saying that the sexual pleasure will be at hammering due to circumcision.

Conclusion: Since male circumcision has been found to decrease risk of HIV infection among men up to 65% in some studies, it is important to know about the attitude of parents and to determine its acceptability as a potential HIV prevention strategy in India. There is also need to bring awareness about the potential role of circumcision as an HIV prevention strategy among all sections and religions of people. This study found male circumcision to be highly acceptable among a wide collection of parents with male children in Visakhapatnam, India.

A Phase I study of the safety and acceptability of 3% w/w SPL7013 (VivaGel) applied vaginally in sexually active young women (MTN-004)

Ian McGowan*[1], Kailazarid Gomez[2], Patricia Emmanuel[3], Irma Febo[4], Beatrice A Chen[1], Barbra Richardson[5, 6], Marla Husnik[6], Edward Livant[7], Jeanna Piper[8], Clare Price[9], and the MTN-004 Protocol Team.
[1]University of Pittsburgh School of Medicine, [2]Family Health International, [3]University of South Florida, [4]University of Puerto Rico, [5]University of Washington, [6]Fred Hutchinson Cancer Research Center, [7]Microbicides Trial Network, Magee-Womens Research Institute, [8]Division of AIDS, NIAID, NIH, [9]Starpharma Pty Ltd.

Background: The study was designed to assess the safety, adherence, acceptability, and effect on vaginal microflora of VivaGel, a novel dendrimer topical microbicide that inhibits HIV and HSV-2 *in vitro*.

Methods: Sixty-one women aged 18-24 were recruited from three sites in San Juan (PR), Tampa (FL) and Pittsburgh (PA). Participants were randomized 1:1:1 to receive VivaGel (V), VivaGel placebo (VP), or the HEC placebo (HEC) twice daily for 14 consecutive days. Safety endpoints included genitourinary (GU) and/or other adverse events (AEs). Acceptability and adherence were determined by interviewer-administered questionnaires. Changes in vaginal flora were determined from Gram-stained vaginal smears and quantitative vaginal culture.

Results: A total of 22, 21, and 18 women were enrolled in the V, VP, and HEC groups respectively. No Grade 3 or 4 AEs, serious AEs, or withdrawals due to AEs were reported. GU symptoms (1 or more attributed to product use) were reported as follows: V (n=14; 63.6%), VP (n=11; 52.4%) and HEC (n=7; 38.9%) (NS, p=0.3). The prevalence of abnormal pelvic exam findings attributed to product use was similar across all arms of the study. Using pair-wise comparison, women in the V arm had a significantly higher incidence of related GU AEs than the HEC gel (0.197 versus 0.083 per 100 person years respectively; p=0.04). Adherence rates including time on product hold were 77% (V), 95% (VP), and 94% (HEC). Thirty-six percent of women in the V arm reported that they would be very likely to use the gel in the future compared to 48% (VP) and 61% (HEC). Exposure to V and VP resulted in shifts in the vaginal microflora but there was no overall impact on BV as assessed by Nugent score.

Conclusions: VivaGel was generally well tolerated and comparable with the VivaGel placebo, although there was lower adherence and acceptability and a higher incidence of related genital AEs compared to the HEC placebo gel

High Resistance Barrier for Macromolecular CCR5 Inhibitors of HIV-1 Entry

Donald Mosier[1], Rebecca Nedellec[1], Mia Coetzer[1], Michael Lederman[2], Robin Offord[3] & Oliver Hartley[4]

[1]The Scripps Research Institute, La Jolla, CA; [2]Case-Western Reserve University, Cleveland, OH; [3]Mintaka Foundation for Medical Research, Geneva, Switzerland; [4]University of Geneva, Geneva, Switzerland

Background: Small molecule, allosteric inhibitors of CCR5 can select for resistant HIV-1 variants that utilize the drug-bound form of CCR5 as the entry coreceptor, but no resistance to macromolecular CCR5 inhibitors (e.g., PSC-RANTES, 5P12-RANTES) had been reported until the recent publication of Dudley *et al*. One SHIV162P3 variant from one macaque exposed to PSC-RANTES in a preclinical microbicide trial harbored two amino acid substitutions that were reported to confer 5- to 7-fold resistance to PSC-RANTES. This result was surprising since multiple long-term selection experiments in vitro (including the one reported here) had failed to select for resistance to either PSC- or 5P12-RANTES.

Methods: The two "resistance" mutations in the above-mentioned report, K315R in the V3 loop and N640D in HR2 of gp41, were introduced into SHIV162P3. Entry function and sensitivity to PSC-RANTES or the small molecule allosteric inhibitor TAK-779 were assessed by single cycle infection of U87.CD4.huCCR5 or rhCCR5 target cells. We also performed long-term selection experiments with escalating concentrations of the small molecule CCR5 inhibitor maraviroc (MVC) or macromolecular 5P12-RANTES in human PBMC cultures infected with HIV-1 CC1/85, an isolate previously demonstrated to develop resistance to MVC after 16 weeks of selection by increasing concentrations of inhibitor.

Results: The combination of K315R and N640D mutations resulted in no significant change in IC_{50} values for PSC-RANTES or TAK-779 from the SHIV162P3 wildtype (K315, N640) sequence. The long-term selection experiment resulted in >1000-fold resistance to MVC by 16 weeks of virus passage, but only transient 4-8 fold resistance to inhibition by 5P12-RANTES after 28 weeks, followed by loss of virus replication. The highly MVC-resistant viruses were fully sensitive to inhibition by 5P12-RANTES.

Conclusions: These results confirm the high barrier to resistance for macromolecular CCR5 inhibitors that act by occluding viral access to CCR5 and/or sequestering CCR5 at intracellular sites. We were not able to confirm the one report of resistance to PSC-RANTES.
The MVC-resistant isolates had identical mutations to those previously reported by the Pfizer group, suggesting a single pathway to resistance to MVC. There is no cross-resistance between small and macromolecular CCR5 inhibitors. Use of 5P12-RANTES in microbicide products would thus not be affected by prior or contemplated use of MVC as a systemic antiviral agent.

Preventative action against HIV/AIDS in nightclubs frequented by people of Antillean and Subsaharan African origin in France

JP. NGUEYA,

Objective: The objective is to communicate with individuals in nightclubs in order to lay the foundations for a process of behavioural change promoting a rise in standards of health, by giving rise to self-questioning, personal reflection, and dialogue on the topic of HIV/AIDS.

The goal is successfully altering common mindsets and negative ways of thinking with relation to HIV/ AIDS (eg. 'condoms are for white people', 'it takes away sexual pleasure', 'it is only used by ''players''', 'AIDS affects those with few morals').

Methodology: To rally about 15 nightclub operators who have signed a charter; to recruit a prevention 'agent' who is specialised in working with migrant communities and whose mission is, amongst other things, to make the DJs, nightclub operators and staff aware of the topic, to offer preventative advice, to distribute material (condoms, brochures, flyers,..), to always be available to negotiate with the organizers, to respond to questions and to construct networks of contacts (connections, figures of authority, etc.).

In order to achieve these objectives, Afrique Avenir produces specific tools (thanks to the support of its partners: Direction Générale de la Santé, Institut National de prévention et d'éducation à la Santé Le CRIPS île de France, DASS de Paris) and distributes them in these places. We use the following: banners, display shelves, charters, engraved glasses, calendars, postcards, posters, brochures and leaflets and condoms. The messages on many of these correspond to the appropriate local sociocultural realities and mental representations of HIV/AIDS.

Results: Approximately 17-20 events are carried out each month, reaching out to 3500-4000 people. Between 2003 and 2008, the number of African women diagnosed as HIV-positive fell, and among African men, the number stabilised. This seems encouraging with regard to the number of new cases, even though the figures are difficult to interpret.

Conclusion: Despite their different set ups, nightclubs are conducive to preventative action against HIV/AIDS.

HIV DRUG RESISTANCE – CHALLENGES FOR REDRESS

Joseph Ndiritu Ngunju, Paul Moses

BACKGROUND

This paper intends to address critical challenges that compromise increased efforts to combat the development of HIV drug resistance in Nakuru, Kenya. The prevalence level of HIV infections have been reported to have risen to 7.4% (National Aids Control report, 2009) which is alarming. Over 84% of people living with HIV are women and girls of reproductive ages. Married couples have also been reported to have increased cases of infections due to various factors which range from trust, inconsistent use of condoms and sexual pleasure, hence the need for added initiatives to address the challenges leading to increased HIV infections and HIV drug resistance.

METHODS

Identified barriers to HIV testing, access to treatment, adherence through patient survey, focused group discussions and qualitative interviews. Literature review on cases detected with HIV drug resistance, policy analysis on HIV prevention programmes. Assessing impact of outreaches, exploring the extent of private practitioners on HIV treatment and follow-up systems, records maintained at HIV treatment clinics and processes of counseling on testing HIV status and adherence procedures at public /private health sector.

FINDINGS

Barriers identified included shortage of Doctors and Nurses at health settings, time use by health professionals to deliver health within the existing economic context, traditional values, practices and attitudes, lack of an effective drug supply and management system, particularly in rural areas, lack of integrated health services, weak health systems and the community lack power of advocacy.

Ineffective HIV prevention strategies, sharing of HIV drugs among patients, misconception held by communities on power of prayers (worship) which lead to withdrawal from use of ART, lack of capacity among care givers to orphans, irregular CD4 count diagnosis on PLWHAs.

CONCLUSIONS:-

- Need for corroborative approach in HIV treatment between private and public hospitals.
- Social environmental controls of infections.
- Joint approaches to strengthen health systems.
- Address the challenges of health care including HIV prevention strategies for the marginalized groups.
- Demystification of HIV.
- Engaging the community in HIV prevention methods eg use of condoms consistently, Behavior change communication (BCC)
- Expanding the capacity of health workforce to deal with HIV drug resistance.
- Improving supply chain management systems for HIV treatment .

A hard way to evidence : Controversies about male circumcision as HIV prevention

Genevieve PAICHELER-HARROUS
National Center of Scientific Research (CNRS); National Agency for AIDS Research (ANRS), France

Background How has been evidence about male circumcision (MC) accepted within and outside the scientific community? This presentation will review the evolution of the researches on MC from 1989 to 2009, before and after the results of the three randomized controlled trials (RCT) showing a significant protection by MC. The background is sociological, i.e. the social construction of evidence. The RCTs, gold standards of evidence-based medicine, are nevertheless questioned on a scientific basis — as RCTs cannot grasp and control all the possible variables — and on a social basis as well, as MC is linked to a cultural and religious background. Distrust and, at an extreme point, plot theories about MC, are then displayed. In brief, this presentation will be based on a questioning of the nature of evidence in evidence-based medicine.

Methods This presentation is based on an analysis of litterature. I searched in different databases all the articles about MC as potential protection against HIV infection in Africa published in medical and scientific peer-reviewed journals, and the correspondence in reaction to them published in the same journals. The analysis of the articles did consider neither their scientific validity nor the relevance of their methodology. As a sociology of medicine investigation, it considers the authors' objectives and conclusions and it deals with the authors' stances, their evolution and their confrontation.

Results Before and after the three RCTs, we are facing the same questions and controversies about the protective role of MC as if the RCTs are not sufficient to close the debate. What is emphasized is the gap between a controlled investigation and the "real life", between efficacy and effectiveness. In fact, the actors at odds with MC did not change their point of view after the demonstration of its protection against HIV transmission.

Conclusions Evidence is not so clear that there is no room for debate. Many questions remain after the RCTs. Were the investigations relevant ? Was the methodology fit to its object ? Where the relevant variables selected ? All these aspects remain unsolved and are the focus of the controversies. Even if it is acknowledged that the quality of evidence has improved with the RCTs, it is still impossible to get rid of all disinclination. Scientific investigations do not take place in a closed world. They are tainted by emotions, passions, prejudice as scientists belong to a social world beyond their research milieu.

The Effects of Twice-daily use of Either VivaGel, VivaGel Placebo, or HEC Placebo on the Vaginal Microflora

Rabe, L.K[1]., Hillier, S.L[1,2]., Meyn, L.[1], Richardson, B. [4], McGowan, I.[1,3]
[1]Magee-Womens Research Institute, Pittsburgh, PA, USA, [2]University of Pittsburgh, Department of Obstetrics, Gynecology, and Reproductive Sciences, Pittsburgh, PA, [3]University of Pittsburgh, Department of Medicine , Pittsburgh, PA, USA, [4]University of Washington, Department of Biostatistics, Seattle, WA, USA

Background: VivaGel is a polyanonic dendrimer based gel that has anti-HIV activity *in vitro*. The objective of this study was to assess the impact of twice-daily VivaGel use on vaginal microflora.

Methods: Healthy, non-pregnant, sexually active women aged 18-24 were enrolled in a Phase I, double blinded, randomized, controlled comparison with 14 days of twice daily exposure to VivaGel, VivaGel placebo, or HEC gel. Women were recruited in Tampa, FL, San Juan, Puerto Rico, and Pittsburgh, PA and screened for sexually transmitted infections prior to enrollment. Vaginal swabs were collected at enrollment, 1 week and 2 weeks after daily use, and at 1 week after completion of product use for quantitative culture in a central laboratory. Vaginal smears were stained and the flora assessed according to the Nugent criteria. Generalized estimating equations were used to evaluate the marginal effect of gel usage on prevalence and concentrations of vaginal microflora and on Nugent scores.

Results: 58 of the 61 women enrolled had culture results for all 4 visits; VivaGel (n=21), VivaGel placebo (n=21), and HEC placebo (n=16). The prevalence of *Enterococcus* increased significantly after 1-2 weeks among women using VivaGel (OR 2.0, CI 1.1-3.5, P=0.01) compared to baseline and final visit off product, whereas women using either HEC or VivaGel placebo had no change. The prevalence of the following organisms decreased significantly (P<0.02) among women using VivaGel: *Lactobacillus* spp., *G.vaginalis*, and pigmented anaerobic gram negative rods (AGNR). With VivaGel placebo there was a significant (P<0.03) decrease in prevalence of H_2O_2 negative *Lactobacillus*, *G.vaginalis*, non-pigmented and pigmented AGNR. Women assigned to HEC gel had a significant decrease in group B Streptococcus (P=0.001). Women using VivaGel also had an increase of > 1 log in the concentration of *Enterococcus* (P=0.002), Group B *Streptococcus* (P=0.03), and coliforms (P=0.005), whereas women using HEC or VivaGel placebo had no significant increase in these organisms. None of the women had significant changes in Nugent scores of the vaginal flora (P>0.6).

Conclusions: Twice daily exposure to VivaGel resulted in shifts in the vaginal microflora including an increased prevalence and concentration of *Enterococcus*, and increased prevalence of GBS, and coliforms. While there was some inhibition of organisms associated with bacterial vaginosis among women using VivaGel, there was no overall impact on BV as assessed by Nugent score.

Exploring the Vif-ABOBEC3G Pathway as Novel Mechanism to Prevent HIV Sexual Transmission

Brigitte E Sanders-Beer[1], Laurent Pessaint[1], Jack Greenhouse[1], Lu Yang[2], Karen M Watson[2], Robert W Buckheit Jr[2], Tariq M Rana[3], J Victor Garcia-Martinez[4], and Mario Stevenson[5]

[1]BIOQUAL Inc., Rockville, MD, [2]ImQuest BioSciences Inc., Frederick, MD, [3]Burnham Institute, La Jolla, CA, [4]University of North Carolina at Chapel Hill, NC [5]Univ. of Massachusetts, Worcester, MA

Background: APOBEC3G (A3G) and ABOBEC3F (A3F) are expressed in the cytoplasm of various immune cells in the human female reproductive tract and in colorectal tissue, two portals of entry for HIV. A3G and A3F are members of the AID/APOBEC family of cytidine deaminases that introduce lethal hypermutations into retroviral cDNA. Vif counteracts A3G/F by targeting these cellular proteins for ubiquitin-mediated proteasomal degradation.

Methods: The Vif inhibitor, RN-18 was identified from a 30K compound library on the basis of its ability to stabilize A3G in the presence of Vif. Two RN-18 analogs, AE-17 and AE-47, were generated. RN-18 and its two analogs were tested for *in vitro* antiviral activity against a primary HIV-1 subtype B isolate (HT/92/599) and *in vitro* toxicity in human PBMC. Also, RN-18 was tested against subtype A, C, D, E, F, G, and O primary isolates and evaluated against two drug-resistant isolates. A TaqMan RT-PCR was developed simultaneously detecting human and monkey A3G RNA using *in vitro* transcribed human A3G cDNA as standard.

Results: Against the HT/92/599 isolate (B clade), RN-18 had an IC_{50} ranging from 9.8-20.8 μM in PBMC cultures from 4 different donors, AE-47 from 6.0-19.7 μM, and AF-17 had an IC_{50}<50μM in 2 of 4 donors (IC_{50}=29.5-31.4 μM). None of the compounds were toxic to human PBMCs (TC_{50}>50μM). RN-18 was highly active against at least 1 out of 3 strains from clade A, C, D, E, F, and G (IC_{50} ranging from 0.5-7.6 μM, an IC_{50} of <10μM was considered active) but not against two subtype O viruses BCF01 and BCF03. There was minor activity against the O type strain BCF02 (IC_{50}=27.7 μM). RN-18 was active against the protease-resistant strain Merck 144-44, but not against the multi-drug resistant strain MDR769. Moreover, it demonstrated activity against several HIV-2 strains and SIVmac251. A3G cDNA was expressed to variable degrees in monkey vagina, cervix, and uterus. Investigation of expression of A3G in the colon and rectum is in progress.

Conclusions: Vif inhibitors will prevent A3G from proteasomal degradation and create a Vif-minus phenotype at mucosal sites. The broad antiviral activity against viral subtypes that are responsible for the majority of mucosal infections worldwide, as well as the expression of A3G in tissues involved in mucosal transmission, support the notion that Vif antagonists, such as RN18, are a potential new class of agents that can be used to prevent mucosal HIV transmission.

The Impact of a Prescription-Only Microbicide on Women's Access in Urban South Africa.

Fern Terris-Prestholt[1], Catherine Macphail[2], Helen Rees[2], Charlotte Watts[1]
1. Social and Mathematical Epidemiology (SAME), London School of Hygiene and Tropical Medicine, UK
2. Reproductive Health and HIV Research Unit, South Africa

Background
With first generation microbicides, there was great hope for an over-the-counter (OTC) product that could be widely distributed and easily accessed outside of health services. Current microbicides in the pipeline are largely ART based and will need to be distributed through health care facilities or pharmacies on prescription. This study looks at women's preferences for different distribution channels to consider the impact of restricted prescription only products in Johannesburg, South Africa.

Methods
A discrete choice experiment was administered to 1017 adult sexually active women in three Johannesburg townships to estimate their preferences for different distribution strategies and predict uptake through each channel (Clinic, Pharmacy, Supermarket, Spaza (township cornershop). Also elicited were women's preferences for how they would be advertised (HIV prevention, pregnancy prevention, enhanced pleasure, women's empowerment).

Results
This study showed that the distribution channels were very important to women. Given the choice of these four channels, 33% would collect from a pharmacy, 32% from a clinic, 20% from a supermarket and 16% from a spaza. Even with restricted, prescription-only access, 65% of women would still be able to access product through their preferred outlet. This was fairly robust across different groups of women (cohabiting, socio-economic status, and employment status). When removing OTC distribution outlets, 49% preferred clinic and 51% chemist distribution, with clinic appealing slightly more to lower SES and unemployed women. We are unable to predict the proportion of women who would no longer access microbicides without the OTC outlets, nor account for reduced uptake of 2nd generation due to required and repeated HIV testing. The type of promotional messaging used was also important, with 'enhanced pleasure' generally least and 'women's empowerment' most liked; preference heterogeneity was identified, suggesting a potential for market segmentation to increase overall uptake.

Conclusions
Though OTC distribution of microbicides was preferred by a third of the participants, the remaining two-thirds would still have access through their preferred channel if it were introduced as a prescription-only product. It will be very important to include both clinic and chemist distribution as together they are likely to provide good access for both higher and lower income women in urban South Africa.

Potential impact of circumcision on herpes simplex virus type 2 prevalence among spouses in five northeastern states of India

K Walia[1] B. Borkakoty[2], D. Biswas[2], J. Mahanta[2]; 1INDIAN COUNCIL OF MEDICAL RESEARCH , NEW DELHI -
110029, DELHI/IN 2 Regional Medical Research Centre for NE Region,
ICMR, Virology, Dibrugarh, ASSAM/IN,

Background
Herpes simplex virus type 2 (HSV-2), the most common cause of genital ulcer disease worldwide has shown increasing evidence to have synergistic activity on human immunodeficiency virus (HIV) acquisition by two fold or more. So, there was a need to know the prevalence of HSV-2 to develop intervention strategy especially in the high HIV prevalent states of northeast India. A study was therefore conducted among antenatal women to assess the prevalence of HSV-2 infection as well the role of spouse's circumcision on HSV-2 prevalence.

Methods
A total of 1640 antenatal women from five different northeastern states of India, namely Assam, Arunachal Pradesh, Manipur, Meghalaya and Mizoram with diverse ethnic background were enrolled after informed consent. They were screened for IgG antibody status against HSV-2 using HerpeSelect 2 ELISA IgG kits form Focus Diagnostics, USA. A structured questionnaire was used to evaluate different risk variables.

Results
The median age of the subjects was 24 years (SD±4.8) with inter quartile age of 22-28 years. The overall prevalence of HSV-2 (IgG) positive was 8.6%, while prevalence was highest in Arunachal Pradesh (15%) and was lowest in Manipur (2.74%). There was a significant association of HSV-2 infection with history of vaginal discharge with pelvic pain (p=0.0001) and genital ulcer (p=0.02). Regular condom user's had a low HSV-2 prevalence of 1 % compared to 10.3 % in infrequent or non-condom users (OR=11.1, 95% C.I.= 3.5 – 35.2, p<0.0001). HSV-2 prevalence was 1.7% in women with circumcised spouses compared to 9.2% among uncircumcised spouse (OR= 5.7, 95% C.I.=1.4- 23.4, p=0.01).

Conclusion
The study documented a variable difference of prevalence of HSV-2 among the different states of northeast India. The independent association of spouse's circumcision with HSV-2 sero-status in pregnant women documents the role for circumcision in decreasing the transmission of HSV-2 in the community. This is the first study from India that substantiates the usefulness of circumcision as a modifiable preventive measure in Indian settings that can be utilized to prevent the spread of HSV-2 which may also have a role in lowering transmission of other STIs and HIV prevalence in the community.

Developing Strategy Responses to HIV Transmission among Adolescents Through Community Engagement.

Julie Wangui, Gladys Wanjiru Nganga

BACKGROUND: Over 84% of people living with HIV/AIDS in Kenya are Women and girls of reproductive ages due to biological factor, cultural background and gender inequalities./

METHODS: literature review, a randomized community survey on HIV surveillance methods, group discussions engaging 147 girls and 29 boys between ages 12-24 years. Designed methods for interventions to reach young girls consistent with cultural traditions in KENYA.

RESULTS: Most young people preferred private clinics for HIV testing and services including when they needed reproductive health care.

- Pregnancy and child birth are vulnerable periods of reproductive ages
- Inconsistent use of both female and male condoms among the youth.
- Matters related to sex including abortion are kept secret and underreported
- Women and girls have no decision making power over sex and family planning.
- Inadequate knowledge among the youths on HIV prevention methods and use of PEP(Post –Exposure prophylaxis).

CONCLUSIONS -Develop youth friendly programs to reduce stigma related to HI
-Engage the community to promote a safe and supportive environment
- Establish accessible and youth friendly VCT and increased post test services focusing on the most vulnerable out-of-school girls in urban areas including domestic workers
-Designing comprehensive post repair programs linking the community with health sector for PEP management and counseling services.
- Encourage discussions between parents, teachers and adolescents on matters of sexuality
-Develop accurate and appropriate messages on HIV modes of transmission “Beyond ABC” methods.
-Challenge deeply rooted cultural believes, attitudes, myths and taboos related to reproductive health.

Safety and Acceptability of Vaginal Ring as Microbicide Delivery Method in African Women

Cynthia Woodsong[1], Ariane van der Straten[2], Gilead Masenga[3], Helen Rees[4], Linda-Gail Bekker[5], Shay Ganesh[6], Katherine Young[1], Joseph Romano[1], Annalene Nel [1]

1. International Partnership for Microbicides, Silver Spring, Maryland, USA
2. Research Triangle Institute, San Francisco, USA
3. Kilimanjaro Christian Medical Centre, Moshi, Tanzania
4. Reproductive Health and HIV Research Unit, Wits University, Johannesburg, South Africa
5. Desmond Tutu HIV Foundation, Emavundleni, Cape Town, South Africa
6. Medical Research Council, Durban, South Africa

Background
Vaginal rings are being explored as a potential delivery method for microbicides to prevent HIV infection. Rings offer the advantage of monthly instead of daily use, which may increase product adherence and therefore effectiveness. Since vaginal rings are not widely used in African countries, safety and acceptability of this method were assessed.

Methods
A safety study of a placebo silicone elastomer vaginal ring was conducted among healthy, sexually active women 18-35 years of age at 5 sites in Africa. 3 sites in South Africa and 1 in Tanzania completed the study. Women were randomized to 3 months of ring use and 3 months of observational no-product use, in a crossover design. Women responded to an acceptability and adherence questionnaire at 5 points during the study. Safety was assessed by pelvic/speculum examination, colposcopy and adverse event monitoring.
Results

152 of the 170 women enrolled at 4 sites completed. No ring-related SAEs were reported; 22 women reported possibly/probably related AEs. Genital AEs were equally distributed between ring and no treatment arm. No safety concerns were identified. More than 90% women reported liking the ring, felt it was comfortable and easy to insert; and liked that it did not alter sexual experience. Awareness of the presence of the ring decreased over time. A minority of women experienced either spontaneous ring expulsion or removal for cleaning during the trial which decreased over time.

Conclusions
Use of a silicone vaginal ring for 3 months was safe and acceptable to African women. The observed rate of expulsion was less than reported with other vaginal rings, but participant removal of the ring for cleaning may indicates a need for enhanced adherence counseling.

Partner HIV Testing as a Strategy for Recruiting HIV Serodiscordant Couples into an HIV Prevention Clinical Trial: Experiences from the Partners Center, Tororo, Uganda

Aloysious Kakia* [1], Richard Businge[1]
[1]The AIDS Support Organization, Tororo, Uganda;

Background: Partners Center Tororo is affiliated to The AIDS Support Organization (TASO); it is one of 9 sites in Uganda and Kenya implementing the Partners PrEP Study, a phase III randomized trial of antiretroviral pre-exposure prophylaxis (PrEP) for HIV prevention. Our site recruitment goal is 500 HIV-1 discordant couples over 2 years. The site works closely with the local TASO center and several VCT sites, and has implemented partner HIV testing, a new approach to identifying serodiscordant couples.

Methods: We identified HIV+ individuals in the TASO Tororo client database who were not on ART and had partners with unknown HIV status; we also gave talks at TASO clinics. TASO counselors, field officers, nurses and community volunteers contacted those identified at their homes. They were told about discordance and the importance and availability of testing their partners for prevention and care. With their permission, we offered their partners an HIV test. All staff involved in tracing and testing had training in home-based HIV testing. Confidentiality was upheld. Couples found to be serodiscordant were told about the Partners PrEP Study; those interested were referred to the study site for screening.

Results: 99% of the partners approached accepted an HIV test. Of these, 64.7% were female, 81.5% were negative. Between Nov 2008 and Nov 2009, a total of 645 HIV discordant couples were screened and 385 enrolled into the Partners PrEP trial at our site. Of those HIV discordant couples screened for eligibility, 345 (53.4%) were identified through the partner testing strategy; 121 (18.7%) from couples tested at VCT centers; 99 (15.5%) from a pool of discordant couples already known before the trial began. The remaining strategies contributed 12.4%. Costs up to the time of screening included allowances for the staff and community volunteers, fuel for the site vehicles, transport refund to couples on screening day. Total costs were $37 for the partner testing strategy, $37 for testing at VCT centers and $100 for couples from the pool of previously known discordant couples.

Conclusions: Multiple concurrent strategies are needed in order to recruit high numbers of eligible serodiscordant couples into clinical trials. Confidential, voluntary HIV testing of partners of HIV+ people whose serostatus is not known is an efficient way to identify HIV serodiscordant couples for HIV prevention trials, and for future implementation of effective HIV interventions.

Need For Positive Responses in The Struggle To Reduce HIV Drug Resistance – A case study in Nakuru , Kenya.

ESTHER WANJIRU GITHAIGA, – BLISS WOMEN AND CHILDREN PROJECT
MOSES NDEGWA MUTIGA, – AMBASSADORS OF CHANGE, NGO

BACKGROUND
HIV drug resistance in Kenya is now complicating management of HIV/AAIDS infections among patients posing a major threat to scaling up of anti retro viral therapy (WHO/UN P rogramme on HIV/AIDS "3 by 5" initiative)

Inadequate clinical and biological follow- up has been linked to high rates of drug resistance (>50% after 8 to 20 months)

Most HIV drugs are reportedly lacking in most public health care centers particularly the far to reach population in rural areas
Shortage of health care workers also contribute significantly to lack of essential information required by HIV positives /

METHODS
Qualitative research ,in- depths interviews among people living with HIV,health providers both in the public and private health sector .Literature review, visits to VCTs and HIV treatment clinics in the country and reproductive health centers

RESULTS
From 84 HIV- 1 plasma samples successfully analyzed 1.9 drug resistance was detected specifically Nevirapine (1.3 %) at G98A 2.60% , K103E (1.3%) and L 100F (3.7%) mutations.

HIV drug resistance among HIV – 1 positive drug naive persons is at low thresholds .Patients sharing drugs due to stigma prevalence level cost of laboratory expenses on diagnosis ,cost of transport to and from hospitals ,stigma in health settings all contribute to non -adherence to HIV treatment . Lack of government political will to increase national budget allocations for health targeting HIV prevention methods and treatment create barriers to universal access to quality treatment

CONCLUSIONS
Need for a screening policy for HIV drug resistance prior to treatment and patients already on ART with suspected ARVs.
Designing large ,effective ART programmes on drug resistance
Planning and working on a plan to replace drugs e.g stavudine which causes HIV patients to loose their body fat(Lipostrophy) and revised national guidelines in line with the World Health Organization Recommendations.