# Monday, November 19, 2007 – 11:15 a.m.

## Beyond HAART

### 101

**DIETARY INTAKE AND PHYSICAL ACTIVITY IN A CANADIAN POPULATION SAMPLE OF MEN WITH HIV INFECTION AND METABOLIC ABNORMALITIES**

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**Plain Language Summary:** Metabolic problems (high blood sugar or lipids, fat redistribution) are common in patients with HIV, especially under antiretroviral therapy. These metabolic abnormalities can be influenced by diet and exercise. Therefore we measured body mass index, dietary intake and physical activity in men with HIV and metabolic problems living in the Greater Toronto Area and compared the data to Canadian recommendations. We found that most of the patients were overweight or obese, even though they did not report high energy intakes, and more than 80% exercised enough when compared to the recommendations of Canada's Physical Activity Guide. However, their diets were often high in fat, cholesterol, and sodium, and low in fiber, vitamin E, magnesium, and other micronutrients. We conclude that nutrition counseling is important for patients with HIV and metabolic problems.

**Objective:** To assess nutritional status, including dietary intake and physical activity in a Canadian population sample of men with HIV and metabolic abnormalities and to compare the data to Canadian recommendations.

**Methods:** Sixty-five HIV-infected men with at least one feature associated with the metabolic syndrome (insulin resistance, dyslipidemia, central obesity, or lipodystrophy) were enrolled. Results from 7-day food records and activity logs were compared to the Dietary Reference Intakes and recommendations of Canada's Physical Activity Guide, respectively. Anthropometric data were also measured.

**Results:** Fifty-two percent of the subjects were overweight, another 15% were obese. However, energy intake (mean±SEM) (2153±99 kcal/d) was lower than the estimated requirement (2854±62 kcal/d; $p<0.0001$), and 85% of the patients reached the recommended daily minimum of 60 minutes of mild or 30 minutes of moderate exercise. Most time was spent on mild activities, but 81% engaged also in moderate to very strenuous activities. Intake was adequate for protein, but high for fat and cholesterol in 40% of patients. No patient reached the recommendation for fiber. Intake from diet alone was suboptimal for most micronutrients. Prevalence was highest for low vitamin E (91% of the patients), magnesium (68%), folate (46%), vitamin C (39%), and zinc (43%) intake, and high sodium intake (72%).

**Conclusions:** A large proportion of HIV patients with metabolic abnormalities were overweight or obese. This was not associated with high energy intake, or reduced physical activity. However, high fat and low fiber intake as well as inadequate micronutrient intakes was prevalent. Therefore, nutrition evaluation and counseling should be an integral part of the care for HIV patients with metabolic abnormalities.

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### 102

**POST VACCINATION HBSAB TITRE IS THE MAJOR FACTOR ASSOCIATED WITH LOSS OF PROTECTIVE LEVELS OF HBSAB AFTER SUCCESSFUL HBSAG VACCINATION AMONG PERSONS WITH HIV**

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**Plain Language Summary:** Co-infection with both Hepatitis B Virus (HBV) and HIV leads to increased liver-related mortality among persons living with HIV. The HBV vaccine provides an opportunity to prevent HBV and it is recommended that this vaccine be provided to all persons with HIV at risk of acquiring HBV. Case reports indicate that protection against HBV may wane after successful HBV vaccine leading to susceptibility to HBV if exposed. This project evaluates factors associated with loss of immune protection after successful HBV vaccination. The major factor associated with loss of protection from HBV is low levels of HBV antibodies measured after HBV vaccination.

**The Challenge:** To determine factors associated with loss of protective levels of HBV surface antibodies (HBsAb) among those who had HBsAb seroconversion in response to the recombinant HBV surface antigen (HBsAg) vaccine.

**Our Approach:** Retrospective cohort study involving two large urban immunodeficiency clinics. Inclusion criteria included: HIV positive, documentation of at least one dose of recombinant HBsAg vaccine after HIV diagnosis, vaccination between January 1, 1998 to June 1, 2005, and HBsAb seroconversion. Individuals were excluded if chronically HBV infected. Saved HIV VL specimens were tested to determine past HBsAb levels. Potential factors associated with loss of protective levels of HBsAb included: Age, gender, duration of follow-up, presence Hepatitis C Virus antibodies, suppressed HIV VL at time of vaccination, CD4 cell count >= 350 cells/ml at time of vaccination, having received at least 3 doses of the HBsAg vaccine and post vaccination HBsAb titres.

**Key Findings:** Post vaccination serology was available on 83 participants. Forty-three had evidence of HBsAb seroconversion and 9 (20.9%) lost protective levels of HBsAb. The only evaluated factor associated with loss of protective HBsAb is post vaccination HBsAb titres. Of participants with a post-vaccination HBsAb titre >= 100 IU/ml none lost protective levels of HBsAb compared to 9 of 21 (42.9%) with HBsAb titres < 100 IU/ml (chisqr, $p = 0.008$).

**Impact on Policy and Practice:** Findings should be interpreted with caution based on the small samples size. Regardless, our findings suggest that among persons with HIV those with a post-HBsAg vaccination HBsAb titre of less than 100 IU/ml be monitored closely for loss of protective level of HBsAb. Based on the persistence of protective levels of HBsAb among those with HBsAb titres of greater than 100 IU/ml serial monitoring of HBsAb levels is likely unnecessary.

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## 103

### GASTROINTESTINAL IMMUNE RESTORATION AND HIV PROVIRAL LEVELS AFTER LONG-TERM SUPPRESSIVE HIV THERAPY

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**Plain Language Summary:** The Gut-Associated Lymphoid Tissue (GALT) is the largest lymphoid organ in the body, housing almost 80% of the total immune cells. Following HIV infection, unlike the slow decline of CD4+ T cell populations observed in blood, CD4+ T cell depletion in the GALT occurs very rapidly, with the disappearance of almost 95% of GALT CD4+ T cells within two weeks. While highly active antiretroviral therapy (HAART) results in the reconstitution of CD4+ T cell populations in blood; reconstitution in the GALT appears to be delayed and/or suboptimal. Since immunodepletion in the GALT may pave the way for progressive HIV immune dysfunction, we evaluated the impact of long term (over 4 years) highly suppressive (always undetectable) HAART on CD4 T cells in the GALT.

**Objective:** To evaluate the impact of long-term completely suppressive HAART on immune reconstitution in blood and the GALT.

**Methods:** Blood and sigmoid colon biopsies were collected from 16 HAART-treated individuals with a persistently undetectable blood HIV RNA load (<50 copies/ml) for at least 4 years. T cell phenotype/function were examined in cells isolated from peripheral blood and the GALT by flow cytometry. HIV proviral DNA was quantified by PCR in purified CD4+ T cells.

**Results:** CD4+ T cell proportions were consistently higher in GALT than in blood (55% vs. 45%, p = 0.004), and were not correlated with proviral load at either site. HIV proviral load was higher in GALT than in blood (mean 3809 vs. 1856 copies/million CD4+ cells, p=0.03), and correlated with levels of gut CD8+ T cell activation (r=0.9, p=0.007). Gastrointestinal HIV Gag-specific T cell responses did not correlate with proviral DNA levels or mucosal activation.

**Conclusions:** In this unusually highly-suppressed population, HAART was associated with complete CD4+ T cell reconstitution in GALT. However, the HIV reservoir remained higher in GALT than blood, and was linked to gut mucosal immune activation.

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### METABOLIC COFACTOR SUPPLEMENTATION DOES NOT IMPROVE LACTATE METABOLISM IN HAART-TREATED PATIENTS WITHOUT SYMPTOMATIC LACTIC ACIDOSIS

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**Plain Language Summary:** Life threatening lactic acidosis is a rare complication of antiretroviral treatment for HIV, but many more patients show long term, asymptomatic elevations in blood lactate levels. This is thought to be a result of drug induced mitochondrial toxicity. Supplementation with riboflavin, thiamin and L-carnitine has been shown to improve outcome in patients with severe lactic acidosis, so we studied the effects of these supplements in HAART-treated patients. Unexpectedly, subjects showed a decrease in lactate clearance and no apparent change in lactate production. Further research is required before these supplements are recommended for prevention or treatment of asymptomatic elevations in blood lactate.

**The Challenge:** Treatment with metabolic cofactors has been shown to improve outcome in patients with life-threatening lactic acidosis. It is thought that cofactor supplementation alleviates drug-induced mitochondrial toxicity, thus decreasing lactate production; whether this occurs in patients with chronic asymptomatic hyperlactatemia is unknown. Our study investigates the effect of treatment with L-carnitine, riboflavin and thiamin on lactate production and metabolism in HAART-treated patients without symptomatic lactic acidosis.

**Our Approach:** We studied lactate metabolism in 10 HIV+ patients on HAART before and after 4-6 weeks of supplementation with metabolic cofactors. An exogenous lactate challenge test (ELCT) was administered on both visits. Blood lactate values were measured for 135 min following the start of infusion to determine lactate clearance. Lactate production was then measured via a forearm ischemia test. Peripheral blood mononuclear cells were also assayed for mitochondrial DNA and RNA content.

**Key Findings:** Following supplementation, area under the lactate curve during ELCT increased while clearance decreased (pre-treatment 16.43±4.0 ml/kg*min, post-treatment 12.08±2.6 ml/kg*min, p<.01). Peak lactate values during the lactate challenge increased (pre-treatment 7.6±0.97 mmol/L, post-treatment 8.6±1.2 mmol/L, p<.01). There was no change in lactate production during forearm ischemia; however, a trend toward increased mitochondrial DNA and RNA content was observed.

**Impact on Policy and Practice:** Our preliminary results suggest that cofactor supplementation in HIV subjects without symptomatic lactic acidosis does not reduce lactate production during exertion and decreases clearance of an exogenous lactate load. One possible explanation is that L-carnitine supplementation may improve insulin sensitivity, increasing glucose disposal and overwhelming the metabolic capacity of the liver to clear the lactate load in subjects with impaired liver function. Further research is required to determine whether cofactor supplementation is safe or effective for use in HAART treated patients to prevent and/or treat asymptomatic hyperlactatemia.

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## Women and Biological Vulnerability

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**ACTIVATION OF ANTIVIRAL IMMUNITY BY TLR LIGANDS LEADS TO PROTECTION AGAINST HSV-2 INFECTION IN PRIMARY GENITAL EPITHELIUM OF WOMEN**

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**Plain Language Summary:** The mucosal lining of the body provides a protective barrier to internal organs including the lungs, gut and genital tract. Epithelial cells that line the mucosa express receptors called Toll-like receptors (TLRs), that activate cells to make defensive factors that can kill the microbes. We used a novel strategy of boosting the natural defensive responses of epithelial cells to protect against sexually transmitted viruses. Molecules that mimic parts of microbes were used to attach to TLRs on epithelial cells, grown from reproductive tracts of women, to show that this can protect these cells against herpes infection. Similar approaches are being used to show protection against HIV-1. This may be a new and unique alternative to topical microbicides that uses body's own defense mechanisms.

**Objective:** To determine whether treatment of primary genital epithelial cells with TLR ligands protects against infection with sexually transmitted viruses.

**Methods:** Genital tissues were obtained from women undergoing hysterectomies. The epithelial cells were isolated from tissues and grown on transwells. Epithelial monolayers were then treated with different TLR ligands including Peptidoglycan, Lipoteichoic acid, Poly I:C, LPS, flagellin, and three different CpG oligos for 24h and then infected with HSV-2. HSV-2 viral loads, Type I Interferon, Nitric oxide, inflammatory cytokines and intracellular viral activation pathways were measured after ligand treatment.

**Results:** Primary epithelial culture model has provided us with useful information regarding the susceptibility of genital epithelium to HSV-2. Peptidoglycan and Lipoteichoic acid (TLR-2 ligands) provided 56% and 49% protection, respectively, against HSV-2 infection. Poly I:C, a TLR3 ligand provided the best protection (99.5%) against HSV-2 infection. TLR4 ligand LPS failed to provide any protection. Flagellin, a TLR5 ligand provided 80% protection. All three types of human CpG oligos, A, B and C (TLR9 ligands) were tested and found effective in providing different degrees of protection against HSV-2 infection in GECs. The antiviral effect of these ligands correlated with Type-1 IFN and NO production by epithelial cells following treatment with TLR ligands. Inflammatory cytokine secretion, including IL-1beta, IL-6 and TNF-alpha were induced following Poly I:C treatment but not other TLR ligands. TLR activation by Poly I:C led to IRF-3 activation and translocation in primary genital epithelial cells.

**Conclusions:** Anti-viral responses induced by TLR activation in GECs may provide a unique alternative to topical microbicides by enhancing body's own innate defense mechanisms against sexually transmitted viruses.

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### 106

**THE HIV-1 GP41 EPITOPE QARILAVERY ELICITS A HIGHER SYSTEMIC AND MUCOSAL IGA RESPONSE THAN THE MPR EPITOPES**

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**Plain Language Summary:** Providing effective mucosal protection is a key objective of future HIV vaccine strategies since HIV is primarily a mucosally transmitted disease. IgA is a crucial component of mucosal protection, therefore it is important to identify and include IgA-eliciting epitopes in vaccine constructs to confer optimal protection. We have shown that an epitope on HIV-1 gp41, QARILAVERY elicits a greater IgA response than the MPR epitopes that have received much attention. This novel epitope is a good candidate to be included in mucosal vaccine strategies against HIV-1.

**Objective:** The peptide QARILAVERY is located on the N-terminus of gp41 of HIV-1 and is highly conserved across HIV-1 clades. It was found to be the target of serum IgA isolated from HIV exposed uninfected individuals by Clerici et al (2002), with neutralizing ability. The objective of this study was to determine the capacity of this peptide to generate systemic and mucosal IgA and IgG in a mouse model.

**Methods:** The peptide sequence GIKQLQARILAVERYLKDQQLLG was inserted in triplicate into the gag gene (p55) of HIV-1 clade A at the C-terminus prior to the stop codon. The Gag+epitope construct was cloned into pcDNA3.1 to generate a DNA vector (pSJ8), and into a replication defective adenovirus vector (rAdSJ4). Female C57bl/6 mice were immunized with a heterologous [pSJ8+CpG] prime intra-muscularly (i.m.) followed by an intranasal (i.n.) rAdSJ4 boost. A second set of DNA and rAd vectors (pSJ10 and rAdSJ6 respectively) was also generated in the same manner, expressing epitopes from the gp41 membrane proximal region (MPR) 635-685, that were inserted into gag. The systemic and mucosal IgG/IgA levels were determined by ELISA against the specific epitopes, QARILAVERY or MPR epitopes (ELDKWAS/NWFDIT), based on the immunization groups and are reported as an end-point dilution (EPD) relative to 1.5x the background.

**Results:** All epitopes elicited IgG and IgA in the systemic (serum) and mucosal (vaginal washes and fecal pellets) compartments. The MPR epitopes elicited significantly higher IgG levels systemically compared to the QARILAVERY epitope (5000X EPD versus 900X EPD respectively) and mucosal levels were comparable at 150-200X EPD. However, there was significantly higher IgA detected against QARILAVERY both systemically, at 1100x EPD versus 850x, and mucosally, at 180x EPD versus 80x in fecal pellets and 100x versus 50x in vaginal washes.

**Conclusions:** The level of IgG generated against the MPR epitopes was significantly higher systemically compared to the QARILAVERY epitope. However, there was significantly higher IgA detected against QARILAVERY both systemically and mucosally, which is ideal for mucosal protection. This implicates QARILAVERY as a good candidate epitope to be used in future mucosally effective vaccine strategies.

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### GLOBOTRIAOSYLCERAMIDE: PROTECTION AGAINST HIV INFECTION

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**Plain Language Summary:** We have proposed the glycosphingolipid, globotriaosylceramide (Gb3) as a natural resistance factor against HIV infection. In this study, we attempt to pharmacologically mimic these genetically defined Gb3 expression phenotypes in a monocytic cell line (THP-1) and determine susceptibility to HIV infection. This was achieved by treating cells with a competitive inhibitor of alpha-galactosidase A, 1-deoxygalactonojirimycin (DGJ) or a glucosylceramide synthase inhibitor, phenyl-2-palmitylamino-3-pyrrolidino-1-propanol (P4). We found that DGJ decreases THP-1 cell susceptibility to HIV infection. In contrast, P4 increased HIV susceptibility.

**Objective:** The glycosphingolipid (GSL), globotriaosylceramide (Gb3) plays a key role in HIV infection. We reported peripheral blood mononuclear cells (PBMCs) from Fabry disease patients, which accumulate Gb3 as a result of defective alpha-galactosidase A-mediated catabolism, were selectively resistant to R5 HIV. PBMCs which accumulate Gb3 due to a genetic anabolic deficiency were resistant to both X4 and R5 HIV. In contrast, genetic lack of Gb3 synthesis results in massive PBMC hyper-sensitivity to X4 and R5 HIV infection. We hypothesize that Gb3 influences the susceptibility to HIV infection at the level of entry and membrane fusion. We attempt to pharmacologically mimic these genetically defined Gb3 expression phenotypes in a monocytic cell line (THP-1) and determine susceptibility to HIV infection.

**Methods:** THP-1 cells were treated with a) a competitive inhibitor of alpha-galactosidase A, 1-deoxygalactonojirimycin (DGJ) to increase Gb3 expression or b) a glucosylceramide synthase inhibitor, phenyl-2-palmitylamino-3-pyrrolidino-1-propanol (P4). In addition, total cellular Gb3 content was monitored by extraction and Verotoxin TLC overlay. HIV susceptibility was determined via measurement of p24gag antigen production by ELISA.

**Results:** We found that DGJ decreases THP-1 cell susceptibility to HIV infection. In contrast, P4 increased HIV susceptibility. Cell GSL analysis verified increased Gb3 expression in cells treated with DGJ and decreased Gb3 in P4-treated cells as compared to controls.

**Conclusions:** Our findings suggest Gb3 provides resistance to HIV infection. Variable Gb3 expression may provide a natural HIV resistance factor in the general population. Individuals with anabolic-based elevated Gb3 levels show no clinical phenotype, suggesting that pharmacological manipulation of Gb3 levels may provide a relatively benign approach to induction of HIV resistance.

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### THE EFFECTS OF GENITAL INFECTIONS ON HIV SUSCEPTIBILITY IN WOMEN

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**Plain Language Summary:** HIV is mainly spread through sexual contact, and two basic steps are required to transmit the virus: 1) HIV must be shed in the genital secretions (cervico-vaginal or rectal secretions, or semen) of the infected partner, and 2) HIV must then infect susceptible genital cells in the uninfected partner. It is clear that common genital infections (including bacterial vaginosis and STIs such as gonorrhea, chlamydia and others), may dramatically increase HIV susceptibility, but exactly how this occurs is unknown. This project aims to understand how common genital infections increase HIV susceptibility in women, and whether treatment reverses these changes.

**Objective:** To determine the effects of genital infections on HIV susceptibility in women. Specifically, we examined the association of genital infections with the number of HIV target cells in the female genital tract.

**Methods:** HIV-negative women genital infections and infection-free controls were recruited through the Hassle Free Women's Clinic in downtown Toronto. Using a cervical cytobrush sample, we measured the number of dendritic cells expressing DC-SIGN, and the number of CD4 T cells expressing CCR5, since these two populations are felt to be the initial HIV target cells in the female genital tract. We present baseline (pre-treatment) associations of genital infections.

**Results:** 40 women have been enrolled to date: 12 with bacterial vaginosis (BV); 11 with lesser alterations in vaginal flora (AVF); 7 with C.trachomatis; 3 with N.gonorrhoeae; 7 with T.vaginalis; and 6 infection-free controls. Women with any genital infection (n=34) had a significant increase in the number of cervical DC-SIGN+ dendritic cells (p=0.003) and CD4/CCR5+ T cells (p=0.007) compared to women with no infection (n=6). Similar effects were seen for BV and all individual STIs; particularly interesting was the association of asymptomatic, lesser alterations in vaginal flora with increased numbers of CD4+ T cells expressing the CCR5 co-receptor.

**Conclusions:** These preliminary results suggest that a wide range of genital infections may increase HIV susceptibility by increasing HIV target cells in the FGT. The association of minor changes in the genital flora with mucosal changes may increase HIV susceptibility and warrants further investigation. Ongoing studies are examining the impact of therapy on HIV genital target cells; these results will be directly applicable in formulating novel strategies for HIV prevention.

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# Monday, November 19, 2007 – 11:15 a.m.

## Engaging Communities in Research

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**OPERATIONALIZING 'COMMUNITY ENGAGEMENT' IN COMMUNITY-BASED RESEARCH: A CASE STUDY OF THE TRANS PULSE PROJECT**

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**Plain Language Summary:** Increasingly, communities and researchers are working collaboratively to address health inequalities facing marginalized peoples. Community-based research (CBR) is grounded in the principles of community relevance, community engagement, and action outcomes and differs from traditional research in that communities are engaged at the levels of input, process and outcome. A large body of evidence points to successes of CBR and its ability to bridge academic research interests and community needs. CBR enhances relevance of research questions, improves data validity, and increases the likelihood of knowledge diffusion to stakeholders. These advantages accumulate only to the extent that a project is successful in community engagement, which typically challenges researchers. We present a case study of community engagement in the Trans PULSE Project, a CBR study exploring social exclusion and HIV vulnerability in Ontario's trans communities.

**The Challenge:** Despite a convincing body of evidence valuing CBR as an approach to address health inequalities, the operationalization of 'community engagement' remains a vague concept.

**Our Approach:** We present strategies used in the Trans PULSE Project to produce partnerships and build capacities among members of the research team and the broader trans community. We also provide concrete examples of operationalizing 'community engagement.'

**Key Findings:** We describe the history of the Trans PULSE Project, the development of its innovative community engagement strategy, and our plans for evaluating future project phases. Our initial strategy addresses community ownership and control and includes: community initiation of study, identification of needs, and choice in research partnerships. A second strategy focuses on broader community input into the informational basis for the project and includes: hosting community soundings to refine the research agenda and forming a community engagement team representing a broad cross-section of the trans community for input at key points in the research process. A third strategy includes capacity-building processes, such as using opportunities to involve additional community members on shorter-term projects and compiling resources.

**Impact on Policy and Practice:** CBR initiatives struggle with how to meaningfully engage community members across input, outcome and process stages of their projects. We offer practical solutions on how to engage community members at each stage as well as advice on how to build capacities in support of such engagement.

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**COMMUNITY ENGAGEMENT AND COMMUNITY-BASED RESEARCH (CBR): LINKING THEORY AND PRACTICE**

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**Plain Language Summary:** In 2004-2006, a team of university and community-affiliated researchers undertook a CBR study of HIV-related stigma among African and Caribbean communities in Toronto (the Stigma Study). The implementation of the study raised a number of challenges particularly related to recruitment of participants, community involvement, interpretation of findings and knowledge production.

**The Challenge:** The African and Caribbean Council on HIV/AIDS in Ontario (ACCHO) instituted a process to understand the level of community engagement in its research. We review and critically assess CBR methodology based ACCHO's experiences with implementing the Stigma Study.

**Our Approach:** The Stigma Study (2004 to 2006) was a qualitative CBR study of African and Caribbean communities in Toronto to examine experiences of and responses to stigma, and understand how social structure influences those experiences and responses. The study personnel included a research team from universities and community-based organizations, a study coordinator, a data analyst and a community advisory committee. The study recruited 30 people living with HIV/AIDS for indepth interviews and 74 other community members for focus groups. This assessment of the study methodology is based on critical reflection and discussion of issues related to the structure of the study, recruitment, and data analysis and interpretation.

**Key Findings:** The study lacked implementation guidelines based on critical race analysis and recognition of the structural and power imbalance between universities, community groups and marginalized populations. Recruitment of participants took place mainly through ASOs, other community-based organizations, and word-of-mouth. This standard process may have limited the participation of a wider cross-section of the target population and prohibited a better understanding of how intersectionality influences secrecy about HIV/AIDS. Research funders, research ethics boards (REBs) and research institutions place much emphasis on the institutional affiliations and formal credentials of people involved in research. This dominant perspective limits the formal or informed involvement of community members who are themselves implicated in the knowledge being produced, and restricts the sexual, gendered and other perspectives that may facilitate a richer interpretation of the research data. The study privileged an instrumentalist perspective of workable solutions to stigma, which may not adequately capture the lived complexity of stigma.

**Impact on Policy and Practice:** Standard approaches to research may further marginalize, disempower and alienate populations that are already marginalized by race and socioeconomic status. University and community-affiliated researchers must advocate to funders, research institutions and REBs how their rules and practices limit community engagement, how research is done and, ultimately, our ability to respond to HIV/AIDS.

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## 111

**BUILDING CBR RESEARCH: WORKING WITH COMMUNITY INTERVIEWERS**

Jann Ticknor [1]; Randy Jackson [1]; Janice Ristock [2]; Joyce Seto [3]; Shari Brotman [4]; LaVerne Monette [5]
1-Canadian Aboriginal AIDS Network; 2-Women's Studies, University of Manitoba; 3-Métis Centre, National Aboriginal Health Organization; 4-School of Social Work, McGill University; 5-Ontario Aboriginal HIV/AIDS Strategy

**Plain Language Summary:** The Canadian Aboriginal AIDS Network is recruiting and interviewing HIV+, two-spirit women (i.e., gay, lesbian, bisexual, transgendered, or wsw) about their experiences accessing HIV-related health services. The term two-spirit encompasses a range of gender and sexuality identities, and can include spiritual aspects. This presentation will highlight the processes shaping our research with two-spirit women, explain why and how we changed our research design to involve community-interviewers, and discuss the benefits and challenges of our approaches.

**The Challenge:** CAAN is used to adapting and adjusting research to meet community needs as well as the challenges of 'doing nationally-situated CBR'. The challenges in this project are reaching the communities of two-spirit women, while providing safe, culturally appropriate opportunities for two-spirit women to speak to their experiences of accessing HIV-related healthcare.

**Our Approach:** The original plan involved one-on-one interviews with women in 6 different sites across Canada to be conducted by a research coordinator. Through our pilot-test, we learned our approach needed adjusting based on the feedback and recommendations coming from pilot-test participants, conversations with service providers, front-line and outreach workers who work directly with two-spirit women, members of our national research advisory committee and two-spirit women who work within CAAN. In response, we have reformed our approach and are now working to engage local community-interviewers at each site. Our approach is still evolving. This presentation is a reflection of 'doing' CBR and will highlight our approach to flexibility and accountability within an Indigenist framework.

**Key Findings:** Recruiting and engaging HIV+ two-spirit women is challenging. While we expected some barriers, it has been more difficult than we anticipated. Using CBR allows some flexibility when challenges are encountered, and we have broadened our recruitment strategy to work more closely with community networks, such as communities of Aboriginal women who are living with HIV/AIDS and HIV+ positive women in general. We will speak to the evolving recruitment strategy we are using, share our learnings, and ideally, contribute to the dialogue about recruiting 'hidden' communities of people living with HIV/AIDS.

**Impact on Policy and Practice:** The focus of this presentation will contribute to the dialogue about practicing CBR with vulnerable populations and working with community-interviewers on a national level. In terms of impacting policy and practice, this presentation will inform new practitioners about the evolving nature of CBR. Further, discussion and dialogue about an alternative approach to addressing recruitment challenges may be of interest to more seasoned CBR practitioners.

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**DOES RESEARCH TRAINING AND CAPACITY BUILDING EFFECTIVELY LEAD TO COMMUNITY EMPOWERMENT? LESSONS LEARNED FROM THE POSITIVE SPACES HEALTHY PLACES COMMUNITY BASED RESEARCH STUDY**

J. Watson [1]; Michael Hamilton [1]; D. Hintzen [1]; Marie Kayitesi [1]; Jim Truax [1]; Pius J. White [1]
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**Plain Language Summary:** People living with HIV/AIDS (PHAs) in Canada are a highly researched population, yet their inclusion in the research process has historically been minimal or non existent. In response to traditional ways of engaging in research that exclude community members from actively participating as research partners, community based research (CBR) has become a recognized tool for addressing urban health issues including HIV/AIDS. A main objective of CBR is to empower and enhance the capacity of communities by inviting their equitable involvement as research partners. This includes a commitment to providing research training and capacity building opportunities for peer researchers throughout the life of the research project. It is therefore suggested that research processes and outcomes should benefit the community through hiring and training community members as community researchers and research assistants whenever possible and appropriate in order to help build and enhance community assets. This presentation will draw on the training and capacity building experiences of seven peer research assistants who were employed and trained through the Positive Spaces, Healthy Places community based research study. A number of issues will be addressed including: the need to equip people with skills and competencies which they would not otherwise have; realizing existing skills and developing potential; promoting increased self-confidence; the need to provide opportunities for people to learn through experience; and involving individuals in collective efforts so that they gain confidence in their own abilities and their ability to influence decisions that affect them. Success, challenges and recommendations regarding the research training and capacity building process will also be discussed.

**Objective:** To develop a more in-depth understanding of the experiences of Peer Research Assistants who participate in community based research; To promote best practices regarding training and capacity building for peer researchers and research assistants in community based research.

**Methods:** In-depth focus groups and training debriefing sessions. Focus group discussions were recorded and transcribed and analzyed thematically.

**Results:** Research training and capacity building for peer researchers and research assistants have both short and long term benefits and challenges. Benefits include increased confidence and self-esteem; community involvement; developing new skills; re-entry into education and employment. Challenges include: questions about sustainable benefits; being viewed as a community spokesperson; and, emotional and physical 'burn out'.

**Conclusions:** Community based research projects that provide training and capacity building of peer researchers and peer research assistants has positive outcomes on self esteem and overall mental health. However, funding is necessary to ensure that there is both the time and resources available to provide adequate training opportunities, support, supervision and debriefing. Links between funding, capacity building, research training and use of skills in the future must be made more explicit in order that community members can benefit from both the short and longer term outcomes of research training and capacity building processes.

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# Monday, November 19, 2007 – 11:15 a.m.

## Back to the Basics

### 113

**DESIGN AND DEVELOPMENT OF NOVEL MULTIGENE SIV VACCINES BASED ON VARICELLA-ZOSTER VIRUS VECTOR**

David Willer [1]; Aruna Ambagala [1]; Jacqueline Chan [1]; Paul Sandstrom [2]; James Brooks [3]; Rick Pilon [2]; Jocelyn Fournier [4]; Kelly MacDonald [1]
1-Mt. Sinai Hospital/University of Toronto; 2-National HIV and Retrovirology Laboratories, Health Canada; 3-National Laboratory for HIV Genetics, Health Canada; 4-Health Products and Food Branch, Health Canada

**Plain Language Summary:** Varicella-Zoster Virus (VZV), the causative agent of chickenpox and herpes zoster, establishes a life-long latent infection in humans, with evidence of periodic reactivation resulting in intermittent immune stimulation even in healthy individuals. This critical feature sets it apart from all vaccine vectors currently in testing for HIV, where severely attenuated or replication-deficient vectors are the standard. This capacity for lifelong infection of the vaccine, together with the proven capacity for self-boosting of the vector, forms a novel paradigm for HIV vaccine development.

**Objective:** To explore the possibilities of using VZV as a vaccine vector for development of an HIV vaccine.

**Methods:** We are developing a series of multi-gene SIV vaccine candidates utilizing VZV as the vector backbone. We have employed "PCR assembly" using a panel of oligonucleotides to generate codon-optimized SIVmac239-derived sequences. SIV expression constructs were engineered into a VZV-BAC (Bacterial Artificial Chromosome) using bacterial recombination (allelic exchange), which permitted the site-specific targeting of SIV gene products into the VZV genome. VZV vectors expressing SIV genes were generated by transfecting VZV-SIV BAC into a human melanoma cell line (MeWO). The necessary removal of intervening BAC sequence from the virus genome was achieved by serial passage of the recombinant virus through Vero cells expressing “Cre” recombinase (Vero-CRE). Growth characteristics, transgene expression, and genetic stability of the VZV-SIV vaccine candidates are being assessed in vitro. Prior to challenge experiments in cynomolgus macaques, immunogenicity and latent infection of the vaccine candidates will be evaluated in guinea pigs and cotton rats respectively. We have recently initiated a preliminary study to assess the viral “take” and immunogenicity of VZV in cynomolgus macaques.

**Results:** Here we highlight the construction of codon-optimized SIV antigenic sequences (Gag, Pol, Env, Gag-Pol polyprotein (GPP), Gag-Pol Fusion (GPF) and a novel fusion protein “NeTaRev” comprised of SIV accessory genes Nef, Tat, and Rev) and the engineering of VZV-based SIV vaccine candidates. VZV expressing SIV genes have being generated and their growth characteristics, transgene expression and immunogenicity are being assessed.

**Conclusions:** This VZV-based SIV vaccine study will address key issues of the immunogenicity and protective efficacy of this herpesvirus vector.

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### 114

**UPREGULATION OF INTERFERON- α INDUCED STAT1 ACTIVATION AND APOPTOSIS IN MONOCYTES FROM HIV+ PATIENTS**

Abdulkarim Alhetheel [1,4]; Yuriy Yakubtsov [1,4]; Khaled Abdkader [1,4]; Nadia Sant [1,4]; Jonathan Angel [4,5]; Ashok Kumar [1,2,3,4]; Francisco Diaz-Mitoma [1,2,3,4]; Marko Kryworuchko [1,2,3,4]
1-Infectious Disease and Vaccine Research Centre, Children's Hospital of Eastern Ontario (CHEO) - Research Institute; 2-Division of Virology, CHEO; 3-Department of Pathology and Laboratory Medicine, University of Ottawa; 4-Department of Biochemistry, Microbiology and Immunology, University of Ottawa; 5-Division of Infectious Diseases, Ottawa Hospital

**Plain Language Summary:** Monocytes/macrophages (M/M) play a major role in inflammatory reactions and pathogen clearance. However, chronic immune activation observed during HIV infection may also cause cellular dysfunction and tissue pathology. Indeed, several M/M defects have been reported during the course of HIV infection. Since M/M function is controlled by growth factors called cytokines via the activation of Signal Transducer and Activator of Transcription (STAT) signaling pathway, we hypothesized that the activation of this pathway in monocytes from HIV+ patients may be disrupted.

**Objective:** To evaluate cytokine-dependent STAT activation in monocytes from HIV+ patients and determine the biological impact and molecular mechanisms responsible for any alterations in signaling observed.

**Methods:** Monocytes from chronically-infected HIV+ patients on and off antiretroviral therapy (ART) were assayed respectively for STAT activation, apoptosis and other downstream effects by flow cytometry, real-time PCR and ELISA.

**Results:** In contrast to STAT activation in response to IFN-α, IL-10, GM-CSF, and IL-4, only IFN-γ-induced STAT1 activation was upregulated in monocytes from off therapy patients compared to those on ART and HIV- controls. Upregulation of tyr-phosphorylated STAT1 correlated with increased total STAT1 expression. Interestingly, spontaneous and IFN-γ-induced monocyte apoptosis was elevated in HIV+ patients compared to HIV- controls. Spontaneous apoptosis correlated with plasma levels of TRAIL. Surprisingly, among the IFN-γ responsive genes (IRF-1, CXCL9, CXCL10, and TRAIL) studied, only CXCL9 expression was elevated in HIV+ patients on ART compared to the other groups.

**Conclusions:** Upregulation of IFN-γ-induced STAT1 activation and apoptosis in HIV+ patient monocytes may be the consequence of chronic immune activation and contribute to the functional impairment observed in these cells through the course of the disease.

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## 115

### UNDERSTANDING THE SUPPRESSION OF HIV-1 PROTEIN SYNTHESIS BY SAM68ΔC

Kim Marsh [1]; Alan Cochrane [1]
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**Plain Language Summary:** Following infection of the cell, HIV-1's capacity to replicate is dependent on its ability to bypass innate anti-viral defences. Understanding the nature of these defences and how they act provides new insights into alternative strategies to control the infection. Our studies have focused on the factor Sam68ΔC which is acts to suppress synthesis of HIV-1 proteins. We have identified that Sam68ΔC acts through a novel mechanism and very selectively providing greater understanding of the process by which HIV-1 proteins are expressed. We hope to exploit these findings to design novel treatment strategies.

**Objective:** Previous analyses had identified Sam68ΔC as a potent inhibitor of HIV-1 structural protein expression. Although previous analysis had suggested a correlation between the inhibitory properties of Sam68ΔC and the dramatic alteration in viral RNA subcellular distribution, we wanted to understand the mechanism in greater detail. Our analyses have determined that suppression of viral RNA translation by Sam68ΔC is not associated with changes in subcellular distribution or modification of the viral RNA but rather by changes in the composition of the viral RNP.

**Methods:** Effects on viral RNA subcellular distribution were examined by in situ hybridization and immunofluorescence. To analyze for alterations in viral RNA structure, ribonuclease protection assays were utilized to determine whether suppression correlated with changes in RNA splicing or abundance. To assess changes in RNA polyadenylation, both fractionation on oligo-dT cellulose and random amplication of cDNA ends poly A test (RACE-PAT) were used. Finally, composition of the viral RNP was probed using Ribonucleoprotein (RNP) immunoprecipitation (RIP) assays.

**Results:** The ability of Sam68ΔC to induce perinuclear bundling of HIV-1 RNA was found to be dependent upon the integrity of the microfilament component of the cytoskeleton. Disruption of this network was found to restore movement of viral RNA throughout the cytoplasm but failed to induce viral protein synthesis. These findings along with the failure to detect changes in viral RNA abundance or polyadenylation suggested that Sam68ΔC acts through modification of the viral RNP. Subsequent RIP assays confirmed this prediction, inhibition being associated with a marked reduction in binding of PABP-1 to HIV-1 RNA. Additional tests highlighted the selective nature of the repression observed, the ability of Sam68ΔC to function being dependent not only the unique features of HIV-1 RNA but also the export pathway used to deliver the viral RNAs to the cytoplasm.

**Conclusions:** Our studies have characterized Sam68ΔC as a very potent and specific inhibitor of HIV-1 structural protein synthesis. Repression is associated with changes in the viral RNP (loss of PABP-1) that are essential for efficient engagement with the translational apparatus. Our finding that Sam68ΔC action not only requires the Rev-RRE RNA complex but also export via Crm1 export pathway indicate that there are pathway dependent differences in RNPs that can be exploited to alter RNA processing and utilization. These unique features of the HIV-1 RNP are currently being studied in an effort to better design inhibitory strategies that exploit these properties.

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## 116

### HIV IMPAIRS CD8 T-CELL FUNCTION BY REMOVING THE IL-7 RECEPTOR ALPHA-CHAIN FROM THE CELL SURFACE AND TARGETING IT FOR DEGRADATION

Elliott Faller [1,2]; Mark McVey [2]; Juzer Kakal [1,2]; Scott Sugden [1,2]; Paul MacPherson [1,2,3]
1-University of Ottawa, Faculty of Medicine, Department of Microbiology/Immunology; 2-Ottawa Health Research Institute; 3-Division of Infectious Diseases, Ottawa Hospital General Campus

**Plain Language Summary:** We have previously shown soluble HIV Tat protein down regulates expression of the IL-7 receptor α-chain (CD127) on CD8 T-cells and in so doing impairs CD8 T-cell proliferation and cytolytic potential. We now show Tat co-localizes with CD127 at the cell surface and targets it for degradation.

**Objective:** To determine the mechanism by which Tat down regulates CD127 on CD8 T-cells.

**Methods:** CD8 T-cells were isolated from healthy volunteers and incubated in media alone or with Tat (10 µg/ml) in the presence or absence of inhibitors as indicated. CD127 surface expression was measured by flow cytometry and fluorescence microscopy, and total CD127 was assessed by Western. CD127 transcripts were measure by Real Time PCR.

**Results:** As expected, Tat protein is taken up by CD8 T-cells and accumulates over 6-12 hours. Once in the cytoplasm, Tat co-localizes with CD127 at the cell surface and increases the rate at which the receptor is internalized and degraded. Indeed, as shown by both flow cytometry and by Western, the half-life of CD127 was decreased by more than half in the presence of Tat. While colchicine does not prevent Tat from entering CD8 T-cells, it does block Tat's ability to remove CD127 from the cell surface indicating a role for microtubules in this process. Proteasome inhibitors (MG132 and Lactacystin) but not lysosome inhibitors (E64 and Leupeptin) also blocked Tat's ability to decrease CD127 indicating Tat likely targets the receptor for degradation by the proteasome. Tat had no effect on the level of CD127 transcripts indicating Tat does not down regulate CD127 at the level of gene transcription or mRNA stability. Similarly Tat did not alter the abundance of transcripts encoding the secreted isoform of CD127.

**Conclusions:** Soluble HIV Tat protein, acting in a paracrine manner, enters CD8 T-cells and increases the rate at which CD127 is removed from the cell membrane. Our data suggest Tat interacts directly or indirectly with CD127 at the cell membrane to induce receptor capping, endocytosis and degradation by the proteasome.

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# Monday, November 19, 2007 – 1:45 p.m.

## Clinical Care and Outcomes

### 117

**THE IMPACT OF HERPES VIRUSES ON CD4 AND VIRAL LOAD IN HIV CO-INFECTED WOMEN NAÏVE TO HAART**

Allyson Ion [4]; Sameer Kassim; Charu Kaushic [3]; Sonya Buracond; Lynn Kelleher [4]; Fiona Smaill [1,4]; Philippe El-Helou [4,5]; Marek Smieja [1,2,4]
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**Plain Language Summary:** Concurrent infections of HIV and HSV-2 can increase susceptibility to other sexually transmitted infections and HIV transmission rates, however, the role of HSV-2 and other herpesviruses in the progression of HIV and the time to needing HAART is not well understood. We sought to determine if sero-positivity for HSV-1, HSV-2 or CMV was associated with a lower baseline CD4 and higher baseline viral load. We also wanted to determine if women infected with HIV plus one or more herpesviruses (including HSV-1, HSV-2 and CMV) immunologically deteriorate more rapidly, measured by decline in CD4 cells and increases in plasma viral load, shortening the time to needing antiretroviral therapy. We found no clear relationship between antibody evidence of previous exposure to three different herpesviruses and subsequent immunogic deterioration amongst HIV-positive women who were not on HAART.

**The Challenge:** To investigate whether sero-status for HSV-1, HSV-2 or CMV is associated with a lower baseline CD4, higher baseline viral load and more rapid CD4 decline amongst women who do not immediately require HAART initiation.

**Our Approach:** Adult female patients at the HIV clinic in Hamilton (n=30) with a mean age of 40.8 (±8.6) were approached and consented for serum antibody testing as part of a study to understand HSV-2 and HIV co-infection. Sera were tested for HSV-1 and HSV-2 with ELISA and confirmed with immunoblot. CMV antibody status was abstracted from routine blood work via chart review. Eligibility for inclusion in the analysis was dependent on two separate CD4 and viral load assessments, a minimum of nine months apart prior to HAART initiation. The average CD4 and log viral load change per year was calculated for each woman. Descriptive statistics and independent samples t tests were conducted using SPSS version 15.0.

**Key Findings:** Our cohort of women (n=30) presented with an overall mean baseline CD4 count of 473 cells/ml (±196) and a mean baseline viral load of 3.6 log copies/ml (±0.92). Women sero-positive for HSV-1, HSV-2 and CMV presented with a baseline CD4 count of 445, 486 and 473 cells/mm3 respectively compared to sero-negative women who had baseline CD4 counts of 504, 460 and 473 respectively, which was not statistically significant (p=0.44, p=0.75, p=0.99). HSV-1, HSV-2 and CMV sero-positive women had an annualized CD4 decline of 42, 39 and 52 cells, respectively, compared to sero-negative women who experienced a loss of 102, 121 and 157 CD4 cells, respectively. Although a greater loss of CD4 cells per year was observed in sero-negative women, this difference was not significant (p=0.29, p=0.16, p=0.21). There was no significant difference in baseline log viral load or log viral load change per year between HSV-1, HSV-2 and CMV sero-positive and sero-negative women.

**Impact on Policy and Practice:** The role of herpesviruses as cofactors for HIV progression deserves continued study, as these are potentially amenable to anti-herpetic suppressive treatment. However, our preliminary results do not demonstrate a relationship between these infections and immunologic decline, and a larger study with prospective follow-up would be needed to more precisely examine their role in HIV progression.

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### 118

**HIV TYPE 1 POL GENE DIVERSITY AND NEVIRAPINE (NVP) RESISTANCE MUTATIONS IN WOMEN FROM NORTH-RIFT, KENYA AFTER NVP SINGLE-DOSE PROPHYLAXIS FOR PREVENTION OF HIV-1 MOTHER-TO-CHILD TRANSMISSION**

Michael Kiptoo [1,2]; James Brooks [3]; Richard Pilon [3]; Hezhao Ji [3]; Harriet Merks [3]; Nathalie Masse [3]; Zipporah Ng'ang'a [2]; Fredrick Okoth [1]; Paul Sandstrom [3]; Elijah Songok [1]
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**Plain Language Summary:** Single dose nevirapine is widely used in developing countries to prevent HIV-1 mother-to-child transmission (PMTCT). In Kenya, this regimen was introduced in the public hospitals in 2003. This regimen selects key drug resistance mutations that can impair further HAART efficacy. This study aimed to find out the prevalence of NVP resistance associated mutations after NVP single dose regimen in women from North-Rift, Kenya. 13.9% of Kenyan women who received single-dose nevirapine for PMTCT harboured significant NNRTI mutations that would impair the effectiveness of an NNRTI based treatment regimen. While single dose nevirapine may be an effective PMTCT tool, consideration needs to be given to alternate treatment regimens for nevirapine exposed mothers.

**Objective:** This study aimed to find out the prevalence of NVP resistance associated mutations after NVP single dose regimen in women from North-Rift, Kenya.

**Methods:** After obtaining informed consent, blood was collected between 6 and 24 weeks post-partum, from 36 women who had been given single-dose nevirapine. The pol gene including the protease (PR) codons 1-99 and reverse transcriptase (RT) codons 1-320 were amplified and sequenced. The HIV drug resistance mutations and clade were determined according to the IAS-USA 2006 mutation list using the Stanford HIV Drug Resistance Database and the Rega subtyping tool respectively.

**Results:** Subtype analysis revealed that 24 (66.7%) were subtype A1, 4 (11.1%) D, 2 (5.6%) C with three recombinants (8.3%) A/D and 1 (2.8 %) K/CRF01_AE. In the PR coding region, high numbers of polymorphisms were found including some identified as secondary PR resistance sites. L10I/V was found in one woman (2.8%), L10I in 2 (5.6%), L10V in 3 (8.3%) and L33F in another (2.8%). One major PI mutation V32I was identified in one woman (2.8%). Nevirapine associated mutations were found in 5 women (13.9%). The K103N mutation was found in 2 women (5.6%), Y181C in 1 (2.8%), Y181C plus Y188C in 1 (2.8%) and Y181C plus G190A in another woman (2.8%). The NRTI mutations detected were K65R and M184V in one woman each.

**Conclusions:** HIV-1 subtype A1 is the predominant circulating strain in this region. Major resistance mutations are archived after single dose NVP. Drug resistance outcomes in women should be considered as an important secondary end point in PMTCT assessment as this may impact on the durability of HIV treatment regimens.

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## 119

### EVALUATION OF THE EXTENT OF HIV RNA SUPPRESSION OVER TIME AMONG PARTICIPANTS IN THE ONTARIO COHORT STUDY (OCS)

Janet Raboud [1,2]; Maggie Li [1]; Ahmed Bayoumi [2,3]; Irving Salit [1,2]; Sharon Walmsley [1,2]
1-University Health Network; 2-University of Toronto; 3-Centre for Research on Inner City Health, The Keenan Research Centre in the Li Ka Shing Knowledge Institute of St. Michael's Hospital

**Plain Language Summary:** This research project examines several aspects of HIV viral load levels among HIV positive individuals who are Ontario Cohort Study participants. We report on the time to virologic suppression, time to virologic rebound and the proportions of individuals whose viral load levels are below the limit of detection (50 copies/ml) by calendar year.

**The Challenge:** To describe changes and patterns of HIV virologic suppression among HIV infected patients who were enrolled in the OCS over the past 8 years.

**Our Approach:** Demographic and clinical data were extracted from the Ontario Cohort Study database. Virologic blips were defined as an increase in viral load above 50 copies/ml at a single visit followed by a viral load < 50 copies/mL at the next evaluation. Median times to virologic suppression and virologic rebound were estimated with Kaplan Meier curves.

**Key Findings:** Viral load (VL) measurements were available for 2519 patients from 1999 to 2006. 2422 patients who have at least 2 viral load measurements were included in this study: 84% were male, median age was 47 yr, median years of HIV infection was 17 years (IQR 13,22), 62% were MSM, 11% IDU, 29% heterosexual contact and 95% were on ARVs. There was a median of 16 (IQR 9 to 24) VL measurements per patient and median follow-up of 58 months (IQR 31, 90). 1875 (77%) of patients achieved virologic suppression (HIV RNA < 50 copies/ml) during the study period, 842 (45%) at their first visit. 1265/1875 (67%) patients experienced viral rebound (VL>50 copies/mL). If virologic blips are not considered as rebounds, then 905/1875 (48%) patients experienced viral rebound. The median time to rebound considering blips as rebounds was 15 (6, 35) months and not considering blips as rebounds was 24 months (8, 53). The proportions of patients achieving virologic suppression at every measurement (ignoring blips) during the year for the years from 1999 to 2006 were 33%, 40%, 44%, 47%, 50%, 55%, 60% and 62%. Of patients with virologic suppression at 1 year, 83% maintained suppression to 2 years, 69% to 3 years and 59% to 4 years. Patients who achieved virologic suppression after the year 2000 rebounded sooner than patients who suppressed before 2000.

**Impact on Policy and Practice:** HAART therapy has steadily increased the proportions of patients with maximal virologic suppression. Suppression at one year predicts long term suppression to 4 years.

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## 120

### CANCER RISKS AMONG HIV-INFECTED PERSONS IN ONTARIO: A LINKAGE STUDY

Siamak Tenzif [1]; Robert Remis [2,4]; Eric Holowaty [3]; Carol Swantee [4]; Karen Hofmann [3]; Keyi Wu [4]
1-Mount Sinai Hospital; 2-University of Toronto; 3-Cancer Care Ontario;; 4-Central Public Health Laboratories, MOHLTC

**Plain Language Summary:** Some forms of cancers have been linked to HIV/AIDS infection. This study examined rates of these cancers as well rates of selected non-AIDS defining cancers in an Ontario HIV cohort and compared them with the general population. Study results show that risks for developing some non-AIDS defining cancers are higher in the AIDS patients. The link between HIV/AIDS and these cancers have clinical care implications and will require a re-examination of management of long-term care of HIV/AIDS.

**Objective:** To investigate: Incidence and mortality rates of HIV/AIDS cancers and non-AIDS defining cancers in a cohort of HIV/AIDS patients compared to general population for Ontario between 1985 and 2004.

**Methods:** This two parts study comprised of: a) an exploratory ecological study and; b) a unique linkage study of cancer and HIV using records from Cancer Care Ontario (CCO) and Ontario Public Health Laboratory (HIV) data. The Ontario Mortality Database was used to determine the living status of the study cases. HIV sero-diagnostic and viral load data sets were reviewed to allow for the creation of a unique HIV file. This file was then linked to the CCO file using deterministic and multiple probabilistic linkage methodology. A study file with no nominal/identifying data was generated. Chi-Square, ANOVA and Person-Years analysis were completed. Standardized incidence ratios (SIR) and standardized mortality ratios (SMR) were calculated.

**Results:** The ecological study results were used to prioritize a list of 11 cancers for the linkage study. The overall study analysis indicated elevated significant ($P < 0.05$) risks of developing anal (SIR 50.3, 95% CI 32.9-72.7), lung (2.0, 4.3-6.3), brain (3.1, 1.7-5.4) cancers, non-Hodgkin's lymphoma (NHL) (37.5, 33.8-41.5), Hodgkin's disease (10.5, 6.8-15.3) and all cancers combined for the HIV cases. Gender specific analysis showed elevated significant ($P < 0.05$) risks for HIV males for anal cancer (67, 43.5-97.7) and for HIV females for lung cancer (2.8, 1.0-5.9) and NHL (28.1, 19.4-39.6). SMR analysis showed that HIV males were at increased significant ($P < 0.05$) risks of death from skin (11.22, 95% CI 1.25-38.73) and Hodgkin's disease (13.52, 4.35-31.29). The study findings support a recent meta-analysis of HIV and cancer by Grulich et al (2007).

**Conclusions:** The study findings further demonstrate the impact of HIV immunodeficiency on risks of developing various types of cancers some of which were not previously linked to HIV infection. Study findings have major clinical impacts on the clinical care management and cancer screening for HIV/AIDS patients.

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# Monday, November 19, 2007 – 1:45 p.m.

## A Window into Transmission and Prevention

### 121

**RATES OF NEW HIV INFECTIONS AMONG PERSONS UNDERGOING REPEAT DIAGNOSTIC TESTING IN ONTARIO, 1993-2006**

Ann N. Burchell [1,2]; Liviana Calzavara [1,3]; Robert S. Remis [1,3]; Ted Myers [1,3]; Carol Swantee [4]; Carol Major [5]; Paul Corey [3]
1-HIV Studies Unit, University of Toronto; 2-Division of Cancer Epidemiology, McGill University; 3-Department of Public Health Sciences, University of Toronto; 4-Public Health Laboratory, Ontario Ministry of Health and Long Term Care; 5- Ontario HIV Treatment Network

**Plain Language Summary:** Monitoring the number of new infections is important to understand the status of the epidemic in Ontario. A review of HIV-antibody test records among people who tested more than once in 1993-2006 found that the rate of new HIV infections in Ontario is not decreasing.

**Objective:** To describe HIV incidence among persons undergoing repeat testing in Ontario in 1993-2006.

**Methods:** People using voluntary, diagnostic HIV testing at least twice were identified by computerized and manual record linkage as of 31/12/2006. The analysis was restricted those with reported risk factors and who met the criteria for (1) men who have sex with men (MSM); (2) injection drug user (IDU); or (3) heterosexual. In the 1993-2006 period, 1,258 seroconverters and 247,044 repeat negative testers contributed 1,016,575 person years (PY) of observation. Annual incidence density estimates were calculated by apportioning seroconversions across calendar years. Poisson regression was used to identify differences in incidence density according to time, age, gender, and region. Results are reported as relative rate ratios (RR) with 95% confidence intervals (CI).

**Results:** The overall incidence rates in 1993-2006 were 0.98, 0.22, and 0.028 per 100PY among MSM, IDU, and heterosexuals, respectively. Among MSM, incidence declined 18% per year in 1993-1996 (RR=0.82, 95%CI 0.72-0.94), then increased 5% per year, on average, in 1997-2006 (RR=1.05, 95%CI 1.02-1.09). In the earlier years, younger MSM (aged 15-39) were at greater risk of infection than MSM 40+, but age differences have diminished over time. Among IDU, incidence was highest in Ottawa-Carleton (RR=5.53, 95%CI 3.81-8.02) followed by the Northern region (RR=2.95, 95% CI 1.97-4.40), and was lowest in other regions of Ontario; no time or gender differences were observed. Incidence rates were highest among IDU aged 30-39 compared to younger and older IDU (RR=1.37, 95%CI 1.02-1.8). Among heterosexuals, incidence was higher among males (RR=2.22, 95%CI 1.68-2.93), among those reporting sexual contact with a person who was HIV-positive or at high risk of being infected (RR=3.79, 95%CI 2.74-5.25), and in Metro Toronto. No time or age differences were observed among heterosexuals.

**Conclusions:** There is no evidence of a decline in HIV incidence among repeat testers in Ontario. Geographic differences were distinct for each exposure category, suggesting that generalizations from one group to another should be avoided. The absence of age differences in incidence among heterosexuals may be a reflection of lower rates of testing among older adults.

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### 122

**HIV SCREENING AMONG PREGNANT WOMEN IN ONTARIO: A SUCCESS STORY**

Robert S. Remis [1]; Carol Swantee [2]; Carol Major [3]; Robert W.H. Palmer [1]; Keyi Wu [2]; Mark Fisher [3]; Juan Liu [1]
1-Ontario HIV Epidemiologic Monitoring Unit, Department of Public Health Sciences, University of Toronto; 2-HIV Laboratory, Central Public Health Laboratory, Laboratories Branch, Ontario Ministry of Health and Long-Term Care; 3-Ontario HIV Treatment Network

**Plain Language Summary:** We examined the uptake in HIV screening in pregnancy in Ontario following the new policy to offer testing to all pregnant women announced in 1999. We found that HIV test uptake increased dramatically and in 2007 over 90% of pregnant women were tested.

**Objective:** Following the ACTG 076 trial in 1994 demonstrating that antiretroviral prophylaxis significantly reduced mother-infant HIV transmission, few pregnant women in Ontario had been tested for HIV. In January 1999, the Ministry of Health introduced a new policy to offer HIV screening to all pregnant women and measures were undertaken to promote this policy. Beginning in 2001, we sent a reminder memo to prenatal care providers who did not order an HIV test. To evaluate the program, we examined patterns of HIV testing among pregnant women in Ontario.

**Methods:** In Ontario, prenatal screening for infectious markers including HIV is carried out at the Public Health Laboratory and data is managed centrally. We determined the number of pregnancies with any test prescribed and the proportion with an HIV test.

**Results:** In the 8.5 years from January 1999 to June 2007, 1,247,678 pregnancies (2,800/week) were tested for at least one infectious marker and included in the analysis. The proportion of pregnancies tested for HIV during the pregnancy increased from 33.4% in the first quarter of 1999 to 91.1% in the second quarter of 2007. 314 pregnant women tested HIV-positive (0.33 per 1,000), of whom 220 tested positive for the first time during the pregnancy. We observed regional differences in HIV testing rates, though much less than in the earlier years of the program. In the second quarter of 2007, HIV uptake among pregnant women by health region varied little, from 90.4% to 91.3%. Uptake by public health unit varied more, from 81.0% to 97.2%. Twenty-five public health units achieved an HIV test uptake of 90% or greater in 2007, compared to five public health units two years earlier.

**Conclusions:** Uptake of HIV testing improved dramatically in Ontario with the implementation of the new screening policy and program. The actual rate of HIV test uptake among pregnant women was likely slightly higher (by 2-3%) due to our inability to identify HIV tests carried out non-nominally in the HIV diagnostic database; an additional 4.2% of women were tested for HIV prior to the current pregnancy. The observed increase was partly due to the impact of a reminder memo sent to physicians who had not prescribed an HIV test beginning in 2001. We estimate that, since the new prenatal HIV screening policy was initiated, at least 60 infant HIV infections have been prevented.

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## 123

### STRATEGIC POSITIONING AND EPISODIC CONDOM USE

Barry Adam [1]; Winston Husbands [2]; James Murray [3]; John Maxwell [2]
1-University of Windsor; 2-AIDS Committee of Toronto; 3-Ontario Ministry of Health and Long-Term Care

**Plain Language Summary:** This study opens up the category of "strategic positioning" to see what role anal intercourse without ejaculation has in attempting to reduce risk. There is a spectrum of gay and bisexual men who report this behaviour, ranging from a small set who believe that taking the top role reduces risk, to those who see their practices as barebacking and also ejaculate in their partners, or whose partners ejaculate in them. Both bareback and nonbareback men who have unprotected sex without ejaculating tend to move in similar circuits, have some shared beliefs, and are more likely to report erectile difficulties.

**The Challenge:** To understand risk practices of gay and bisexual men who report unprotected anal intercourse without ejaculating.

**Our Approach:** Toronto Pride survey 2005 plus follow-up interviews with men having unprotected sex most or all of the time.

**Key Findings:** This report examines the characteristics of the 7.8% of the Toronto Pride survey of 2005 (N=72) who stated that in the previous 6 months, they had unprotected anal intercourse (UAI) with a casual male partner but did not ejaculate, and on subsequent interviews with 34 men have UAI most or all of the time. Forty percent (40%) of them indicated they participate in bareback scenes and websites. This set of men was also more likely to have UAI and ejaculate with a casual partner (OR=3.83, p=.006) than other men in the Pride survey. Men reporting UAI without ejaculating, compared to those who do not, are more likely to agree: A lot of guys I go home with have no desire to use condoms (OR=5.74, p<.001), I respect whatever the wants regardless of whether he's positive or negative. If he wants to use a condom, that's fine, and if he doesn't, that's fine too. (OR=3.76, p<.001), I like the emotional rush of pushing my limits (OR=2.72, p<.001), Sometimes I feel depressed about not having a relationship and give in when it comes to sex even if it is without a condom (OR=2.43, p<.001), It is not up to me to take responsibility for guys I meet for sex. They are adults who can make their own decisions around risk (OR=2.36, p<.001), and I find drugs are good for making sex hotter and raunchier (OR=2.13, p<.01). The 60% nonbareback group shows that 33 of them report taking a top role and only 18, a bottom role, suggesting some intend to limit risk. This set of men is more likely to agree, "If I lose my erection with a condom on, I prefer to have sex without it," than other men in the survey (OR=5.08, p<.001), suggesting that erectile difficulties play a significant role in this sexual adaptation. Excerpts from interviews help illuminate these experiences.

**Impact on Policy and Practice:** Survey and interview findings suggest that erectile difficulties, especially with condoms, underlie the UAI of men who attempt to reduce risk through taking the top role or episodic use of condoms. A large portion of men reporting UAI without ejaculating, report participation in bareback scenes and websites and also have UAI and ejaculate. A significant number of men often placed in the "strategic positioning" category are, then, not trying to practise "harm reduction," while those who are tend to move in similar circles, share similar beliefs, and may have the potential, over time, to shift toward barebacking.

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### CIRCUMCISION AMONG MEN WHO HAVE SEX WITH MEN (MSM) IN THE POLARIS HIV SEROCONVERSION STUDY

Liviana Calzavara [1,2]; Robert Remis [1,2]; Ted Myers [1,2]; Gerald Lebovic [1]; Nancy Ramuscak [1]; and the Polaris Study Team
1-HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto; 2-Department of Public Health Sciences, Faculty of Medicine, University of Toronto

**Plain Language Summary:** The evidence that male circumcision significantly reduces the risk of HIV infection among heterosexual men is now compelling. Our analysis suggests that circumcision may also have an impact on HIV infection for MSM who have unprotected insertive anal sex. Additional analysis is being conducted to further assess this relationship.

**Objective:** To explore the association between circumcision and HIV seroconversion among those who engage in unprotected insertive anal sex.

**Methods:** Polaris is a cohort study of recent HIV seroconverters and HIV-negative controls in Ontario. Participants were recruited through Ontario's HIV diagnostic testing database, physicians, community organizations and media. In total 240 MSM enrolled in Polaris were asked their circumcision status (84 cases, 156 controls). We examined circumcision status and socio-demographic characteristics and HIV seroconversion. We used multiple logistic regression to examine the impact of circumcision on HIV infection among those who engaged in unprotected insertive anal sex. Unprotected insertive anal sex was defined as not having used a condom for insertive sex, or having a condom break, slip, removed before ejaculation or having delayed application of the condom.

**Results:** Overall 69% (165) of MSM surveyed were circumcised, 70% of cases and 72% of controls. The majority (88%; 145/165) were circumcised in infancy. 15% were circumcised for religious or cultural reasons and 20% for medical reasons. Significant predictors of circumcision were being born in Canada (p = 0.0005) and being Jewish/Muslim or Christian compared to other religions (p= 0.0079). There was a trend suggesting those born after 1970 were less likely to be circumcised in infancy compared to those born earlier (p = 0.078). During the time period of infection, 47% of MSM reported no unprotected anal sex, 11% had only unprotected receptive anal sex, 15% had only unprotected insertive anal sex and 26% had both unprotected insertive and receptive anal sex. Among those who had only unprotected insertive anal sex (n=35), circumcision may have a protective effect (ORcrude = 3.19, 95%CI 0.70-14.56, p = 0.151). Preliminary models suggest that being uncircumcised and engaging in unprotected insertive anal sex has a significant relationship with HIV infection (ORadj 4.91, 95%CI 1.43-16.93).

**Conclusions:** The majority of MSM in Polaris are circumcised, mostly during infancy. Preliminary analyses suggest that uncircumcised men who engage in unprotected insertive anal sex may be at higher HIV risk than those circumcised. Additional analysis is being conducted to further assess this relationship.

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# Monday, November 19, 2007 – 1:45 p.m.

## Vulnerable Populations: Building on Strengths

### 125

#### THE IMPACT OF ERASURE ON HIV VULNERABILITY IN ONTARIO'S TRANS COMMUNITIES

Greta Bauer [1]; Rebecca Hammond [2,3]; Robb Travers [2]; Matthias Kaay; Michelle Boyce [4]; Scott Anderson [2]
1-Epidemiology & Biostatistics, The University of Western Ontario; 2-Ontario HIV Treatment Network; 3-Community Health & Epidemiology, Dalhousie University; 4-TGStation.com

**Plain Language Summary:** For trans people in Ontario, social determinants of health (SDOH) -- including income, housing, and access to social services and health care -- have a broad range of effects on health and well-being and can impact vulnerability to HIV. Using specific examples from Phase I of the Trans PULSE Project, we explore how social determinants are mediated by social exclusion and examine how the concept of erasure can enhance our understanding of social exclusion as a meta-determinant of health.

**The Challenge:** To develop a theoretical framework that explains how erasure functions to impact SDOH for trans people.

**Our Approach:** The Trans PULSE Project is a community-based research project. We held a series of community soundings in 2006 to explore health issues affecting trans people in Ontario. Transcripts from soundings were analyzed by a team of community and allied investigators to elucidate the processes that impacted health.

**Key Findings:** We identified three forms of erasure, each of which can take either passive or active forms: 1) Self erasure involves intentionally or unintentionally passing as a cisgendered person. 2) Institutional erasure occurs through a lack of health care, social service, education or hiring policies that accommodate trans identities or trans bodies, including the lack of knowledge that such policies are even necessary. 3) Information erasure includes a lack of existing knowledge regarding trans people and trans issues, the failure to generate this information, and the assumption that such knowledge does not exist, even where it may. We demonstrate how these three processes work together in a mutually reinforcing manner to produce a system where the appearance of a trans person as applicant, patient or client is seen as an anomaly, one not backed by a visible community of any number or strength. Thus, the impetus falls too often on individual trans people to attempt to remedy systematic deficiencies and policies, and to acquire the knowledge necessary to address their needs. Underlying these processes is cisnormativity, the assumption that people will be cisgendered, which disallows the possibility of trans existence or trans visibility. Vulnerability of trans people within trans-inappropriate systems may make visibility difficult or dangerous, and thus institutional and information erasure are identified as necessary sites for intervention.

**Impact on Policy and Practice:** Our analysis informs strategies for improvement in SDOH and reductions in vulnerability to HIV. Our findings may have relevance for other communities where invisibility and "passing" affect community visibility and access to adequate financial resources, housing, social services and health care.

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### 126

#### MABWANA. REACHING BLACK MEN WHO HAVE SEX WITH MEN IN TORONTO: THE IMPORTANCE OF COMMUNITY

Clemon George [1,2]; Winston Husbands [2,3]; Lydia Makoroka [3]; Barry Adam [4]; Robert Remis [2,5]; Sean Rourke [6]; Joseph Beyene [7]
1-Mental Health Services, St. Michael's Hospital; 2-African and Caribbean Council on HIV in Ontario; 3-AIDS Committee of Toronto; 4-Department of Sociology, University of Windsor; 5-Department of Public Health Sciences, University of Toronto,; 6-Department of Psychiatry, University of Toronto; 7-Public Health, Hospital for Sick Children

**Plain Language Summary:** In Canada, surveillance data indicates that Black men, particularly Black MSM, are disproportionately affected by HIV, when compared to the proportion of non-black male and black females infected. However, there is a paucity of research evidence to inform program and services for this population. Due to the lack of evidence on HIV transmission risks for this population, we began our study by soliciting information from key community members on Black MSM networks, their needs and other issues of relevance that make them vulnerable to HIV.

**Objective:** The general objectives of the study are to: 1. Characterize BMSM in Toronto in terms of their socio-demographic characteristics, sexual relationships and sexual behaviour; 2. Determine correlates of sexual risk behaviour; 3. Determine differences among BMSM related to their sexual behaviour; 4. Examine the experiences, influences and decision-making associated with (un)protected sex among BMSM, and how these factors may define microcultures of BMSM; 5. Understand how BMSM interpret and assess current HIV prevention campaigns, and the extent to which the campaign messages influence their sexual behaviour.

**Methods:** Key Informants (KI) from organizations serving Black men in Toronto, and individuals who had an intimate knowledge of BMSM communities in Toronto, were selected for in-depth interviews. Questions were designed to solicit information on health and social agencies organizational structure and how this fits with working on behalf of Black MSM. Questions were also asked on BMSM community relationship and social support of Black MSM in black communities. Participation in the KI interviews was voluntary and all participants were consented for the interview. Key Informants were interviewed at the study's office or at another private location. Interviews were approximately 1 1/2 hours in length, and conducted by two researchers. Notes were taken during the interviews and later transcribed.

**Results:** The nine KI were Black men, all active in the BMSM community. They identified the following main issues facing Black MSM: The structure of Black service organizations is not welcoming; Education around HIV/AIDS is confusing - resulting in insufficient knowledge on sexual health and inadequate skills in risk negotiations; HIV campaign have not been inclusive of Black MSM; Complexities in sexual identity become a barrier to disclosing sexuality; Sense of isolation, depression and addiction pervasive in BMSM communities but often not acknowledged by service providers; Lack of a well defined support mechanism; Homophobia in Black communities including important community stronghold such as churches, which exacerbates social isolation; Racism within the broader gay community; Generally, there was a sense of lack of support for Gay, bisexual and other MSM from Black communities.

**Conclusions:** There is a sense of fragility in BMSM communities with regards their position within Black communities and the broader gay community. Key Informants recommended that regardless of the study's outcome, results should be reported in a way that minimizes discrimination of BMSM and further marginalization of BMSM and Black Communities. Most respondents emphasized the need to address homophobia in a way that is respectful of Black community standards in order to open a dialogue within the communities.

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### UNDERSTANDING AND RESPONDING TO DEPRESSION IN ABORIGINAL PEOPLE LIVING WITH HIV/AIDS: SERVICE PROVIDER PERSPECTIVES

Evan Collins [1]; Randy Jackson [2]; Roy Cain [3]; Tracey Prentice [2]; Judy Mill [4]; Kevin Barlow [2]
1-Department of Psychiatry, University of Toronto; 2-Canadian Aboriginal AIDS Network; 3-School of Social Work, McMaster University; 4-Faculty of Nursing, University of Alberta

**Plain Language Summary:** This study interviewed service providers who work with Aboriginal people living with HIV/AIDS who also experience depression. The service providers, from different backgrounds, see depression as a complex problem and emphasize the role of social issues, the impact of residential schools, and the loss of culture and tradition in contributing to depression. They support the use of Aboriginal traditional healing as long as it is complementary, and not contradictory, to mainstream treatment of HIV and depression.

**Objective:** This OHTN-funded research project explores how Ontario service providers view depression in Aboriginal persons living with HIV/AIDS (APHAs). We examine how service providers understand depression and its relation to HIV; how they respond to depression in their clients; and the challenges they face in providing service.

**Methods:** We conducted in-depth interviews of 24 service providers from 4 Ontario cities. Professional background included psychiatrists, social workers, nurses, addiction counselors, community support workers, elders and traditional healers. Eleven worked in Aboriginal services and the rest for non-Aboriginal agencies/programs. Using a narrative, qualitative approach, verbatim transcripts were coded and analyzed for emergent themes.

**Results:** In general, service providers viewed depression in a Western paradigm as an emotional state with feelings of sadness and hopelessness accompanied by physical signs (loss of sleep, appetite, etc). Most emphasized the multi-factorial and complex nature of depression including the interplay with drug and alcohol abuse, and the contribution of social determinants, intergenerational trauma and the impact of residential schools. A dominant theme was the experience of loss in APHAs with depression whether the loss was physical, psychological, social or cultural. In responding to depression, both Aboriginal and non-Aboriginal service providers endorsed the role of Aboriginal healing and traditions for their clients. Generally they viewed this as complementary to Western approaches to depression and cautioned against situations where it might be contradictory. Service providers discussed numerous challenges in dealing with depression in APHAs.

**Conclusions:** Service providers from varied backgrounds tended to view depression from a Western lens but recognized the complexity of HIV and mental health. There was emphasis on loss, especially related to culture, traditions and the social determinants of health, and an endorsement of Aboriginal healing and traditions playing a role in supporting APHAs with depression. They called for greater organizational resources and better partnerships between programs to address the complexities of mental health problems in Aboriginal people living with HIV/AIDS.

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### POSITIVE SPACES, HEALTHY PLACES: HEALTH OUTCOMES AT 6 MONTHS

Ruthann Tucker [1]; Saara Greene [2]; Michael Sobota [3]; Jay Koornstra [4]; LaVerne Monette [4]; Dale Guenter [6]; Steve Byers [7]; James Dunn [8]; Stephen Hwang [8]; Sean B. Rourke [1,8]
1-Ontario HIV Treatment Network; 2-Fife House; 3-AIDS Thunder Bay; 4-Bruce House; 5-Ontario Aboriginal HIV/AIDS Strategy; 6-McMaster University; 7-AIDS Niagara; 8-Centre for Research on Inner City Health, St. Michael's Hospital; University of Toronto

**Plain Language Summary:** This is the first systematic and longitudinal community-based research initiative in Canada to examine and demonstrate that the type, quality and stability of housing for people living with HIV and AIDS affects health outcomes and health-related quality of life.

**The Challenge:** Executive directors and front-line support workers in community-based AIDS service organizations know first-hand that the availability, quality and access to stable housing significantly affects the health, well-being and quality of life of people living with HIV in Ontario. What has not yet been available is systematic data to support the pervasiveness of the problem across the province, and the extent to which the social determinants of health increase the risk for unstable housing and also contribute in a detrimental way to the health and wellbeing of people living with HIV.

**Our Approach:** A total of 605 face-to-face surveys with people living with HIV and AIDS from across Ontario were collected at baseline (one year follow-up underway) to examine: (a) the housing status of people living with HIV in Ontario; (b) the range of housing and supportive housing options available across Ontario, including those provided by community-based health and social service organizations and other housing agencies; (c) variations in the housing and/or homelessness experiences of people with HIV from specific communities, including aboriginal communities, ethnocultural communities, women, families, sexual minorities, youth and ex-prisoners; and (d) the kind of housing options desired or required by people with HIV that will ensure access to, and utilization of, health care, treatment and social services for optimal health. As part of our 1-year mixed-method prospective study, short interviews were conducted at 6 months by phone on all participants to determine any changes in housing and health status. This study will highlight these findings:

**Key Findings:** For those housed at baseline (either with and without support services) 20% had a change in their housing at 6 months compared with 48% who were unstably housed ($p < 0.01$). Those who had a change in housing were more likely to have had substance use problems at baseline and experiences of housing discrimination ($p < 0.01$). All participants were asked to rate their physical and emotional condition at the follow-up interview compared to 6 months ago: 33% of those housed with support services reported their status as "better" – a rate almost 2 times higher than those unstably housed; in addition, those housed without support services and those unstably housed were twice as likely to report that their status was "worse" compared with those who were housed with support services. Several factors were found to be associated with increasing housing risk at 6 months: (1) geographic location (highest risk in Thunder Bay, medium risk in Ottawa and Kingston and lowest in remaining regions); (2) Presence of depression and alcohol misuse problems at baseline were associated with a 3-fold increase in perceived housing risk at 6 months; (3) Those who felt anxious about being forced to move out or had experienced 1 or more events of housing discrimination were twice as likely to feel that their housing was at risk at 6 months.

**Impact on Policy and Practice:** Housing stability and access to support services affect health outcomes in people living with HIV. Strategies and interventions that address housing and the social determinants of health are needed to improve the health and well being of people living with HIV/AIDS. Further evidence of the relationship between housing and health will be available shortly from Positive Spaces, Healthy Places as we complete our qualitative interviews and detailed surveys at 1 year.

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# Monday, November 19, 2007 – 1:45 p.m.

## Harm Reduction: Facts, Attitudes and Solutions

**129**

### CRYSTAL METHAMPHETAMINE USE AMONG POLY-DRUG USING MEN WHO HAVE SEX WITH MEN: WHO IS USING?

Sandra Bullock [1]; Ted Myers [2,3]; Alicja Krol [1]; Liviana Calzavara [2,3]; Dan Allman [2,4]; Peggy Millson [2,3,5]
1-Department of Health Studies and Gerontology, University of Waterloo; 2-HIV Social, Behavioural and Epidemiological Studies Unit, University of Toronto; 3-Department of Public Health Sciences, Faculty of Medicine, University of Toronto; 4-University of Edinburgh, Scotland;
5-Ontario HIV Treatment Network

**Plain Language Summary:** Previous research has indicated that crystal methamphetamine (crystal) use may be related to increased participation in unprotected anal intercourse among men who have sex with men (MSM). Earlier analysis of poly-drug using MSM in Toronto indicated that crystal use was affiliated with unsafe sex primarily among HIV positive men (who were HIV positive prior to using crystal). HIV negative men were much less likely to use crystal and have unsafe sex. This analysis looks further into the history of MSM to highlight correlates and predictors of crystal use.

**Objective:** To gain an understanding of who in the Toronto MSM community is using crystal, to further our understanding of how it may be involved in risk behaviour.

**Methods:** 300 MSM were interviewed about their use of crystal and 19 other substances during their lifetimes and in the past 90 days. They also were asked about their identity, sexual and substance use histories, and other determinants of health. Logistic regression was conducted to determine the primary correlates of current (past 90 day) crystal use.

**Results:** In total, 83 men (27.6%) had used crystal in the 90 days prior to interview, and 164 (54.7%) had used it within their lifetime. Odds of current crystal use increased with being somewhat (OR=7.64) or very attached (OR=10.43) to the Toronto gay community, being HIV positive (OR=2.87), the perception of having no one "who cares for you" (OR=4.56), perceiving that crystal makes sex better (OR=1.97), seeking sex partners through sex parties and the internet (OR=2.89) or via other impersonal means (OR=19.27), and having an income between $40,000 and $59,000 (OR=3.06). Men who lived in a common-law relationship (OR=0.17), were satisfied with their social lives (OR=0.38), and who had experienced mental abuse in the past year were less likely to have used crystal in the past 90 days.

**Conclusions:** While many studies have examined the relationship between crystal and participation in unsafe sex, few have studied the predictors of crystal use itself in the MSM community in Toronto. Expected correlates were often not significant (e.g., gay bar and circuit party attendance). More research must be conducted to understand who is currently using crystal in Toronto, and their motivations for using the drug.

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**130**

### INJECTING GENDER: ATTITUDES AMONG WOMEN AND MEN IN OTTAWA WHO INJECT DRUGS TOWARDS A POTENTIAL SAFER INJECTING FACILITY

Emily De Rubeis [1]; Lynne Leonard [1]; Carol Strike [2]; Emily Medd [1]; Aideen Reynolds [1]
1-HIV Prevention Research Team, Department of Epidemiology and Community Medicine, University of Ottawa; 2-Centre for Addiction and Mental Health

**Plain Language Summary:** Safer injecting facilities (SIFs) provide users with a safer place to inject drugs. Results of recent studies suggest that SIFs have several positive benefits. These findings are important given that Ottawa continues to report high levels of HIV and HCV infections among injection drug users (IDUs). We compared the attitudes between women and men IDUs in Ottawa towards a potential SIF. We found that the majority of both genders would use a SIF. More women reported that they did not want to use a SIF because they did not want to be seen. Other differences between women and men included that more women reported that it was not acceptable to prohibit getting help injecting from other users of the site. The findings suggest that women and men IDUs have different harm reduction needs which need to be addressed.

**Objective:** Based on emerging evaluation data, a SIF in Ottawa may have the potential to address elevated levels of HIV and HCV infection among IDUs and widespread engagement in public injecting and other HIV- and HCV-related risk practices. The objective of this study was to characterize attitudes of Ottawa IDUs towards operational policies and services in an attempt to optimize uptake by and benefits for both women and men.

**Methods:** In 2005, 250 IDUs consented to personal interviews. A gendered analysis comparing attitudes and preferences towards a potential SIF was undertaken.

**Results:** Sixty-four percent of IDUs reported willingness to use a SIF. Reasons for not wanting to use a SIF differed between genders; significantly more women (67%) than men (23%) reported not wanting to be seen using a SIF. While the majority of both genders reported that most proposed policies were acceptable, gender differences existed towards policies prohibiting assisted injections and sharing drugs. However, 67% of women reported a willingness to learn how to inject themselves – a teaching component that could be provided in a SIF. In terms of service preferences, nearly all participants reported the importance of overdosing care, HIV and HCV testing, needle exchange, medical care and teaching, and referrals to other services.

**Conclusions:** Although the majority of IDUs were willing to use a potential SIF, gender differences existed with regards to reasons for not wanting to use a SIF, and towards proposed policies. In order to maximize utilization of a potential SIF or other harm reduction services, it is important to characterize gender-specific attitudes and preferences towards these important services.

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## 131

### LEGAL ISSUES SURROUNDING THE DISTRIBUTION OF "SAFER CRACK USE KITS"

Richard Pearshouse [1]; Richard Elliott [1]
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**Plain Language Summary:** The legal issues surrounding the distribution of sterile pipes in 'safer crack use kits' are contentious. However, little accurate analysis of such legal issues has been undertaken. This research seeks to provide clarity to this issue, and identify avenues to remove the uncertainties currently found in the law.

**The Challenge:** Oral crack use (crack smoking) has been identified as a possible risk factor for transmission of HIV and HCV. Recent research among people who smoke (rather than inject) crack and heroin has found that the prevalence of HCV is substantially higher than in the general population. The distribution of sterile pipes in 'safer crack use kits' is an important component of a broader harm reduction approach. The legal issues surrounding the distribution have been the subject of much misinformation. The challenge is to provide accurate legal information regarding the distribution of the pipes, and identify avenues to law reform in this area.

**Our Approach:** This research discusses areas of criminal and civil liability under Canadian law for health service providers and clients of safer crack use kit distribution programs. It also considers the issue from a human rights perspective. Finally, it discusses appropriate reform to law and policy to remove the legal uncertainty around such harm reduction activities.

**Key Findings:** The distribution of unused, sterile crack pipes within 'safer crack-use kits' is unlikely to attract criminal liability. The crack pipes are distributed as devices in the prevention of disease. This is an important consideration in determining how Canadian criminal law may treat these items. However the status of used crack pipes is less clear. According to the definition in section 2(2) of the CDSA, a "controlled substance" includes "anything that contains or has on it a controlled substance and that is used or intended or designed for use … in introducing the substance into a human body". In theory, an individual in possession of a used crack pipe (which contains traces of crack) is vulnerable to arrest and prosecution for possession of a controlled substance. In practice, people have been convicted for possession of trace amounts of crack cocaine on crack pipes.

**Impact on Policy and Practice:** This research provides greater clarity as to the potential legal liability regarding the distribution of crack pipes. It also identifies areas of potential law reform to remove the uncertainty identified in the law.

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## 132

### "THEY'RE ALL CONNECTED TOGETHER": THE EXPERIENCE OF SUBSTANCE USE AND DEPRESSION AMONG CANADIAN ABORIGINAL PEOPLE LIVING WITH HIV/AIDS

Tracey Prentice [1,5]; Randy Jackson [1]; Roy Cain [2]; Evan Collins [3]; Kevin Barlow [1]; Judy Mill [4]
1-Canadian Aboriginal AIDS Network; 2-McMaster University; 3-University of Toronto; 4-University of Alberta; 5-University of Ottawa

**Plain Language Summary:** This presentation will describe the results of our study on the experience of depression among Aboriginal People Living with HIV/AIDS (APHAs), with a particular focus on the use of substances. We briefly outline our approach to research, our objectives and our methods, before highlighting the complexity of the relationship between substance use and depression as reported by the APHAs in our study. We conclude with recommendations for service providers.

**Objective:** The purpose of this academic – community partnership is to explore the experience of depression from the perspective of Canadian Aboriginal people living with HIV/AIDS (APHAs). In particular, the study examines how participants understand the roots of their depression, what they do about their depression, and how formal service provision might better respond to their needs. The experience of substance use is the focus of this presentation.

**Methods:** In partnership with community collaborators in 6 Canadian cities we recruited 72 individuals (men=45; women=23; and transgender=4) at various ages and stages of HIV infection to participate in in-depth interviews. Verbatim transcripts were coded and analyzed for emergent themes.

**Results:** For participants in this study, the relationships between HIV/AIDS, substance use and depression is complex and multi-directional. Excessive substance use is reported as both cause and effect of depression and plays multiple roles in relation to living with HIV. Many of our participants reported growing up in homes where excessive alcohol use (and to a lesser extent drugs) was a regular occurrence that sometimes led to violent or abusive episodes. To escape this, participants reported leaving their family homes to engage in street-life where substance use is often learned as a 'survival technique' and vulnerability to HIV is increased. Many APHAs reported injection drug use as the means by which they were infected; however, many more participants reported only initiating, or increasing, substance use immediately following diagnosis. A cycle of depression and alcohol or drug dependence is a common experience in which the importance of managing HIV is temporarily forgotten (e.g., taking HIV meds, proper nutrition, rest, etc.). This frequently leads to further depression. However, many participants were able to overcome or manage their substance abuse and find alternate ways of coping with their HIV and/or their depression. Both Aboriginal and non-Aboriginal services (e.g., addiction treatment centres or AIDS service organizations, etc.) were instrumental in finding new approaches to supporting APHAs in which re-connecting participants to Aboriginal culture and traditions was key.

**Conclusions:** Our findings suggest ways formal services might better respond to the needs of Aboriginal people living with HIV and depression. In particular, while incorporating cultural elements, services can also attend to the unique challenges faced by Aboriginal people living with HIV/AIDS. Addressing past trauma and facilitating access to traditional ceremony and culture are key elements to how services might better respond.

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# Tuesday, November 20, 2007 – 2:45 p.m.

## Clinical Complexities of Co-Infection

### 133

**GONORRHEA AND HIV: FRIENDS OR FOES?**

Wendy N. Dobson-Belaire [1]; Anuradha Rebbapragada [2]; Alan Cochrane [1]; Rupert Kaul [2]; Mario Ostrowski [3]; Scott D. Gray-Owen [1]
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**Plain Language Summary:** Gonorrhea is a sexually transmitted infection caused by the bacterium Neisseria gonorrhoeae (Ngo). Clinical and epidemiological studies have demonstrated that N. gonorrhoeae promotes HIV-1 transmission by stimulating viral shedding and increasing the chance of seroconversion upon exposure to the virus. How Ngo mediates these effects are unknown. We found that the bacteria can directly stimulate HIV-1 expression in HIV-infected T cell lines, however when examining actual white blood cells from donors, Ngo was found to cause an anti-HIV response mediated by the anti-viral protein interferon-alpha (INFα).

**Objective:** While clinical and epidemiological studies clearly demonstrate that N. gonorrhoeae promotes HIV-1 transmission, the reason for this relationship remains poorly defined. This study aims to understand the molecular and immunological aspects of this interaction by examining the effect of N. gonorrhoeae infection on HIV-1 replication in peripheral blood mononuclear cells (PBMCs).

**Methods:** Four different models were employed. The Jurkat CD4+ T cell line or primary CD4+ T cells were transduced with a pseudotyped HIV-1, or CD8-depleted PBMCs from HIV+ donors or HIV- donors infected with HIV in vitro. These were infected with various defined bacterial strains and HIV-1 expression was measured by p24 ELISA. In some instances, the culture supernatants from bacterial infected PBMCs were transferred onto HIV-infected cells to monitor the effect.

**Results:** N. gonorrhoeae was found to increase HIV-1 expression in the Jurkat CD4+ T cell line but had no detectable effect on primary CD4+ T cells. In addition, gonococcal infection of CD8+-depleted PBMCs resulted in profound inhibition of HIV replication that we have attributed to the release of a soluble factor(s). Analysis of culture supernatants indicates that the type I interferon, IFNα, is expressed in response to N. gonorrhoeae, and anti-interferon receptor antibodies suppress the supernatants' HIV-inhibitory effect.

**Conclusions:** Infection with N. gonorrhoeae stimulates HIV production by infected CD4+ T cells, yet simultaneously stimulates a potent IFNα-dependent innate response that opposes this effect. This implies that the bacteria's impact on HIV-1 will ultimately rely upon on how the balance between these two opposing effects is maintained during coinfection.

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### 134

**ANAL DYSPLASIA (THE TRACE STUDY): COMPARATIVE EFFECTIVENESS OF ABLATIVE THERAPIES**

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**Plain Language Summary:** Anal cancer occurs at higher rates in HIV-positive gay men. Anal pre-cancerous changes have been detected in the TRACE study. These pre-cancers can be treated to remove them. In this study, we compare different treatment strategies.

**Objective:** Anal cancer occurs at high rates in HIV-positive gay men. Screening studies can detect pre-cancerous changes in the anal canal. TRACE is an anal cancer screening study designed to determine the characteristics of tests used to detect high-grade pre-cancer (AIN 2/3). High-grade pre-cancer can be treated but optimal therapy is uncertain. Our objective in the TRACE cohort was to compare some of these treatment modalities.

**Methods:** Subjects were HIV+ men who had a history of anal receptive intercourse (ARI). Cytology and biopsy specimens were independently assessed by 2 blinded pathologists. All subjects with AIN 2/3 were offered Trichloroacetic acid (TCA) applied once monthly x 4 months, Infra-red Coagulator (IRC) as 1-2 treatments or no therapy (surveillance). Follow-up visits were every 3-6 months and the index lesion was re-biopsied. Therapeutic failure was defined as recurrence of AIN 2/3 at the same or an adjacent site; success was the presence of AIN 1 or normal histology after treatment.

**Results:** There were 90 subjects with 148 AIN 2/3 lesions and 43% had >1 lesion. Treatment and follow-up was completed for 80 lesions (54%): IRC (57), TCA (16), Aldara (5), surgery (2), no therapy (8). Subjects had a median age=45, CD4=350, median viral load <50, 77% were on HAART. Patient characteristics were equivalent between groups. Complications after IRC occurred in <5% and included prolonged pain, bleeding or fever; there were no complications from TCA. Successful ablation of individual lesions occurred after these therapies: IRC (39/57, 68%); TCA (14/16, 87%); surgery (2/2). For IRC vs TCA, P=0.2 (NS). Forty-three lesions were not treated because of personal preference, pts. were lost to follow-up or the lesions were too large (>50% of the transition zone): remissions occurred in 6 of 8 untreated lesions. The median duration of follow-up was 13.5 months in all pts. with no significant difference between the groups.

**Conclusions:** High rates of high-grade dysplasia have been detected during anal cancer screening. Treatment effectiveness of the Infra-red Coagulator (IRC) and topical Trichloroacetic acid (TCA) are similar. IRC requires fewer treatment visits but is associated with greater morbidity.

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## 135

### HIV-HCV CO-INFECTION THERAPEUTIC OUTCOMES HAVE NOT IMPROVED OVER TIME

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**Plain Language Summary:** HIV medications have improved with time. This has resulted in improved treatment outcomes for those living with HIV. Many HIV-HCV co-infected individuals have a heavy burden of other challenges (i.e. poverty, addictions, mental health illness) that make successful treatment more difficult to achieve. Our work suggests that HIV-HCV co-infected individuals are not benefiting as much from improvements in treatment as other populations.

**Objective:** HIV management has improved in terms of multidisciplinary delivery of care, HAART side effect profile, frequency of dosing and pill count. It is unknown whether this has improved suboptimal treatment outcomes previously observed in HIV-HCV co-infection.

**Methods:** Clinical, immune and virologic therapeutic outcomes of Ottawa Hospital Immunodeficiency Clinic patients treated between January 1996 and February 2007 were evaluated by database analysis (SPSS 13.0). Outcomes and reasons for interruption or change in therapy were compared before and after the midpoint of the HAART era (approximately January 2001) in HIV-HCV co-infected patients initiating a first course of HAART.

**Results:** Table 1 Treatment Outcomes

| | N | Median Time to HAART Interruption Or Change (months) | Baseline Mean CD4 (cells/μL)) (SD) | Mean CD4Increase at Month 6 (cells/μL) (SD) | Mean CD4 Increase at Month 12 (cells/μL) (SD) | HIV RNA below Detection at Months 6 and 12 | |
|---|---|---|---|---|---|---|---|
| 1996-2000 | 108 | 20 | 380 (291) | 90 (143) | 116 (136) | 67% | 85% |
| 2001-2007 | 63 | 22 | 206 (187) | 82 (96) | 134 (135) | 85% | 91% |

By multivariate Cox regression analysis the median time to interruption or change in initially prescribed HAART in HIV-HCV did not differ by era (OR 1.2, p=0.2). In those on treatment, CD4 recovery did not improve in the recent era (month 6, p=0.87; month 12, p=0.67 by t-test). The on-treatment proportion achieving HIV RNA suppression below detection improved at month 6 (p=0.05, $\chi 2$).

Table 2

| Proportion Interrupting or Changing HAART for: | Gastrointestinal Intolerance | Poor Adherence | Lost to Follow-Up | Substance Abuse | Liver Toxicity |
|---|---|---|---|---|---|
| 1996-2000 | 24% | 19% | 11% | 8% | 5% |
| 2001-2007 | 21% | 23% | 14% | 5% | 3% |

There was no change in the proportions of key reasons explaining why patients interrupted or changed their initially prescribed HAART.

**Conclusions:** Early virological measures of treatment success improved modestly in those remaining on HAART in more recent times. However, improved characteristics of HIV management did not increase treatment duration, improve CD4 recovery, increase adherence or diminish lost to follow-up in HIV-HCV co-infection. Strategies which target adherence and substance abuse may increase uninterrupted duration of HAART use, and the benefits of that achievement, in HIV-HCV.

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## 136

### ABNORMAL VAGINAL FLORA IN HIV INFECTED WOMEN IS ASSOCIATED WITH INCREASED HIV SHEDDING AND REVERSIBLE GENITAL INFLAMMATION AND ACTIVATED T CELL POPULATIONS

Anuradha Rebbapragada [1]; Kathryn Howe [1]; Charles Wachihi [2]; Christopher Pettengell [1]; Sherzana Sunderji [1]; Blake T. Ball [3]; Francis Plummer [3]; Walter Jaoko [2]; Rupert Kaul [1]
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**Plain Language Summary:** Perturbations in vaginal flora, defined as altered vaginal flora (AVF; minor perturbations) and bacterial vaginosis (BV; more severe perturbations), may be associated with increased HIV transmission. To understand the mechanisms behind this observation, we investigated the changes in cervical cell populations and protein levels associated with BV in HIV-infected women. Our findings suggest that BV infection may alter the local genital tract milieu to promote local HIV replication and consequently secondary transmission.

**The Challenge:** BV is very common, and has been associated with genital tract inflammation and increases in both HIV acquisition and transmission. However, the changes in the female genital tract (FGT) mucosal immune milieu that accompany BV, as well as lesser perturbations in vaginal flora (AVF), have not been elucidated.

**Our Approach:** In an initial cross-sectional study we examined the association of BV and AVF with cervical immune cells, cytokine levels and the cervical shedding of HIV, Herpes simplex virus 2 (HSV2) and cytomegalovirus (CMV) in HIV-infected Kenyan female sex workers (FSWs). Next, we examined the effect of BV therapy (500 mg of oral metronidazole twice daily for a week) on FGT immunology.

**Key Findings:** In the cross-sectional analysis of 70 FSWs, HIV genital shedding was associated with both AVF (OR 3.8; P=0.05) and BV (OR 4.3; P=0.04). AVF was associated with increased genital tract levels (P<0.05) of IL1β and TNFα, two pro-inflammatory cytokines that may enhance HIV replication. In the prospective study, effective BV therapy reduced genital tract levels of IL1β (P<0.05), and was associated with reduced numbers of overall cervical CD4+ T cells, as well as the number of activated CD4+ cells expressing CD69 and the CCR5 HIV co-receptor (P<0.01 for all).

**Impact on Policy and Practice:** This study is the first to demonstrate that effective BV therapy reduces genital tract inflammation in HIV-infected women. We postulate that perturbations in the FGT immune milieu due to changes in vaginal flora may drive secondary transmission of HIV via two possible mechanisms: (i) increased levels of IL1β may directly activate HIV-LTR and enhance viral replication; or (ii) increased numbers of activated T cells during BV may serve as a reservoir for increased HIV replication in the genital mucosa. Strategies to maintain/restore normal vaginal microbial flora have the potential to reduce HIV transmission.

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# Tuesday, November 20, 2007 – 2:45 p.m.

## Immune Processes and Vulnerability

### 137

**TOLL-LIKE RECEPTOR EXPRESSION AND RESPONSIVENESS IS INCREASED IN HIV-1 INFECTION AND NORMALIZED WITH ANTIRETROVIRAL THERAPY**

Richard Lester [1,2]; Xiao-Dan Yao [3]; Blake T. Ball [1]; Lyle McKinnon [1]; Rupert Kaul [4]; Charles Wachihi [2]; Walter Jaoko [2]; Francis Plummer [1]; Kenneth Rosenthal [3]
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**Plain Language Summary:** The role of innate immunity in HIV is poorly understood. Our innate immune system uses receptors, including Toll-like receptors (TLRs), as an early warning system to detect infection and rapidly activate inflammation and immune responses. Here, we studied the effect of HIV infection in treated and untreated women from Kenya on TLR expression and function. We found that chronic, untreated HIV infection was associated with greatly increased expression of TLRs. We also showed that HIV infection leads to markedly increased TLR-triggered inflammatory responses. Increased TLR expression was associated with viral load in subjects and anti-retroviral treatment normalized TLR expression. Together, these data indicate that chronic HIV infection is a driver of increased innate immune sensitivity, and this may contribute to the chronic immune activation that underlies AIDS. This mechanism may lead to potential new targets for therapy.

**Objective:** The role of innate immunity in HIV disease is poorly understood. Toll-like receptors (TLRs) are important in rapidly recognizing infection and triggering innate immune responses. The objective of this study was to evaluate the effect of chronic untreated and treated HIV-1 infection on TLR expression and signaling.

**Methods:** Two hundred high risk HIV-infected and uninfected women from a Kenyan cohort participated in these studies. TLR1-10 mRNA expression was determined by quantitative reverse transcriptase polymerase chain reaction (qRT-PCR). TLR ligand responsiveness was determined ex vivo by cytokine production in culture supernatants.

**Results:** Chronic, untreated HIV-1 infection was significantly associated with increased expression of TLR6, TLR7, and TLR8 and TLR2, TLR3, and TLR4 were additionally elevated in individuals with advanced disease. Elevation of select TLR expression was positively associated with plasma HIV RNA load, suggesting that either increased virus replication and/or higher levels of circulating virus may drive increased TLR expression in vivo. Further, TLR expression was increased by single-stranded RNA from HIV in vitro, whereas decreased TLR4 expression was observed with its ligand lipopolysaccharide (LPS). Peripheral blood mononuclear cells (PBMCs) of HIV-infected subjects also demonstrated profoundly increased proinflammatory responsiveness to TLR ligands. Finally, TLR expression was normalized in subjects taking antiretroviral therapy, independently of CD4+ T-cell recovery.

**Conclusions:** Together, these data indicate that chronic viremic HIV-1 is associated with increased TLR expression and responsiveness which may perpetuate immune dysfunction and activation that underlies HIV pathogenesis, and thus reveal potential new targets for therapy.

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### 138

**THE RESCUE OF FUNCTIONALLY IMPAIRED HIV SPECIFIC CD8 T CELLS**

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**Plain Language Summary:** During chronic infection, HIV-specific CD8 T cells exhibit progressive signs of functional impairment, attributed to persistent antigenic stimulation, upregulation of the inhibitory receptor PD-1 and declining T cell help. Strategies that directly improve CD8 T cell function offer the potential of restoring immune control of HIV.

**The Challenge:** Although PD-1 expression has been identified as a cause of functional impairment in HIV, in this study PD-1 expression was observed on only a subfraction of HIV-specific CD8 T cells in a subfraction of donors, whereas HIV-specific CTL from all donors exhibited a limited repertoire of effector functions. Blocking the PD-L1/PD-1 axis might also lead to autoimmunity. Thus, Ag-specific strategies for improvement of CTL function during chronic viral infection in the context of high PD-1 expression remain an important therapeutic target for HIV.

**Our Approach:** CD137L (4-1BBL) is emerging as an important stimulator of anti-viral CD8 T cell responses.

**Key Findings:** Regardless of the PD-1 status of the donors, here we show that 4-1BBL, when combined with CD80 or CD70, expands a population of antigen specific CD8 T cells expressing multiple markers of effector function, from the functionally impaired starting population. In contrast, CD70 in combination with CD80 was insufficient for these effects and the related TNF family ligand, LIGHT, had negligible activity. The unique contribution of 4-1BBL correlated with downregulation of the proapoptotic molecule Bim in activated CD8 T cells. Decreasing the level of TRAF1 in T cells using siRNA resulted in increased levels of Bim in the 4-1BBL-stimulated T cells. Thus, costimulation via 4-1BBL leads to TRAF1-dependent Bim downmodulation in T cells, resulting in increased T cell expansion.

**Impact on Policy and Practice:** These studies identify 4-1BBL as a critical component in therapeutic strategies aimed at improving CD8 T cell function.

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## 139

### EXPRESSION AND FUNCTIONAL SIGNIFICANCE OF SOLUBLE IL-7R ALPHA (CD127) IN HIV INFECTION

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**Plain Language Summary:** Interleukin-7 signalling is important for T-cell development and the survival of naïve and memory T-cells. The expression of membrane-associated IL-7R alpha (CD127) is decreased in HIV disease although the mechanism by which this occurs and its role in HIV infection is not known. We have shown that IL-7 induces the shedding of CD127 by CD8+ T-cells in vitro and this is coincident with the downregulation of membrane associated CD127. Soluble CD127 may have a significant effect on the bioavailability of circulating IL-7, blocking its biological effect or altering signalling strength. This may have a role in the pathogenesis of HIV disease, particularly given that plasma IL-7 concentrations are elevated.

**Objective:** To evaluate the regulation and functional significance of soluble CD127 in health and HIV infection.

**Methods:** The effects of soluble CD127 on IL-7 signalling pathways in CD8+ T-cells were assessed by measuring STAT-5 and PI3K activation by flow cytometry or Western blotting. Downstream IL-7 activities such as intra-cellular Bcl-2 expression and CD8+ T-cell proliferation (CFSE) were also investigated. Experiments were conducted using increasing concentrations of a commercially available IL-7R alpha-Fc fusion protein or a native source of soluble CD127 (WI-26VA4 culture supernatant). The concentration of CD127 in human plasma from HIV- and HIV+ individuals was detected by Western blot and quantified using a novel CD127-specific antibody-microfluorosphere Luminex assay.

**Results:** The IL-7-induced expression of phosphorylated STAT-5 in CD8+ T-cells was significantly decreased by soluble CD127. These results were confirmed using antibodies blocking IL-7. Soluble CD127 moderately decreased Bcl-2 expression and IL-7-induced proliferation of PHA-activated CD8+ T-cells. The quantitative CD127 assay has been validated and standardized with a sensitivity of 0.1 ng/ml. In HIV-infected individuals, increased plasma concentrations of soluble CD127 were detected compared to HIV- individuals, by both Western blot and Luminex assays. In addition, plasma CD127 concentrations were negatively correlated with CD4+ T-cell counts in HIV+ individuals.

**Conclusions:** Soluble CD127 negatively affects IL-7 activity by downregulating IL-7-induced STAT-5 activation, Bcl-2 expression and proliferation in CD8+ T-cells. In addition, the detection of CD127 in human plasma is a novel discovery. The increased concentrations of CD127 in plasma in HIV disease may influence IL-7 activity in vivo and may be influenced by disease stage. Furthermore, these findings may bring clinical significance to previous in vitro studies of IL-7's effects on CD127 expression, as well as the downregulation of membrane-associated CD127 observed in HIV disease.

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## 140

### TIM-3 EXPRESSION DEFINES A NOVEL POPULATION OF ANERGIC T CELLS WITH HIGHLY ELEVATED FREQUENCIES IN PROGRESSIVE HIV-1 INFECTION

R. Brad Jones [1]; Lishomwa Ndhlovu [2]; Jason Barbour [2]; James Rini [3]; Aashish Jha [2]; Jessica Wong [1]; Malathy Satkunarajah [3]; Joan Chapman [2]; Douglas Nison [2]; Mario Ostrowski [1]
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**Plain Language Summary:** The human immune system has demonstrated the ability to control HIV. This is clear in early HIV infection, where an initial burst of virus is brought under control. It is also evident in rare HIV-infected individuals who are able to control their virus for many years without therapy. In the large majority of cases, however, the immune system proves incapable of long-term control of HIV and, in the absence of antiretroviral therapy, progression to AIDS occurs. We have identified one way HIV shuts down this initially effective immune response, by causing cells to express a molecule called Tim-3. By blocking this effect we were able to restore function to immune system cells from HIV-infected individuals. This raises the possibility that a therapy which blocks Tim-3 could help the immune systems of HIV-infected individuals control their virus without antiretroviral therapy.

**The Challenge:** Tim-3 is an immunoglobulin superfamily member surface glycoprotein. Interaction of mouse Tim-3 with its ligand, galectin-9, regulates Th1 responses by promoting T cell death. We hypothesized that, in humans, chronic immune activation in HIV-1 infection would evoke Tim-3 expression to dampen T cell function. We sought to determine whether Tim-3 expression on T cells was elevated in HIV-1 infected individuals, and whether Tim-3 signaling plays a role in the establishment of T cell exhaustion.

**Our Approach:** Tim-3 expression on PBMC from HIV-1-infected and uninfected subjects was profiled by flow cytometry. The maturation status of Tim-3+ versus Tim-3- T cells was assessed by multiparameter flow cytometry, and the kinetics of STAT5, Erk and p38 phosphorylation (pSTAT5, pErk and p38 respectively) in Tim-3+ versus Tim-3- cells assayed using phosphoflow. The effect of blocking the Tim-3 signalling pathway on proliferation and cytokine production was assessed using a sTim-3 recombinant protein to saturate Tim-3 ligands.

**Key Findings:** We observed elevated frequencies of Tim-3 expression on CD8+ T cells from acute, and chronically HIV-1-infected individuals relative to uninfected individuals (49.0 +/- 16.2% - chronic, 52.8 +/- 17.5% - acute, versus 28.5 +/- 6.8% for HIV-1 uninfected). The frequency of Tim-3+ CD8+ T cells correlated positively with viral load ($p < 0.0001$) and inversely with absolute CD4+ T cell counts ($p = 0.0397$). Tetramer analysis revealed significantly higher levels of Tim-3 expression on HIV-1-specific versus CMV or EBV-specific CD8+ T cells. Tim-3 expressing CD8+ T cells from acute and chronically HIV-1-infected individuals, were distributed across a range of phenotypic profiles and retained functional but impaired STAT5, Erk and p38 signaling pathways. Tim-3+ T cells failed to produce cytokine, or to proliferate in response to stimulation with antigens or SEB, while cytokine production and proliferation were readily detected in the Tim-3– population. Blocking the Tim-3 signaling pathway using sTim-3 resulted in a dose-dependent enhancement of proliferation and cytokine production by both CD4+ and CD8+ T cells from HIV-1-infected subjects, with disproportionate enhancement of HIV-1-specfic immune responses.

**Impact on Policy and Practice:** This work presents an entirely new therapeutic target for enhancing immune responses in HIV infected individuals. This work will be pursued towards the ultimate goal of developing therapeutics capable of boosting immune responses in HIV-infected individuals. This may enable long term immune control of virus without the need for antiretroviral therapy.

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# Tuesday, November 20, 2007 – 2:45 p.m.

## Reducing Vulnerability: Traditions, Tools and Perspectives

### 141

**ADDRESSING SOCIAL VULNERABILITIES TO IMPROVE MENTAL HEALTH SERVICE ACCESS FOR IMMIGRANT, REFUGEE AND NON-STATUS PEOPLE LIVING WITH HIV/AIDS**

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**Plain Language Summary:** In 2006, 5 ethno-racial communities collaborated with health service sectors and academic partners on a community based action research project to gain insight on the complex mental health needs and challenges faced by immigrant and refugee PHAs and to develop a best practice framework to address their mental health needs. 7 key domains of best practices were identified including: PHA empowerment; intensifying social support; addressing service inequities and improving accountabilities; bridging gaps in healthcare coverage; reducing stigma and discrimination; promoting service providers' cultural competency; enhancing service coordination; and, improving policies. This presentation will present the key findings and policy implications of the study.

**Objective:** Immigrants, refugees, and non-status people living with HIV/AIDS (I/R/N-PHAs) have complex psychosocial needs and face profound barriers when accessing mental health services. The Committee for Accessible AIDS Treatment (CAAT) undertook participatory action research to identify best practice framework that would foster equitable mental health service access for I/R/N-PHAs.

**Methods:** 47 I/R/N-PHAs and 103 service providers were engaged in the study through focus groups, individual interviews, and surveys to identify access barriers, service gaps and elements of best practices to address their mental health needs. The data were then integrated with input from 22 I/R/N-PHAs and 6 service providers/researchers and then rated and sorted using the process of Concept Mapping. Multidimensional scaling and hierarchical cluster analyses were performed to generate and identify key domains of best practices in providing mental health services for I/R/N-PHAs.

**Results:** I/R/N-PHAs face compounding mental health stressors, including uncertainty of migration status, physical and psychological demands of HIV, lack of information on available services, lack of access to health determinants, social isolation, stigma, discrimination, bridge of confidentiality and mistreatment by service providers. Lack of specialized knowledge and skills, resources, and systemic support were cited by service providers as the main barriers to providing adequate care. The research process identified 124 elements of best practices that was clustered into 7 key domains: intensifying social support and capacity building for I/R/N-PHAs; addressing service inequities and improving accountabilities; bridging gaps in healthcare coverage; reducing stigma and discrimination through public education; promoting service providers' cultural competency; enhancing service delivery and coordination; and, improving policies.

**Conclusions:** Improvement of I/R/N-PHAs' mental health requires a comprehensive strategy involving at its centre systemic support and commitment to facilitate the empowerment and leadership of affected PHAs. The strategies require all stakeholders to collaboratively address the social and political determinants of health, eliminate deep-rooted social inequities, and create an accountable and responsive health system.

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### 142

**COMMUNITY PERSPECTIVES ON RESOURCE ALLOCATION DECISIONS WITH A FOCUS ON HIV CARE**

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**Plain Language Summary:** We asked members of the general public and people living with HIV (men and women) what they thought about how resources allocation decisions should be made, using interviews and focus groups. We found that there was broad recognition of the importance of both efficiency in health care spending and fairness and compassion. Respondents recognized that such decisions are hard and frequently challenge individual values. Many people do not want to be involved in such decisions.

**Objective:** Health care resources decisions are often complex and must balance such concerns as efficiency and equity, particularly when health benefits accrue at high costs, as is commonly encountered in the treatment of HIV infection. We explored the concept of fairness in resource allocation from the perspective of community members, focusing on issues relevant to people living with HIV.

**Methods:** We conducted 4 key informant interviews to test and refine an interview guide, followed by 4 focus groups, one for HIV-positive men, one for HIV-positive women, and one each for men and women from the general population. We transcribed and coded the interviews and focus groups using qualitative methods based on grounded theory techniques, looking for emergent themes.

**Results:** We identified 6 themes: 1) Efficiency is important, but should be defined broadly. It may be defensible to withhold resources when treatment is futile or the "return on investment" is slim; 2) Alongside efficiency, resource allocation decisions should value compassion and equity; 3) Resource allocation decisions are inherently complex, involve difficult trade-offs and may lead to situations where individual values may be compromised. Reasons for complexity include uncertainty, exceptional circumstances, and the difficulty in putting aside considerations about individuals (including one's self); 4) Many individuals do not want to be involved in such decisions. Instead of being asked to make decisions themselves, individuals suggested alternatives include nominating others to make decisions or putting trust in "research" to find solutions; 5) Resource allocation decisions are often viewed as inherently political and distrust of how decisions are made and the reasons for the decisions; 6) Some see solutions in working outside of official systems, but such suggestions remain contentious. People living with HIV generally gave similar responses to individuals from the general public.

**Conclusions:** Community members have a good appreciation for the complexities of resource allocation decisions but are often reluctant to partake in such processes. Our findings have implications for the movement to involve "consumers" in policy-level decision making as many individuals find such issues so challenging that they are unable to make principled decisions and others prefer to have "experts" make such decisions for them

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## 143

### WISE PRACTICES IN PROVIDING TRADITIONAL SERVICES TO ABORIGINAL PEOPLE LIVING WITH HIV/AIDS

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3-All Nations Hope AIDS Network; 4-Community Health Research Unit, University of Ottawa

**Plain Language Summary:** Interviews with Aboriginal people living with HIV/AIDS and focus-groups with primary and community-based health professionals provide evidence of the benefits of traditional Aboriginal wellness practices for improved health outcomes. Health professionals who care for Aboriginal PHAs suggest that knowledge about and referrals to traditional healers and practitioners is an important component of culturally competent care.

**Objective:** The Canadian Aboriginal AIDS Network [CAAN] study, Canadian Aboriginal Cultural Competence for HIV/AIDS Health Care Providers, investigates issues related to the cultural skills and competence among primary and community-based professionals who provide care, treatment and support to Aboriginal people living with HIV/AIDS (PHAs) in Canada. The purpose of this study is to better understand the unique health care needs of Aboriginal PHAs and how culturally competent care affects the health outcomes of this population.

**Methods:** This three year project (2005-2008) employs semi-structured interviews with Aboriginal PHAs (n=35) and focus-groups with primary and community-based health professionals (n=52) in five regions of Canada. Verbatim transcripts are coded and analyzed for emergent themes. This presentation focuses on wise practices in providing traditional services to Aboriginal people living with HIV/AIDS.

**Results:** Being receptive to and knowledgeable about traditional Aboriginal healing practices can benefit Aboriginal PHAs' physical, mental, emotional and spiritual wellness. For many Aboriginal PHAs, exploring traditional approaches to wellness is an important component of reconnecting with their cultural identity. However, service providers must be cognizant that participation in sweet grass smudges, sweat lodges, fasting and other traditional ceremonies and practices is a very personal decision, varying according to family, religious and cultural backgrounds, as well as individual experiences and beliefs. HIV/AIDS health professionals who care for Aboriginal PHAs indicate that those who participate in traditional practices seem better able to "come to terms with HIV", to "deal with addictions" and to adhere to treatment regimes. Improved health outcomes are due in part to a relationship of trust and openness with service providers who ensure Aboriginal PHAs have access to a range of choices and strategies for living with HIV.

**Conclusions:** Among Aboriginal PHAs who participate in traditional wellness practices, health outcomes include improved adherence to treatment regimes. In regions where a significant proportion of PHAs are of Aboriginal descent, culturally competent care is evident among primary and community-based HIV/AIDS health professionals who engage in and promote strong networks of information and referrals to Aboriginal service providers including Elders and traditional healers.

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### INTEGRATING TREATMENT INFORMATION AND PREVENTION EDUCATION IN COMMUNITY-BASED AIDS ORGANIZATIONS: A PROCESS EVALUATION OF A NATIONAL CAPACITY-BUILDING INITIATIVE

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**Plain Language Summary:** This paper reports on the results of a process evaluation of Canada's first national HIV/AIDS integration capacity building project (CB Project) developed by the Canadian AIDS Treatment Information Exchange (CATIE). The CB Project aims to help small ASOs increase the organizational presence of treatment information services in their work and better link them with established prevention and education activities. Our findings highlight key design and implementation issues related to the conceptualization of integration and the development of curriculum for community-based integration-related education.

**The Challenge:** At the 2006 International AIDS Conference, a strong call was made to respond to HIV through approaches that integrate prevention and treatment. Most research on integration focuses on epidemiological forecasts about the use of HAART for prevention or on broad policy issues related to treatment roll-out. In North America there is little research that explores integration from the perspective of PHAs or that addresses the concept at the level of community-based service provision. Our study responded to this gap in research.

**Our Approach:** In 2006-7 we conducted a multi-method qualitative study based on individual interviews but also including participant observation of CATIE planning meetings and text analysis of key policy documents. Thirteen individual interviews were conducted: five with CATIE staff, telephone interviews with representatives from six sites across Canada involved in the CB Project and two interviews with funders. Interviews lasted from 30 to 90 minutes, were tape-recorded and transcribed. Analysis was approached as an ongoing process of dialogue with the data that continued reflexively throughout the study. The first three authors hand coded transcripts and compared, contrasted and revised analytic themes. Preliminary findings were assessed in a workshop involving 25 representatives from 15 ASOs across Canada.

**Key Findings:** We argue for the strategic need to distinguish a community-based perspective on integration and identify three foundational principles of such a perspective: (1) an expanded notion of treatment information, (2) the importance of context, and (3) the significance of community-based language. We also argue for the need to balance flexibility and standardization in curriculum design and identify two key issues for curriculum development: 1) information on integrated service models, and (2) information on the relationship between viral load and HIV transmission.

**Impact on Policy and Practice:** This study helps to frame an emerging discussion of the form, possibilities and challenges of community-based approaches to integrating HIV treatment information, prevention and care and support services in Canada. It offers a community-based model of integration that ASOs can draw on in moving toward integrated models of service delivery.

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# Tuesday, November 20, 2007 – 2:45 p.m.

## Global Vulnerability and Opportunities

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### HIGH RISK AND BRIDGE POPULATIONS FOR HETEROSEXUAL HIV TRANSMISSION IN INDIA: BEHAVIOURAL SURVEYS OF FEMALE SEX WORKERS AND MALE CLIENTS

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**Plain Language Summary:** A key issue for HIV control in India is the role of female sex workers (FSWs) and their clients in increasing heterosexual HIV transmission. The government of India has undertaken behavioural surveillance surveys of FSWs and clients in 2001 and 2006 to determine sexual risk behaviours and self-reported HIV testing and sexually transmitted diseases. South India has a higher prevalence of HIV in the general population than the north, and more HIV prevention programming has been undertaken there. This analysis compared findings within and between north and south India. Significant increases in condom use were reported by both FSWs and clients in both north and south between 2001 and 2006, with condom use reported as significantly higher in the south than the north.

**Objective:** This study examines changes in reported demographic characteristics and risk behaviours of female sex workers and their male clients between the Indian National AIDS Control Organization's behavioural surveillance surveys (BSS) in 2001 and 2006, with a focus on comparison between north and south India.

**Methods:** BSS prevalence rates for the different survey questions were imputed into Excel files and summary estimates of percentage for all indicators of interest were calculated. We compared similar indicators among female sex workers (FSW) and male clients of FSW in north and south India, and examined changes in measures between 2001 and 2006. Summarized proportions were weighted by population size of the relevant state based on the 2001 Indian census. The T-test was used to investigate the statistical significance of differences in measures.

**Results:** Shifts in demographics including age, relationship status, and literacy levels between 2001 and 2006 raise questions about comparability of the two survey samples. Significant increases in condom use were reported by both FSWs and their clients, in both the North and South. At the same time, however, self-reporting of STI symptoms increased among FSWs, although generally remaining stable or declining slightly among clients. HIV testing was also reported as significantly increased in both North and South.

**Conclusions:** Results suggest increases in condom use in commercial sexual activity throughout India. The higher rates of safer sex behaviour in the south may relate to more intensive prevention programs there. It is essential that prevention for FSWs and their clients be continued and expanded. BSS are primarily useful for tracking trends, and as such, it is important that they be repeated more frequently than every five years to examine the effects of prevention programming.

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### GENDER EQUITY, HIV/AIDS, AND DEMOCRACY IN RURAL SOUTH AFRICA SINCE 1994

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**Plain Language Summary:** This paper is draws on field research undertaken during November 2005 to January 2006 in the service of a project investigating the connections between HIV/AIDS and gender based coercion and violence in rural Kwa-Zulu/Natal, South Africa. The project, funded by the Canadian Institutes of Health Research and initiated in 2003, aimed to shed light on the ways in which gender based coercion and violence contribute to the spread of HIV/AIDS. Since then, these two scourges have been labeled the "dual epidemics" of South Africa. The research was undertaken in a desperately poor municipality in the interior of KwaZulu Natal, namely the District of Sisonke. We explore the nature of the relations between genders by outlining prominent themes drawn from the interviews, namely: the impact of actual changes to traditional notions of familial structure, and the corresponding changes in expectations of family members; and the ways in which commodification of gendered roles has an impact on the relations between men and women, most notably in the phenomenon of trans-generational sex.

**The Challenge:** To research 1) how rural men and women themselves perceive of relations between the sexes in the era of the post-apartheid epidemic; 2) to understand how men and women relate to the provisions of the Constitution affecting relations between the sexes, especially in terms of the provisions regarding women's equal rights; 3) to involve both men and women in discussions that might highlight how communities themselves might frame approaches to interventions targeted at gender-based coercion and violence in ways that decrease, rather than increase, tensions and hostilities between men and women.

**Our Approach:** Four semi-structured focus groups were conducted with men, grouped according to age: ages 18-24 (n=5); ages 25-34 (n=4); ages 36-45 (n=4); and ages 46-55 (n=3). Four focus groups were conducted with women ages 18-24 (n=4); ages 25-35 (n=4); ages 35-45 (n=4) and ages 45 and up (n=4).

**Key Findings:** Democratic individualism and gender equality, as entrenched in the constitution and the new marriage laws, offer alternative, potentially more effective, protections for women but are perceived by some of our male and female informants to come at a definite cost. To provide gender equality by law but then to fail to enforce it, as is currently the case in many instances, may end up putting women in a worse position in practice than their situation before such laws were passed. Our research in Sisonke turned up definite evidence of that negative outcome.

**Impact on Policy and Practice:** Highlights the fact that positioning rural men and women, who see the constitution's democratic provisions as alien to their culture, as "ignorant," fails to confront the problem of conceiving of human security as an individual, rather than a community-oriented, task.
Proposes that working with women on issues related to the "twin epidemics" (GBV and HIV), without initiating and sustaining intense community programs for boys and men, is futile, and possibly even damaging in the long term. Proposes a series of moderated, co-educational community activities to provide forums for women and men to raise the issues of self-esteem, social and financial security that "drive" gender-based violence and HIV in non-threatening environments, so that vocabularies can be developed for discussing the interlinked, deeply stigmatized (and therefore censored) challenges of HIV and gender-based coercion and violence.

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### PREPARING FOR FUTURE HIV VACCINE DISSEMINATION AMONG VULNERABLE COMMUNITIES IN THAILAND

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**Plain Language Summary:** Thailand (pop. 65 million), with 2.2% HIV seroprevalence and 50,000 HIV/AIDS deaths per year, has enrolled the greatest number of volunteers in HIV vaccine trials in the developing world. Thailand is also home to the only current large-scale HIV vaccine efficacy trial. Social justice and population health paradigms support the need to ensure access to future approved HIV vaccines, particularly among vulnerable communities who have been engaged in HIV vaccine testing and development. Nevertheless, limited attention to social, cultural and structural dimensions of future HIV vaccines among vulnerable communities in Thailand may impede broad acceptability and access.

**Objective:** To engage vulnerable communities in exploring acceptability and access to future HIV vaccines in Thailand and implications for dissemination.

**Methods:** Participants were recruited, based on purposive sampling, from community-based organizations serving vulnerable subpopulations in 4 cities across Thailand. We conducted in-depth, semi-structured, 45-60 minute interviews with community members, service providers and HIV/AIDS experts to explore HIV vaccine acceptability and concerns about future dissemination. Interviews were administered predominantly in Thai, digitally recorded, transcribed and translated into English. Data were analyzed by three independent investigators using line-by-line, axial and thematic coding, and a constant comparative method, with N-VIVO. Triangulation of data sources and investigators, member checking, and prolonged engagement increase trustworthiness of the findings.

**Results:** Thirty-five community members and service providers representing gay youth, transgenders, male and female sex workers, and injecting drug users (IDUs)(11 women, 3 transgender women, 21 men; aged 18-45 years) and 4 Thai HIV/AIDS experts were interviewed. Four primary themes emerged around future HIV vaccine acceptability: 1) vaccine-specific concerns: efficacy, safety and false HIV-positives; 2) policy and structural barriers: prohibitive costs/government subsidies, criminalization of IDU and sex work, and ethics of clinical trial implementation; 3) social and cultural influences: HIV stigma, confidentiality, hierarchical doctor-patient relationships, stigma and discrimination against vulnerable communities in the healthcare system, and family and peer approval; and, 4) behavioral disinhibition.

**Conclusions:** HIV vaccine acceptability was generally high among individuals from vulnerable communities in Thailand. Nevertheless, social and structural barriers—criminalization/extra-judicial executions of IDUs, criminalization of sex work and unsafe working conditions, stigma and sexual prejudice in the healthcare system, and vaccine costs—threaten to subvert access and acceptability. Structural interventions are needed to ensure broad HIV vaccine dissemination to communities at greatest risk. Proactive community education and engagement focused on marginalized subpopulations may be crucial to the success of future HIV vaccines in controlling the epidemic in Thailand.

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### ECONOMIC GLOBALIZATION, GROWTH AND HIV/AIDS: STIMULATING THINKING IN A NEW FIELD

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**Plain Language Summary:** HIV/AIDS is now a fact of life in many countries where efforts are taking place to build economic growth for the poor. But there hasn't been much attention to how HIV/AIDS might impact on these growth efforts, or vice versa. We're trying to encourage researchers to explore this area by offering funding for case studies that look at how economic globalization and growth interact with HIV/AIDS. This information is important because it can help policy-makers figure out how to better design both HIV/AIDS policy and inclusive economic policy.

**Objective:** In many countries, HIV/AIDS has become the biggest challenge to reducing poverty and inequity. HIV/AIDS has also become part of the environment within which efforts to address poverty reduction and inclusive, pro-poor economic growth take place. Such efforts need to take this major challenge into consideration. However, the ways in which HIV/AIDS interacts with economic growth, poverty, inequity, resilience and vulnerability are not well understood.

**Methods:** In response to these knowledge and policy gaps and in consultation with experts in the field, the International Development Research Centre (IDRC) in Canada and the Health Economics and HIV/AIDS Research Division (HEARD) in South Africa jointly developed a research funding programme aimed at providing empirical evidence on linkages amongst economic globalization, growth and HIV/AIDS. The programme will support case studies in low- and middle-income countries that examine policy-relevant research questions within two themes: 1. How HIV/AIDS interacts with efforts to facilitate inclusive, pro-poor growth strategies; 2. The impacts of economic globalization and growth on vulnerability and resilience to HIV/AIDS.

**Results:** By far, the most challenging component has been conceptualizing the substantive net to cast for the case studies. To date, most studies of economics and HIV/AIDS have focused on projecting differences in growth rates between 'With-AIDS' and 'No-AIDS' scenarios, which provides little policy guidance. An iterative process was conducted over one year to arrive at the elaboration of thematic areas that were sufficiently narrow to provide a coherent contribution, but also broad enough to be inclusive of a range of feasible case studies. Furthermore, the thematic areas had to be grounded in real-life experiences for which additional insight could help inform policy to mitigate vulnerability to HIV/AIDS.

**Conclusions:** The entire project has been designed with policy relevance as a central goal. Incoming proposals are being judged on the significance of their findings for policy makers and on their plans for disseminating results to key decision makers.

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