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ELUCIDATING THE IMPACT OF GENITAL INFECTIONS AND THEIR THERAPY ON HIV SUSCEPTIBILITY IN THE FEMALE GENITAL TRACT

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Plain Language Summary: It is estimated that HIV currently infects over 30 million worldwide, with women being disproportionately affected (UNAIDS/WHO in July 2008). Genital infections enhance HIV susceptibility in women (Plummer 1991 JID), and we hypothesized that this might relate to infection-induced changes in the immunology of the genital tract. This project aims to define the effect of several common genital infections (bacterial vaginosis and the STDs gonorrhea, chlamydia and trichomoniasis) on HIV susceptibility in the female genital tract, and to examine whether effective therapy reverses these changes.

Objective: To examine the impact of treating common genital infections on mucosal immune markers of HIV susceptibility in women.

Methods: HIV-negative women, with or without genital infections, were recruited through the Hassle-Free Women's Clinic in downtown Toronto. From a cervical cytobrush sample, we measured the number of cervical dendritic cells expressing DC-SIGN, and the number of cervical CD4 T cells, since these two cell populations are felt to be the initial targets for HIV infection in the female genital tract. We present baseline (cross sectional) associations of genital infections, and a prospective analysis of the mucosal immune effects of therapy.

Results: 68 women have been enrolled to date: 20 with bacterial vaginosis (BV); 19 with lesser alterations in intermediate flora (IF); 11 with C.trachomatis; 4 with N.gonorrhoeae; 8 with T.vaginalis; and 14 infection-free controls. Women with classical STDs (n=21) had a significant increase in the number of cervical CD4+ T cells (p=0.01) compared to infection-free controls (n=14), although DC-SIGN expression levels were similar. When cervical cell populations were compared before and after effective therapy in a paired analysis (n=17), the number of cervical DC-SIGN+ cells was significantly reduced (p=0.04), and a similar trend was seen in cervical CD4+ T cell populations (p=0.08).

Conclusions: These preliminary findings demonstrate that genital infections, particularly bacterial STDs, may increase the risk for HIV acquisition through reversible effects on mucosal immune markers of HIV susceptibility. Longer term follow up is ongoing to address this question. These results will directly impact the design of clinical interventions to prevent and/or treat genital infections to reduce HIV acquisition.

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PREDICTORS OF NEUROSYPHILIS AMONG HIV-POSITIVE AND HIV-NEGATIVE PATIENTS WITH SYPHILIS.

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Plain Language Summary: The diagnosis of neurosyphilis (NS) is based on the detection of antibodies against syphilis in the cerebrospinal fluid (CSF), requiring the physician to conduct a lumbar puncture (LP). The majority of patients with syphilis do not have neurological symptoms and there is conflicting evidence on whom to perform this invasive procedure to exclude NS. This is particularly difficult in the presence of HIV co-infection, as the risk of NS appears to correspond with the immune status of the patient. This study is a review of the clinical and laboratory data on patients with syphilis infection and had undergone a diagnostic lumbar puncture to check for NS, with a goal to determine which features were associated with NS.

Objective: Individuals co-infected with syphilis and HIV could be at high risk for developing NS. The Centers for Disease Control and the Public Health Agency of Canada (PHAC) have made broad guidelines for performing a diagnostic LP in HIV-infected individuals with syphilis infection. PHAC guidelines suggest that an LP be conducted in the diagnostic evaluation of asymptomatic patients with an RPR titer of ≥1:32 or CD4 count ≤350 cells/mm3. We aim to determine if these specific criteria are predictive of NS.

Methods: We conducted a retrospective review of adults with serological evidence of syphilis infection who had undergone a diagnostic lumbar puncture. Cases were identified by screening all CSF specimens sent to the Ontario Public Health Laboratory for syphilis testing by the participating 5 Toronto hospitals (2000-2007). Patients were included if at the time of the LP, they were ≥18 years of age, had serological evidence of syphilis infection by serum testing, and were not previously treated for NS.

Results: Of the 475 patients reviewed, 110 met our inclusion criteria and 21 had NS. Among these 110 patients, 95 (86%) were male and 15 (14%) were female. An RPR titer of ≥1:32 was associated with NS (OR=4.53, 95%CI=1.5-13.8). In patients with HIV infection, an RPR titer of ≥1:32 was also associated with NS (OR=2.71, 95%CI=1.1-32.6). Among HIV-positive patients who had a CD4 cell count 90 days prior to their LP, a CD4 count ≤350 cells/mm3 was associated with NS (OR=4.95, 95%CI=1.85-43.1).

Conclusions: We demonstrated that an RPR titer of ≥1:32 and CD4 cell count of ≤350 were predictive of NS. Our findings support the use of RPR titer and CD4 counts to identify patients requiring a diagnostic LP.

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QUESTIONNAIRE ON VALUES AND KNOWLEDGE REGARDING GENITAL HERPES INFECTION IN HIV

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Plain Language Summary: Herpes treatment may benefit people living with HIV, but it is important to understand patients' perspectives regarding such treatments to improve their acceptability. In this survey of 100 patients, we found a fair level of knowledge about herpes and HIV, and determined what patients would value in future treatment strategies.

Objective: Herpes simplex virus type 2 (HSV-2) may exacerbate HIV disease by increasing HIV viral load, and clinical trials are needed to evaluate whether treatment with anti-HSV medications is beneficial. We conducted an exploratory, cross-sectional survey of HIV-infected individuals to better understand patients' knowledge and values regarding herpes and HIV, and to determine how understandable and acceptable such strategies would be.

Methods: Patients attending regular follow-up appointments at the University Health Network Immunodeficiency Clinic were asked to complete a 29-item survey regarding herpes and HIV. Items included a) demographics and medical history, b) true-false knowledge questions; c) values questions using Likert scales ranging from 1 ("not at all important to me") to 5 ("extremely important to me"). Participants received printed and verbal answers to knowledge questions upon completion.

Results: 100 patients completed the survey, of which 90% were on HAART. 73% were male, 26% female and 1% male-to-female transsexual. Median age was 47 years (interquartile range, IQR=42, 51), median years since HIV diagnosis was 11 (IQR=5, 18), 53% were Canadian-born, and 73% had a college education or higher. Median percentage of questions answered correctly was 47% (IQR=29%, 62%), with most incorrect answers relating to the prevalence and transmission of HSV. Patients valued safely delaying HAART initiation, taking medications once versus twice daily, and decreasing the likelihood of both transmitting herpes to partners and decreasing the likelihood of developing herpes symptoms, with 74%, 64%, 93% and 97% of respondents respectively rating these items as '4' or '5'.

Conclusions: Knowledge about herpes and HIV was fair in this sample of HIV-infected persons but common misconceptions about herpes persist. Patients valued delaying HAART initiation, less frequent dosing schedules, and decreasing both herpes transmission and symptoms, suggesting that treatment strategies meeting these criteria would be welcomed in this population.

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HIV PAIN NEEDS ASSESSMENT STUDY: ASSESSING THE PREVALENCE OF PAIN, PAIN TREATMENT NEEDS, AND BARRIERS TO ACCESSING TREATMENTS FOR PAIN IN THE HIV COMMUNITY.

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Plain Language Summary: This needs assessment study documents the pain-related treatment needs, preferred treatment options, and barriers to accessing pain-related treatment among people living with HIV/AIDS (PHAs). Results indicated that there is a high prevalence (54%) of pain among PHAs. PHAs reported the greatest interest in treatment options such as education about pain management options, and better management of pain-related symptoms (e.g., insomnia, depression). PHAs preferred individual pain management over group-based treatments. They also preferred that group treatments only include group members with HIV or HCV. Barriers to treatment identified by PHAs included: difficulty communicating pain-related needs, fear related to pain medications, and difficulty accessing treatment for pain.

Objective: Pain negatively impacts quality of life and is a growing problem among PHAs. Pain-related treatments, such as multidisciplinary treatment programs, are shown to be effective among the general population; however, clinicians and researchers do not understand well the pain-related treatment needs specific to PHAs. This study assessed the prevalence of pain, need for pain-related treatments, barriers to obtaining pain treatments, and pain treatment preferences among PHAs.

Methods: PHA (N=101) were recruited during regular HIV clinic visits at The Ottawa Hospital. Participants completed questionnaires that assessed mood, experience with pain, pain knowledge and treatment preferences, and barriers to pain treatment.

Results: More than half of PHA participants reported moderately severe pain on a 0 – 10 pain-rating scale, where "10" indicated "pain as bad as you can imagine." Those with pain were more likely to report depression or anxiety, sleep disturbance, and to be on disability. Treatment options of greatest interest to PHAs included education about ways to treat pain, better sleep management, and learning about medication options. PHAs were also interested in multidisciplinary treatment programs. Treatment options of lesser interest included help finding employment that could accommodate the needs of those living with pain. Barriers to pain treatment among PHAs included: difficulties describing/communicating symptoms of pain to health care providers, fears about pain medication (e.g., addiction), and difficulties with transportation to pain treatment programs.

Conclusions: Pain is a highly prevalent and significant issue among PHAs. An important need identified by PHAs was for more information/education about ways to better manage pain. PHAs also identified that treatment options to address factors often associated with pain (e.g., poor sleep, depression) was a key need. Novel psycho-educational and other pain treatment programs need to be developed to address HIV community needs. Ways to reduce barriers to receiving pain treatment must be explored.

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IMPACT OF STATINS ON CD4 COUNT IN HIV-INFECTED INDIVIDUALS ACHIEVING VIROLOGIC SUPPRESSION ON INITIAL HAART REGIMENS

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Plain Language Summary: Statins are medications that are widely used to treat high cholesterol levels. Some evidence suggests that these drugs may also benefit patients living with HIV infection. We reviewed the medical records of 306 HIV-infected persons using HAART, but found no evidence of improved CD4 counts in those using statins.

Objective: To determine whether hydroxymethylglutaryl-coA reductase inhibitors (statins) are associated with improved CD4 counts in patients starting their first HAART regimen and achieving virologic suppression between 2000-2007.

Methods: Individuals with ≥3 CD4 count measurements after achieving 2 consecutive HIV RNA <50 copies/mL on their first HAART regimen were included. Baseline was defined as the time of initial virologic suppression. GEE linear regression was used to model the impact of statin use on CD4 count, with baseline CD4 count, type of HAART regimen, age, gender and time since starting HAART as covariates. Patients who used a statin at any time on this regimen were included in the statin group.

Results: 306 individuals were included, of whom 46 (15%) were receiving statin therapy. 97 (32%) were female and the median age at the time of achieving virologic suppression was 39.8 years. At the time of VL suppression, the median CD4 count was 252 and 296 cells/mm3 in the statin and comparison groups respectively (p=.12). The HAART regimens included NNRTI/2NRTI (42%), boosted or unboosted PI/2NRTI (50%), 3NRTI (4%), PI/NNRTI/NRTI (4%). Statins used included atorvastatin (60%), pravastatin (17%), rosuvastatin (20%) and simvastatin (4%). 41 of 46 statin users (89%) had started the statin after starting HAART, a median of 27.8 months later. CD4 count was significantly associated with female gender [β=40.1, 95%CI (14, 66.3), p=0.0026], years since starting HAART [β=59.3, 95%CI (50.7, 67.9), p<0.0001], baseline CD4 per 100 [β=83.9, 95%CI (75.9, 92) p<0.0001], and baseline age per decade [β=-26.2, 95%CI (-42.4, -9.9), p=0.0016]. There was no significant association with statin use [β=26.3, 95%CI (-19.5, 72.2), p=0.26].

Conclusions: Although statins have immunomodulatory and anti-replicative effects on HIV-1 in vitro, statin use was not associated with improvements in CD4 count reconstitution in this retrospective cohort of HIV-infected individuals with HAART-induced virologic suppression.

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HIV POSITIVE MEN WITH NON-ALCOHOLIC FATTY LIVER DISEASE HAVE ALTERED HEPATIC FATTY ACID COMPOSITION COMPARED TO HIV NEGATIVE CONTROLS WITHOUT FATTY LIVER

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Plain Language Summary: Many people with HIV/AIDS (PHA) have fatty liver, and in some of them this progresses to inflammation or even cirrhosis of the liver. The kind of fat stored in the liver might play a role in the progression of the liver disease. Therefore we compared the hepatic lipids in PHA with fatty liver to HIV-negative controls with normal liver. We found that PHA with fatty liver had altered fat composition compared to controls, and this was more pronounced in those who had fat+inflammation. This might be due to altered lipid metabolism in the liver and/or different dietary fat intake.

Objective: To compare hepatic fatty acid (FA) composition in PHA with non-alcoholic fatty liver disease (NAFLD) to HIV-negative controls without fatty liver.

Methods: Prospective, cross-sectional study including 19 male PHA with NAFLD (HIV/NAFLD) (6 simple steatosis, 13 non-alcoholic steatohepatitis (NASH)) and 7 HIV-negative men with minimal findings on liver biopsy (MF). FA in liver and erythrocyte total lipids (gas chromatography), liver lipid peroxidation and antioxidant power (testkits), blood biochemistry, anthropometry, medical history, dietary intake, and physical activity were assessed.

Results: HIV/NAFLD had higher serum triglycerides than MF, but other clinical, demographic or anthropometric data and oxidative stress in the liver were not different. The n 6/n 3 ratio in hepatic lipids was increased in HIV/NAFLD (mean±SEM) (8.3±1.0 vs. 5.4±0.5) and the ratios of active metabolite / essential FA precursors were reduced for n-6 and n-3 polyunsaturated FA (PUFA): arachidonic/linoleic acid: (0.30±0.05 vs. 0.61±0.12); (eicosapentaenoic+docosahexaenoic)/linolenic acid (1.9±0.4 vs. 8.4±3.4). In erythrocytes, total PUFA were reduced (31.6±2.4 vs. 38.7±3.6 mol%), and dietary intake of vitamin E was lower (7.2±1.4 vs. 9.3±0.6 mg/d) in HIV/NAFLD. We also compared HIV/NASH to HIV/steatosis. HIV/NASH patients were older (47±2 vs. 40±2 y) and had higher ALT (77±11 vs. 41±5 U/L). They had lower hepatic arachidonic (1.4±0.4 vs. 3.0±0.5 mol%) and docosahexaenoic acid (0.37±0.86 vs. 0.86±0.10 mol%) and the arachidonic/linoleic acid ratio was reduced (0.24±0.04 vs. 0.45±0.12).

Conclusions: Male PHA with NAFLD show altered hepatic FA composition compared to MF, and this was more pronounced in patients with NASH. Changes seem to be due to altered essential FA metabolism. Reduced intake of polyunsaturated FA, reflected in erythrocyte FA profile, might also contribute. In contrast, oxidative stress does not seem to play a predominant role for the development of NAFLD in PHA. Studies on possible mechanisms, e.g. impaired desaturase and elongase activity, are necessary.

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MICRONUTRIENT STATUS OF CHILDREN WITH HIV: A RETROSPECTIVE REVIEW

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Plain Language Summary: Nutrition plays a role in the health of people with HIV. We conducted a review of vitamin and micronutrient levels in our HIV-infected pediatric patients, and found low levels of zinc and vitamins A and D.

Objective: Nutritional status is thought to be closely related to immune function in HIV-infected individuals. Specific micronutrient deficiencies, including selenium, vitamin B12, vitamin A, carotenoids, and zinc are associated with excess morbidity/mortality in observational studies of HIV-positive adults. Micronutrient supplementation was shown to be beneficial to HIV-positive individuals in some studies, with outcomes including decreased mortality, decreased morbidity, and increased CD4 cell counts. Few studies of micronutrient status or supplementation have been done in HIV-infected children. We conducted a retrospective review of our patients' vitamin and micronutrient levels, as well as their immunologic and clinical parameters.

Methods: The health records of HIV-positive children 0-18 years attending the Immune Deficiency Clinic at the Children's Hospital of Eastern Ontario were reviewed from Sept/2006 - Sept/2008. Vitamin A, vitamin D, vitamin E, zinc, selenium, iron, and albumin levels were noted, as well as clinical data including demographics, CDC immunologic stage, viral load, treatment, and growth parameters. Descriptive statistics and basic statistical analyses were used to determine associations between vitamin/micronutrient levels and immunologic and growth parameters.

Results: The health records of 26 patients aged 3-17 years (median 12y) were reviewed. All were being treated with HAART, for a duration of 2 weeks to 11 years (median 7.5y). Most children were of black race (22), with a small number being white (2) or aboriginal (2). Seven were Canadian born, while the remainder had immigrated to Canada 2-14 years previously (median 9y). Evaluation of growth parameters revealed that 3 children were below the 10th percentile for weight and BMI, while 6 were below 10th percentile for height. All had CD4 counts in CDC immunologic stage 1 or 2, and viral loads were undetectable in 16 patients, between 50 and 1000 copies/mL in 5 patients, and greater than 1000 copies/mL in 5 patients. Low levels of vitamin A, vitamin D, iron, and zinc were noted in 6/25, 8/25, 1/25, and 9/26 patients respectively.

Conclusions: Micronutrient deficiencies were common in HIV-infected Canadian children on HAART, particularly deficiencies of zinc and vitamins A & D. The effect of vitamin and micronutrient supplementation on children with HIV in resource-replete countries such as Canada is not known, and bears further investigation.

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MICRONUTRIENT SUPPLEMENTATION INCREASES APOLIPOPROTEIN A1 LEVELS IN PERSONS LIVING WITH HIV

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Plain Language Summary: Increased levels of apolipoprotein A1, the primary protein component of HDL ("good") cholesterol, are associated with decreased heart disease risk, and may reduce inflammation and viral replication. We showed that 4-6 weeks of micronutrient supplementation increased ApoA1 levels in HIV-infected subjects. Supplementation may help to reduce heart disease risk and improve immune function in persons living with HIV.

The Challenge: Apolipoprotein A1 (ApoA1), the primary protein moiety of the high density lipoprotein (HDL) particle, has attracted recent attention, both as a marker of cardiovascular risk and in the treatment of inflammatory disorders. In addition, both HDL and ApoA1 have been shown to have anti-HIV properties in vitro; longitudinal observation of patients on HAART have shown a direct correlation between serum HDL and maintenance of viral suppression. Thus, ApoA1 may help to inhibit HIV replication and maintain viral suppression. We examined the effect of micronutrient supplementation with riboflavin, thiamine and L-carnitine on ApoA1 levels in persons living with HIV.

Our Approach: As part of an ongoing study of the effects of micronutrient supplementation on lactate metabolism in HIV, twenty-two subjects were given thiamine 50 mg OD, riboflavin 100 mg OD, and L-carnitine 1000 mg BID. Lipid profile values including serum levels of ApoA1 and HDL-C were measured before and after four to six weeks of supplementation, and were compared in HIV-infected subjects on HAART, untreated HIV-infected subjects, and seronegative control subjects.

Key Findings: At baseline, all HIV-infected subjects showed lower levels of ApoA1 ($p<0.01$) and HDL-C ($p<0.05$) than control subjects. Treated HIV-infected subjects displayed higher ApoA1 levels than those who were untreated ($p<0.01$); there was no significant difference in HDL-C. After four to six weeks of supplementation, all HIV-infected subjects showed a significant increase in serum apoA1 (0.145+/-0.057 g/L increase on HAART, 0.112+/-0.049 g/L untreated, $p<0.03$). No change was seen in serum HDL-C or other lipid values.

Impact on Policy and Practice: As demonstrated in previous studies, HIV-infection is associated with decreased serum HDL levels, as well as lower levels of ApoA1. Our results suggest that supplementation with specific micronutrients may increase levels of ApoA1 in persons living with HIV. This increase was comparable to levels associated with decreased cardiac risk in population studies. While further research is needed to determine the clinical significance these changes, the indirect evidence for immunomodulatory and antiviral effects of ApoA1 is intriguing and understudied. Micronutrient supplementation may represent a useful adjunct to increase efficacy and help alleviate the adverse effects of HIV treatment.

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EFFECT OF METABOLIC COFACTOR SUPPLEMENTATION ON LACTATE METABOLISM AND MITOCHONDRIAL PROTEIN EXPRESSION IN HIV: TWO CASES.

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Plain Language Summary: Treatment with nucleoside/nucleotide analogues (NRTIs) has been linked to disturbances in mitochondrial function and an increased risk of developing serious lactic acidosis. Supplementation with thiamine, riboflavin and L-carnitine may help to reduce the effects of NRTIs on mitochondria and improve the body's ability to metabolise lactate. As part of an ongoing study of lactate metabolism and mitochondrial protein expression in persons living with HIV, we present the cases of two subjects on long term therapy with NRTIs. Supplementation increased the rate of lactate clearance from the bloodstream and increased levels of certain proteins associated with mitochondria, suggesting that these nutrients may be beneficial in reducing some of the adverse effects of HIV therapy.

The Challenge: Use of NRTIs has been linked with disturbances in mitochondrial DNA replication and gene expression, with resultant disturbed lactate metabolism and an increased risk of fulminant lactic acidosis. Supplementation with certain cofactors of mitochondrial metabolism may reduce mortality in patients with NRTI-associated lactic acidosis by ameliorating the effects of mitochondrial damage and improving lactate metabolism. We examined the effects of these supplements on lactate metabolism and mitochondrial protein expression in subjects without acute illness.

Our Approach: HIV-infected subjects on HAART regimens containing d4T were tested before and after four to six weeks of supplementation with thiamine 50 mg and riboflavin 100 mg once daily, and L-carnitine 1 g twice daily. Lactate metabolism was assessed using an exogenous lactate challenge test, in which subjects were infused with a standardized dose of sodium lactate. Lactate levels were measured over the course of 135 minutes post-infusion in order to calculate the rate of lactate clearance. Blood cells were tested by immunoassay to determine the levels of various protein components of the respiratory chain as a measure of mitochondrial protein expression.

Key Findings: Here we present the results obtained for two subjects, both HIV-infected men on long-term treatment with d4T-containing HAART. Peak lactate levels during the lactate infusion decreased, while the rate of lactate clearance increased after four to six weeks of supplementation. We observed a trend toward increased expression of representative proteins for complexes II, IV and V following supplementation.

Impact on Policy and Practice: These findings, although preliminary, provide evidence for a beneficial effect of micronutrient supplementation on lactate metabolism in persons receiving antiretroviral therapy. This effect was accompanied by an increase in mitochondrial protein expression, providing further support for a role of these nutrients in ameliorating the effects of NRTI-mediated mitochondrial toxicity.

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ASSESSMENT OF KNOWLEDGE AND ATTITUDES OF PHYSICIANS INVOLVED IN THE CARE OF HIV-INFECTED PATIENTS WITH RESPECT TO NUTRITION AND NUTRITIONAL SUPPLEMENTS

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Plain Language Summary: Patients living with HIV (PLWH) often ask physicians about nutrition and the use of supplements. However, most physicians have received little training in this area. The purpose of this study was to assess the nutritional knowledge of physicians involved in the care of PLWH using a survey questionnaire. Among the 38 respondents, 50% reported having some nutritional knowledge while 5% rated themselves as very knowledgeable and 53% as having minimal knowledge. Knowledge was acquired through: post-secondary courses (13%), attending conferences/reading medical journals (79%), and the internet (32%). Seventy-one percent reported often being asked about nutrition by PLWH, with 37% often providing some nutritional advice. Only 29% generally refer PLWH to a dietitian. The formula to calculate body mass index was known to 50% of respondents and 47% knew the recommended range for % energy from dietary fat. When asked about potential vitamin toxicity resulting from over consumption of Cod liver oil, only 34% gave the correct answer as vitamin A. Based on this survey, physicians involved in the care of PLWH have sub-optimal knowledge in nutrition.

Objective: To assess the nutritional knowledge of physicians involved in the care of PLWH.

Methods: A questionnaire was distributed to 105 physicians who provide care for PLWH in the Province of Ontario. Among those, 38 responded.

Results: Among the 38 respondents, 50% reported having some nutritional knowledge while 5% rated themselves as very knowledgeable and 53% as having minimal knowledge. Knowledge was acquired through: post-secondary courses (13%), attending conferences/reading medical journals (79%), and the internet (32%). Seventy-one percent reported often being asked about nutrition and/or supplements by PLWH, with 37% often providing some nutritional advice. Only 29% generally refer PLWH to a dietitian. The formula to calculate body mass index was known to 50% of respondents and 47% knew the recommended range for % energy from dietary fat. When asked about potential vitamin toxicity resulting from over consumption of Cod liver oil, only 34% gave the correct answer as vitamin A.

Conclusions: Physicians involved in the care of PLWH have sub-optimal knowledge in nutrition. Since many PLWH request advice about the use of nutritional supplements, physicians involved in their care need to be better educated in this area.

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THE EFFECT OF BETA-CAROTENE SUPPLEMENTATION ON CD4+ T LYMPHOCYTE COUNT IN TREATED HIV INFECTED PATIENTS

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Plain Language Summary: Micronutrient supplementation may have a role in boosting immunity in individuals with HIV infection. We showed that supplementation of anti-HIV drug treated HIV patients with beta-carotene for 28 days increased CD4+ cell counts, a good measure of immunity.

Objective: To analyse the effect of beta-carotene supplementation on serum carotene levels and T lymphocyte counts in treated HIV infected patients.

Methods: We analysed data from our pharmacokinetic study of the effect of beta-carotene supplementation on the pharmacokinetics of nelfinavir in HIV patients for a carotene supplementation effect on immunophenotype subsets. 11 HIV infected adults, receiving stable antiretroviral treatment including nelfinavir 1250 mg twice daily, received beta-carotene supplementation (25,000 IU twice daily) for 28 days. Baseline and day 28 serum carotene and T lymphocyte immunophenotype subsets were analysed.

Results: The 11 study participants were mostly male (9), aged 45.5±9.4 years, with baseline CD4+ T lymphocyte count 592.3±245.6 and viral load <50 copies/mL (one had 63 copies/mL). As micronutrients can lose potency in storage, we showed that the product was stable, with less than 10% degradation over two years, carotene content still being 17% more than label claim. After 28 days of beta-carotene treatment, mean serum carotene increased significantly from baseline 3.35±1.29 to 5.16±1.61 µmol/L (p=0.008). Also, with beta-carotene treatment, mean CD4+ count increased by 75.1±1.126 cells/µL from baseline 592.3±245.6 to 667.4 ± 330.5, although the change did not reach statistical significance (p=0.131). Other immune cell parameters, however, changed significantly with treatment: mean CD4% increased by 3.8% from 29.5±8.6 to 33.3±10.3 (p=0.007) and CD4:CD8 ratio changed by 0.17 (p=0.008) from 0.89±0.55 to 1.06±0.65 (p=0.008). There was no change in viral load with treatment and no serious adverse events or complaints of yellow-orange skin discoloration.

Conclusions: In this small study of short duration, treatment with beta-carotene increased serum carotene levels significantly. The increase was accompanied by improvement in T cell subsets, which measure immune activation and reconstitution. Our findings warrant controlled clinical trials of the effect of carotene supplements on immunity and health of HIV patients.

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DEVELOPMENT OF A PROTECTIVE HUMAN IMMUNODEFICIENCY VIRUS (HIV) VACCINE BASED ON A SELF-BOOSTING HUMAN CYTOMEGALOVIRUS (HCMV) VECTOR

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Plain Language Summary: Human cytomegalovirus (HCMV) is a ubiquitous herpesvirus responsible for asymptomatic, dormant, lifelong infection in healthy individuals. The ability of HCMV to: 1) induce a strong, mucosally-oriented immune response, 2) frequently reactivate and self-boost the immune response, 3) re-infect immune individuals', are key advantages over other vaccine vectors tested to date. Cytomegaloviruses are highly species-specific viruses and generally restricted in ability to infect even closely related hosts. Therefore, to test our hypothesis, we propose to use rhesus cytomegalovirus (RhCMV), a non-human primate cytomegalovirus, as a vaccine vector to induce protective immunity to simian immunodeficiency virus (SIV).

Objective: To explore the use RhCMV as a vaccine vector for development of an HIV/SIV vaccine using cynomolgus macaques by characterizing the primary and secondary immune responses against endogenous CMV followed by the super-infecting RhCMV vaccine strain.

Methods: Specific aim 1: Test if CMV sero-positive cynomolgus macaques can be re-infected with RhCMV and to evaluate immunogenicity of the vector. To differentiate RhCMV from endogenous cynomolgus CMV, a recombinant RhCMV expressing green fluorescent protein (RhCMV-EGFP) has been constructed. Specific aim 2: Characterize the anti-CMV-vector based immune responses to understand their impact on protective efficacy of the subsequent vaccine. Specific aim 3 Construction of RhCMV expressing codon-optimized SIV antigens gag, pol, env or a Nef-Tat-Rev fusion, and assess the levels and pattern of SIV antigen expression and growth in vitro. Specific aim 4: Compare the in vivo growth and immunogenicity of these vectors and their ability to confer protection following a multi-low dose mucosal challenge with pathogenic SIVmac239 in macaques. The data from these experiments will be analyzed to determine the immunologic parameters predictive of protection.

Results: Using a bacterial artificial chromosome derived RhCMV 68.1 pathogenic strain, we have constructed a RhCMV recombinant virus constitutively expressing enhanced green fluorescence protein (EGFP) under control of the HCMV immediate early promoter (RhCMV-EGFP). Currently we are in the process of plaque purification, in vitro characterization and growing high titer virus stocks necessary for the animal inoculation. The codon-optimized SIV genes encoding gag, pol, env and Nef-Tat-Rev fusion proteins have been already cloned into mammalian expression vectors, and their expression levels have been confirmed by Western blot analysis. Infection of immunocompetent adult 10 macaques will allow characterization of immune responses prior to and after the super-infection with RhCMV-EGFP.

Conclusions: This RhCMV-based SIV vaccine study will address key issues of the immunogenicity, protective efficacy and self boosting-capacity of this herpesvirus vector.

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ENHANCEMENT OF THE CTL RESPONSE OF HIV CANARYPOX VACCINE BY MOLECULAR ADJUVANT OX40L

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Plain Language Summary: Effective vaccines are urgently needed to control the continuing spread of HIV. HIV vaccine made from canarypox virus (ALVAC), a weakened virus vector, has been FDA approved and shown to be safe in humans. However, it does not make strong immune responses in vaccinated persons. We have used state of the art techniques in immunology and virology to design a more effective HIV ALVAC vaccine. We tested OX40 ligand (OX40L), a costimulatory molecule that can increase immune responses, alone or in combination with CD40L, another costimulatory molecule, and found OX40L can markedly enhance the cytotoxic T lymphocytes (lymphocytes that can kill HIV infected cells, therefore inhibit HIV replication) immune response of the HIV ALVAC vaccine in mice. Adding CD40L to OX40L cannot further enhance CTL responses. Our findings may lead to novel HIV ALVAC vaccine that is both safe and more effective than current vaccine.

Objective: To augment the CTL response of HIV canarypox vaccine, vCP1452, with OX40L expressed from canarypox vector.

Methods: Recombinant ALVAC virus that can express murine OX40L, vmOX40L, was constructed and characterized. Female Balb/c mice were immunized intramuscularly 3 times with vCP1452 together with vmOX40L, vmOX40L plus vmCD40L, or control empty ALVAC vector. Six weeks after the last time immunization, mice splenocytes were prepared and CD8 T cell responses were analyzed with IFN-□ ELISPOT, HIV Gag epitope tetramer staining and intracellular cytokine staining.

Results: OX40L can augment CD8 T cell responses of vCP1452. Compared with control mice immunized with vCP1452 and empty ALVAC, CD8 T cell responses of the mice immunized with vCP1452 together with vmOX40L increase by 2 folds ($p<0.05$). Coadministration of vmCD40L cannot further enhance CD8 T cell responses compared with vmOX40L alone.

Conclusions: OX40L can enhance CTL response of HIV canarypox vaccine. Our findings may lead to novel HIV vaccine that is both safe and more effective than current vaccine.

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HERPESVIRUSES AS HIV VACCINE VECTORS: INFECTIVITY AND IMMUNOGENICITY OF VARICELLA-ZOSTER VIRUS IN THE CYNOMOLGUS MACAQUE NON-HUMAN PRIMATE MODEL.

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Plain Language Summary: In this work, we are examining the feasibility of using a herpesvirus as a viral vector for a novel HIV vaccine. This herpesvirus is called Varicella Zoster Virus (VZV) and is used today as a vaccine against chickenpox. We have assessed the ability of this virus to infect and elicit an immune response in a non-human primate model. Furthermore, we have generated a panel of novel HIV vaccines using VZV as a vector backbone and will assess their protective efficacy in future trials in this primate model.

Objective: Varicella-Zoster Virus (VZV), the causative agent of chickenpox and herpes zoster, establishes a life-long latent infection in neural ganglia, with evidence of periodic reactivation even in healthy individuals. In addition to the proven safety and efficacy record of the live-attenuated VZV Oka vaccine strain, the large DNA genome can be readily manipulated for the accommodation of foreign genes. Together with the ability to induce broad-ranging cellular and humoral immune responses, and the key feature of durable immunity, VZV is an attractive candidate for use as a vector in HIV vaccine development.

Methods: Live, parental Oka VZV was assessed for viral infectivity and immunogenicity in cynomolgus macaques following intra-tracheal and intravenous inoculations. The ability of the virus to replicate was assessed by quantitative PCR and shell vial/DFA analysis of whole blood, bronchial alveolar lavage and nasopharyngeal samples. Humoral and cellular immune responses to VZV were monitored longitudinally by ELISA and interferon-gamma ELISPOT and multi-colour FACS/ICS, respectively.

Results: Following VZV inoculation, a productive infection was detected in at least one animal. Robust humoral responses were readily detected by day 15 post-inoculation in all animals with a subsequent anamnestic response generated following an intravenous boost. Cell mediated immunity was detected by ELISA and FACS/ICS following antigenic stimulation with a VZV lysate. Phenotypic surface staining and intracellular cytokine staining of PBMCs revealed significant CD4 and CD8 T-cell activation (CD69 or CD107a) and cytokine expression (IFN-gamma, TNF-alpha, and IL-2). Noteworthy, is the elicitation of a CD8 T-cell response which is difficult to detect in humans following VZV vaccination. The extent to which VZV is able to establish latency in this animal model will be ascertained following necropsy.
Concurrently, we have generated an extensive panel of recombinant VZV vectors expressing various combinations of SIV genes to be assessed as potential vaccine candidates. These VZV-SIV recombinants demonstrate high-level transgene expression, genome stability, and wild-type growth characteristics in preliminary in vitro testing.

Conclusions: Our preliminary data suggests that cynomolgus macaques may provide an appropriate setting in which to assess recombinant VZV vectors as SIV/HIV vaccine candidates. Intratracheal inoculation resulted in robust humoral and cell mediated immunity at comparable or elevated levels to those seen in humans following vaccination against chickenpox. This study has provided critical data with respect to dosing and routes of inoculation for future trials. A multi-low dose mucosal challenge trial will be initiated to assess the protective efficacy of various VZV-SIV vectors is slated to begin in early 2009.

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HIV REGULATES IL-23 AND IL-27 EXPRESSION

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Plain Language Summary: The human immunodeficiency virus (HIV) is responsible for the loss of immune system function leading to the development of AIDS. HIV can evade the host immune system by modulating cytokine expression and function. HIV-mediated modulation of crucial Th1 cytokines such as interleukin (IL)-12, IL-23 and IL-27 may play an important role in HIV pathogenesis by controlling the immune response to pathogen infection. The effect of HIV on the expression and function of IL-23 and IL-27 is presently unknown. However, IL-27 has been shown to be a potent inhibitor of HIV replication in vivo. Moreover, low levels of IL-23 have been reported in HIV-infected individuals. Our hypothesis is that HIV and HIV regulatory proteins (Tat and Vpr) modulate IL-23 and IL-27 expression as well as activity, contributing to the loss of cell-mediated immunity and disease progression.

Objective: The objective of this study is to determine the effect of HIV, Tat and Vpr on IL-23 and IL-27 promoter activity and expression.

Methods: The promoters of the IL-23 and IL-27 subunits, p19, EBI3 and p28, up to -3000bp upstream of the start codon were cloned from the genomic DNA of human peripheral blood mononuclear cells (PBMCs) into the pGL3B luciferase reporter plasmid. Plasmid sequences were subsequently confirmed by DNA sequencing. Truncated promoter constructs were also prepared as short as -250bp upstream of the start codon of each gene. Luciferase activity was determined in LPS-stimulated promonocytic HL-60 cells. LPS-stimulated IL-23 and IL-27 protein production was also assessed by ELISA. The effect of Tat and Vpr on IL-23 and IL-27 expression will be determined using retrovirally-expressed viral proteins.

Results: Preliminary results suggest that luciferase activity is stimulated by LPS in the longer (-3000 and -2000 bp) promoter constructs for each of the p19, EBI3 and p28 genes. IL-27 production in the cell culture supernatant is induced by LPS whereas IL-23 levels appear to be unaffected or slightly decreased. The Tat and Vpr genes have been cloned from the p89.6-HIV genome plasmid into the pLXIN retrovirus expression system and transfected into the PT67 retrovirus packaging cell line. The Tat and Vpr expression retroviruses are currently being characterized.

Conclusions: IL-23 and IL-27 may be critical to the modulation of HIV pathogenesis. While both cytokines appear to be regulated by LPS at both the promoter and protein levels, further study is required to fully characterize the effect of HIV and its regulatory proteins Tat and Vpr on IL-23 and IL-27 expression.

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HIV VIRUS REGULATES IL-12 FAMILY CYTOKINES (IL-23 & IL-27) IN THP-1 CELLS

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Plain Language Summary: HIV virus is involved in immune dysregulation. Recently, a growing number of cytokines are discussed in terms of their perturbation in HIV infection and of their effects on virus replication. It is well known that HIV infection itself has a critical role in cytokine dysregulation in HIV/AIDS patients. Among the potential cytokine dysregulation in HIV infected cells; IL-12 and its new family members (IL-23 and IL-27) are important because of their crucial role in cell mediate immune response (CMIR) and fighting against intracellular micro-organisms.

Objective: To determine the role of HIV infection in regulation of IL-23 and IL-27in THP-1 cells as a model systems. Also, to study the impact of HIV infection on THP-1 cell response to microbial products such as LPS.

Methods: We have elucidated the effects of in vitro HIV infection on spontaneous and LPS-induced IL-23 and IL-27 production by THP-1 cells (a human monocytic cell line). To evaluate HIV infection effects on these cytokines production, we have measured IL-23 and IL-27 expression at mRNA levels by Real-Time PCR. Also we have evaluated the levels of IL-23 and IL-27 production at protein level by ELISA.

Results: We have shown that HIV virus properly replicates in THP-1 cells. HIV virus triggers IL-23p19, IL-12p40 mRNA expression in THP-1cells. HIV-1 does not induce IL-27p28 mRNA expression, but it does induce IL-27EBI3 mRNA expression in THP-1 cells. HIV infection inhibits LPS-induced IL-23 at messenger RNA and protein levels in THP-1 cells.

Conclusions: HIV infection impact on the cytokine network represents a crucial determinant of virus replication and immunologic dysregulation. The approaches directed at understanding CMIR regulation by HIV will likely play a key role in the development of effective strategies of HIV prevention and immunologic reconstitution.

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IMPACT OF HIV INFECTION ON IL-23 INDUCED SIGNALING AND GENE EXPRESSION IN HUMAN T CELLS.

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Plain Language Summary: Interleukin-23 (IL-23) is a heterodimeric cytokine consisting of two subunits, one called p40, which is shared with another cytokine, IL-12, and another called p19 (the IL-23 alpha subunit) (1). IL-23 belongs to the IL-12 family of cytokines and shares some features with IL-12 in that it can stimulate the proliferation of memory CD4+ T cells. Unlike IL-12, IL-23 plays a critical role in the induction of the novel IL-17 producing T helper (Th) cell subset called Th17 (2). IL-23 signal transduction is mediated through activation of the Jak-STAT pathway. The components of the signaling pathway for IL-23 are similar to IL-12 and involve two receptor chains: IL-12Rβ1and IL-23R and the signaling proteins: Jak2, Tyk2, STAT1, STAT3, and STAT4 (3).

Objective: The aim of this study is to examine the effect of HIV infection on IL-23-induced signaling in human T cells as well as on the induction of genes expressed by Th17 cells.

Methods: Primary CD4 T cells from healthy controls and HIV-infected patients were isolated by negative selection using Rosettsep magnetic beads (Stem Cell Technologies) using protocols approved by the Queen's University Research Ethics Board. Cells were treated with recombinant human IL-23 (5µg/ml) and untreated cells were used as a control. Total protein was isolated from cells pellets and total RNA was prepared by using TriReagent. All samples were evaluated for the activation of the Jak/STAT pathway and the expression of immunoregulatory genes by Western analysis and reverse transcriptase polymerase chain reaction (RT-PCR) respectively.

Results: We demonstrate that IL-23 can induce the phosphorylation of STAT-1, STAT-3, STAT-4, JAK-2, and TYK-2 and also Th17-expressed genes such as ROR-γt and CCR6 in healthy control CD 4 T cells. In a primary HIV isolates, these affects of IL-23 are lost. These results also show that CD4 T cells from HIV patients constitutively express activated signaling compared to healthy controls.

Conclusions: Our results indicate that the function of IL-23 may be deregulated during HIV infection and represents an important area of cytokine biology for further understanding of the role played by IL-23 in HIV infection.
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INFLUENCE OF INNATE FACTORS AND ANTIBODIES ON HIV-TRANSMISSION THROUGH BREAST MILK

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Plain Language Summary: Human breast milk (HBM) provides both nourishment and protection of the health of newborns. In HIV-infected mothers, HBM contains cell-free and cell-associated virus which accounts for one to two thirds of pediatric HIV cases worldwide. Surprisingly, recent studies have shown that transmission through HBM is less likely to occur if the mother is exclusively breast-feeding compared to women who do not exclusively breast feed their babies. It is our hypothesis that the child's protection from HIV is closely linked to innate factors present in the mother's breast milk. Through the use of a multi-analyte assay developed in our lab, we have begun measuring innate factor levels and antibodies in HBM.

Objective: We will start by establishing normal ranges of innate factors in HIV-uninfected breast milk. Once baseline levels have been measured, we will continue looking at these innate factors in blinded historical HBM samples from South African HIV-infected mothers who either did or did not exclusively breast feed their newborns. Additionally, viral load and specific anti-HIV immunoglobulins will be measured. These data will then be compared to show any correlation between innate factor levels and mother-to-child HIV-transmission rates.

Methods: Our mutli-plex bead assay platform will be used for detecting multiple innate factors in HBM. This platform allows us to measure multiple innate factors and HIV-specific antibody in very small HBM samples. HBM samples will be collected from mothers within one week, one month, and three months after normal vaginal delivery. The samples will arrive at our lab the same day they are collected and processed.

Results: We have successfully designed and are standardizing and optimizing custom beads capable of detecting multiple innate factors in HBM through flow cytometry. In preliminary experiments completed with HBM from HIV-uninfected women, innate factor levels were consistent with published papers that specifically measured IL-8, SLPI, IL-7, lactoferrin, lysozyme, and RANTES in HBM from HIV-uninfected women.

Conclusions: Preliminary results using our platform show high levels of sensitivity and specificity for detection of multiple specific innate factors in HBM. Further testing is required on a larger number of samples to conclusively address our hypothesis.

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INTERNALIZATION OF THE INTERLEUKIN-7 RECEPTOR ALPHA-CHAIN OCCURS VIA AN ENDOCYTIC PATHWAY IN THE PRESENCE OF HIV TAT PROTEIN

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Plain Language Summary: The IL-7 receptor, composed of a unique alpha-chain (CD127) and a common gamma-chain, is essential for T-cell homeostasis and function. We have previously demonstrated soluble HIV Tat protein down regulates CD127 on the surface of CD8 T-cells leading to impaired cell proliferation and cytolytic potential. We now know Tat enters CD8 T-cells and interacts with the cytoplasmic tail of CD127 inducing receptor capping, internalization and degradation. While this process is dependent on microtubules, the exact pathway and intermolecular interactions involved have yet to be fully elucidated.

Objective: The purpose of this study is to elucidate the endocytic pathway through which HIV Tat removes CD127 from the cell surface.

Methods: After treating primary CD8 T-cells with soluble Tat protein, immunostaining coupled with confocal microscopy is used to co-localize CD127 with proteins specific to various endocytic pathways.

Results: To date, we have been able to visualize CD127, transferrin and Tat in primary CD8 T-cells. Interestingly, while CD127 is found over the entire cell surface, its distribution is not uniform. Consistently, CD127 is polarized towards one side of the cell surface. Preliminary results indicate that transferrin has a similar distribution although not as pronounced. Our next step is to determine by co-staining and confocal microscopy if CD127 and transferrin co-localize in early endosomes.

Conclusions: Understanding the pathway by which HIV Tat is able to remove CD127 from the surface of CD8 T-cells will not only provide important information on the pathogenesis of this disease but may also reveal potential targets to disrupt this effect and preserve CD8 T-cell function.

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REGULATION OF IL-12 CYTOKINE FAMILY IN HUMAN MONOCYTES

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Plain Language Summary: Cytokines are a group of small proteins that serve as signaling compounds, allowing cells to communicate with one another. My project focuses on two cytokines, IL-23 and IL-27 that have important roles in regulating cell-mediated immune responses. My research will ultimately focus on the signaling pathways that HIV-infection employs to target cellular mechanisms, and start the progression of the disease. These results will help elucidate the molecular mechanisms by which HIV changes the expression of IL-23 and IL-27 cytokines. As a result, further understanding of the effects that HIV has on cytokine expression will be provided and novel strategies may be developed, enhancing the host immune response against HIV infection.

Objective: My experimental objectives are as follows:(1) To determine the signaling pathways involved in IFN-γ-induced IL-23 and IL-27 expression in human monocytes, (2) To characterize IL-23 and IL-27 expression in HIV-infected individuals and following in vitro infection with HIV of monocytes and (3) To determine the mechanisms by which HIV regulatory proteins modulate the signaling proteins implicated in IFN-γ-induced IL-23 and IL-27 expression in human monocytes.

Methods: Human primary monocytes are obtained from peripheral blood mononuclear cells (PBMCs) of healthy donors. Monocytes are isolated and cultured in IMDM supplemented with 10% FBS , 100 units/ml penicillin, 100μg/ml gentamicin, 10mM HEPES, and 2mM glutamine. In order to study the regulation of IL-23 and IL-27, specific signaling pathways are studied. By using a series of small protein inhibitors I am able to investigate the MAPK signaling pathways using SP600125, SB203580 and PD98059, which are JNK, p38 and ERK inhibitors respectively. PI3K signaling pathway is examined using the LY294002 inhibitor. Once I have determined the signaling pathways induced by IFN-γ stimulation, the effect of HIV regulatory proteins on IL-23 and IL-27 expression will be established.

Results: JNK, p38 MAPK and PI3K negatively regulate IFN-γ-induced IL-23p19 mRNA production in human monocytes. Moreover, ERK does not have a role in the IFN-γ-induced IL-23p19 mRNA production. Furthermore, in the presence of JNK, p38 and PI3K inhibitors, production of IL-23p19 mRNA significantly increased in a dose-dependent manner.

Conclusions: The purpose of my project is to provide further insight into the effect that HIV and its regulatory proteins have in the modulation of Th1 cytokines. By understanding the mechanisms that HIV uses to minimize a Th1 response, novel therapeutic approaches can be used to attenuate the HIV-associated immune deficiency.

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SURVIVAL AND FUNCTION OF MEMORY CD8+ T CELLS IN RESPONSE TO IL-7 AND ANTIGEN

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Plain Language Summary: During a secondary immune response, memory CD8+ T cells are stimulated to proliferate and gain effector function. While antigen is the primary stimulus for proliferation and differentiation of these cells, it is possible that IL-7 may enhance CD8+ T cell function, as IL-7 is an important stimulus during a primary immune response. During HIV infection, CD8+ T cell function is impaired, and this could be due to the down-regulation of the IL-7Rα (CD127), or could be due to impaired IL-7 signaling within the CD8+ T cells.

Objective: To evaluate the effect of IL-7 on the proliferation and function of memory CD8+ T cell subsets in the presence or absence of antigen, and determine if this is impaired in HIV infection.

Methods: CD8-depleted peripheral blood mononuclear cells were pulsed with a peptide pool (CMV, EBV, influenza), and co-cultured with autologous memory CD8+ T cells (CD45RA-CCR7+/-) in the presence or absence of IL-7 (1-50 ng/ml). Cellular function (IFN-γ and CD107a/CD107b) was measured after 6 hours of co-culture, and cell division was analyzed (CFSE) after seven days of co-culture by flow cytometry. Central memory (CD45RA-CCR7+, TCM), effector memory (CD45RA-CCR7-, TEM), and terminally-differentiated effector memory (CD45RA+CCR7-, TEMRA) T cell populations were also determined.

Results: Stimulation with IL-7 increased CD107a/107b surface expression, specifically in the TCM and TEM subsets. In the presence of antigen, the addition of IL-7 resulted in a minor increase of IFN-γ production in the TEM and TEMRA cell subsets. Proliferation of CD8+ T cells increased in response to IL-7 in a dose-dependent manner in the TCM and TEM subsets compared to antigen alone, and to a lesser extent in the TEMRA subset. Studies of CD8+ T cells from HIV infected individuals are underway.

Conclusions: The addition of IL-7 during a secondary immune response can lead to an increase in proliferation and function of memory CD8+ T cells. Whether this effect is impaired in HIV infection is the subject of ongoing study. These results further our understanding of the mechanisms required during a secondary immune response, and is relevant to the ongoing studies of HIV pathogenesis and of IL-7 as a therapeutic in HIV infection and other diseases.

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THE EFFECT OF HIV INFECTION ON THE INTERLEUKIN-27-INDUCED CYTOKINE PROFILE IN PRIMARY HUMAN MONOCYTES.

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Plain Language Summary: Interleukins, cytokines secreted by leukocytes, are predominant messengers that modulate immune responses. There are over 30 different types of human cytokines called interleukins (IL) that have been identified. During HIV infection, cytokine expression and function become deregulated. Of particular note is IL-12, a cytokine which has suppressed production in the setting of HIV infection (1). Interestingly, IL-12 has been investigated as a potential therapy for HIV infection (2). IL-12 shares receptor components as well as downstream signaling components with a newly described cytokine, IL-27. IL-27 exhibits pro- and anti-inflammatory properties and can be regarded as an immunomodulator. Although IL-27 has recently been shown to act as a novel anti-HIV cytokine (3), the effect of HIV infection on IL-27 function has not been characterized. IL-27 induces the activation of human monocytes (4,5) and studies have shown distinct IL-27-mediated cytokine profiles in human monocytes/macrophages (4,6). We have recently demonstrated that IL-27 induces a subset of pro-inflammatory cytokines in human monocytic cells. The purpose of this study is to understand how IL-27-induced cytokine production in human monocytes is affected by HIV infection.

Objective: We sought to identify the effect of HIV infection on IL-27 functions, including IL-27-mediated signaling and resulting cytokine expression in monocytic cells.

Methods: In accordance with Queen's University Research Ethics Board approval, informed consent was obtained from HIV patients willing to participate in this study. Primary human monocytes were isolated from HIV-infected blood donors and were stimulated with rIL-27 or left unstimulated. Primary monocytes were also isolated from healthy, uninfected volunteers. Cell pellets were processed for RT-PCR analysis and Western Blotting to examine the effect of HIV infection on IL-27-induced cytokine expression and signaling pathways, respectively.

Results: Preliminary results have shown that HIV infection alters IL-27 functions, including dysregulation of the IL-27-induced cytokine profile in monocytic cells.

Conclusions: How IL-27 functions in HIV-infected patients is not well characterized. This study is a critical first step to discover how this cytokine may helpful towards the identification of novel treatment modalities or potential prognostic indicators. This work is supported by the OHTN.
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THE MECHANISM OF IL-7-INDUCED SECRETION OF SOLUBLE IL-7R ALPHA (CD127) IN HEALTH AND HIV DISEASE

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Plain Language Summary: In HIV infection, decreased expression of membrane bound IL-7 receptor alpha (CD127) on CD8+ T-cells correlates with decreased CD4 counts, increased plasma IL-7 and decreased HIV-specific CD8+ T-cell function. In vitro, increasing concentrations of IL-7 result in the downregulation of CD127 on CD8+ T-cells, a process independent of receptor internalization or altered mRNA. Furthermore, IL-7 induces the release of a soluble form of CD127 (sCD127) by CD8+ T cells in vitro. The mechanism(s) responsible for the release of sCD127 have not yet been elucidated and the role of sCD127 in HIV pathogenesis is not known.

Objective: To investigate the potential mechanisms involved in the IL-7-mediated secretion of sCD127 by CD8+ T-cells.

Methods: Isolated CD8+ T-cells were pre-incubated with increasing concentrations of potential receptor cleavage inhibitors (matrix metalloprotease (MMP) inhibitors, calcium chelator EDTA) or an inhibitor of IL-7 signaling (Jak-inhibitor) for 2 hours and subsequently cultured with IL-7 (10 ng/ml). After 24 hours, culture supernatants were collected and assayed for the release of sCD127 using a CD127-specific Western blot. To determine whether surface CD127 is directly released by CD8+ T-cells in the presence of IL-7, cells were coated with biotin and cultured with medium or IL-7 for 24 hours. Biotinylated proteins were isolated from culture supernatants and cell lysates using a biotin affinity column and then assayed for sCD127 release by Western blot.

Results: IL-7-induced down-regulation of surface CD127 can be inhibited through the inhibition of Jak-STAT signaling pathway while MMP inhibitors had no effect. EDTA significantly inhibited IL-7's downregulation of surface CD127 in a dose dependent manner. In addition, EDTA and Jak inhibitors reduced the amount of sCD127 released by CD8+ T-cells into culture supernatants in response to IL-7.

Conclusions: These data suggest that the secretion of sCD127 may be mediated through an IL-7-initiated pathway involving calcium signaling. Furthermore, this is the first report regarding the detection of human sCD127 by Western blot using a monoclonal antibody and this method will provide a means to measure sCD127 in culture supernatants. The relevance of IL-7 signaling inducing sCD127 secretion is important in HIV infection given the increased plasma IL-7 and sCD127.

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TRANSCRIPTIONAL REGULATION OF THE CD127 GENE IN CD8 T-CELLS

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Plain Language Summary: Expression of the interleukin (IL)-7 receptor alpha-chain (CD127) is tightly regulated throughout the life-span of a CD8 T-cell. How this receptor's expression is controlled both at the level of transcription and post translationally is currently under investigation. While IL-7 down regulates CD127 providing negative feedback to this signaling pathway, glucocorticoids have been shown to enhance expression. Here we describe the human CD127 promoter and identify key elements important to its transcriptional regulation.

Objective: To understand the transcriptional regulation of the CD127 gene

Methods: CD8 T-cells were isolated from healthy volunteers and incubated with IL-7 (10 ng/ml), dexamethasone, or inhibitors as indicated for 24 hours. Total RNA was harvested and CD127 mRNA transcripts were quantified using both real-time PCR and semi-quantitative PCR normalizing to RPS18 expression. The putative CD127 promoter was cloned from human genomic DNA. The 3 kb promoter and a series of deletion mutants were cloned into a luciferase reporter plasmid and analyzed in primary CD8 T-cells.

Results: The core promoter element of the CD127 gene lies within the first 600 bp upstream of the TATA box. This region provided luciferase expression 4-fold over empty vector and was absolutely essential for transcription. Additional cis-regulatory elements were identified from -1468 to -1760 bp and from -1760 to -2406 bp each increasing luciferase expression 2-3-fold over the basal promoter (12 to 14-fold over vector alone). A glucocorticoid responsive element was identified between -2269 and -2255 bp. While IL-7 efficiently down regulated both CD127 mRNA and protein expression in CD8 T-cells within 24 hours, IL-7 did not down regulate luciferase expression from the cloned 3 kb promoter. Whether the IL-7 responsive elements lie outside this region or IL-7 does not down regulate CD127 mRNA at the level of transcription is currently under investigation. Interestingly, cycloheximide blocked IL-7's ability to down regulate CD127 suggesting a requirement for de novo protein synthesis.

Conclusions: Basal CD127 promoter activity in human CD8 T-cells is controlled by a core promoter region located within 600 bp upstream of the TATA box. Additional positive cis-acting elements including a glucocorticoid-responsive element have also been identified. While IL-7 down regulates CD127 mRNA and protein within 24 hours, de novo protein synthesis is required suggesting suppression by IL-7 is indirect. The exact mechanism by which IL-7 suppresses CD127 expression is currently being investigated.

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TRAPPIN-2/ELAFIN AND INNATE ANTIVIRAL IMMUNE RESPONSES IN THE HUMAN GENITAL MUCOSA

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Plain Language Summary: We are largely protected against sexually-transmitted infections (STIs) by potent mucosal immune responses in our genital tracts, where innate immune factors may play a significant yet not well elucidated role. Since HSV-2 genital infection predisposes to HIV-1 acquisition/exacerbation and since women are at greater risk of HIV infection, our goal is to understand the mechanisms of how innate factors can contribute to protection of female genital tract against both viral infections.

Objective: Several factors contribute to HIV-1 resistance, including antimicrobials trappin-2/elafin. We aimed to characterize its contribution to innate antiviral responses against Poly(I:C), a synthetic mimic of viral dsRNA and a potent inducer of an antiviral protection. Antiviral inhibitory potential of trappin-2/elafin was also tested against HSV-2 and HIV-1 viruses.

Methods: The role of adenovirus(Ad)-delivered and human recombinant trappin-2/elafin in altering inflammation and antiviral responses elicited by Poly(I:C) was assessed using human endometrial carcinoma (HEC-1A) cell line in vitro. Levels of expression of pro-inflammatory mediators and antiviral innate factors were assessed by ELISA and quantitative RT-PCR. Antiviral state after Poly(I:C) treatment was assessed by VSV-GFP plaque reduction assay. Antiviral properties against HSV-2 and HIV-1 were assessed using a transcytosis model with HEC-1A cells grown in tissue culture inserts by determining viral loads in supernatants. The potential of trappin-2/elafin to alter host's recognition and responsiveness to viral agents was assessed by measuring levels of expression of PRRs using quantitative RT-PCR and nuclear translocation of transcription factors using confocal microscopy.

Results: Experiments showed that Ad-mediated augmentation of trappin-2 resulted in statistically significant reduction of IL-8, TNFα, and IFNβ in supernatants of HEC-1A cells following Poly(I:C) treatment as well as mRNA levels of RIG-1, MDA-5, IFNβ, but not TLR3. Nuclear translocation of NF-kB and IRF3, as well as induction of an antiviral state, however, was enhanced in presence of trappin-2. Adenoviral delivery of trappin-2 as well as pretreatment of HEC-1A cells with human recombinant trappin-2/elafin prior to challenge with HSV-2 and HIV-1 resulted in reduced viral shedding post infection and lower levels of IL-8 and TNFα.

Conclusions: Trappin-2/elafin has a potential to impact on innate antiviral responses against viral agents, which may result in lower HSV-2/HIV-1 mucosal transmission across human genial epithelial cells. However, specific mechanisms of action remain to be elucidated.

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VPR INDUCED APOPTOSIS IN HUMAN MONOCYTIC CELLS.

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Plain Language Summary: AIDS progression is characterized by rapid depletion of immune cells, primarily T cells, rendering the host incapable of defending himself against any opportunistic infection. Monocytic cells survive HIV replication and cytopathic effects because of their decreased sensitivity to HIV-induced apoptosis. Determining how HIV induces resistance against apoptosis in human monocytic cells and how this resistance can be reversed is vital for designing AIDS treatment regimes aimed at destroying viral persistence in monocytes. Here are results suggesting, for the first time, the role of Toll like receptors in Vpr induced apoptosis in human monocytic cells. HIV-1 Vpr (Viral protein R), is an accessory protein of HIV known to cause apoptosis in various cell types. Using Vpr-52-96 synthetic peptides as a model apoptosis-inducing protein, I have shown that pre-treating THP-1 cells and primary human monocytes with TLR4, TLR3 and TLR9 agonists LPS, Poly I:C and CpG, respectively, induces resistance against Vpr mediated apoptosis in monocytic cells. Moreover, my results indicate that this resistance is mediated by endogenously produced TNFα.

Objective: To investigate the mechanism by which TNFα, TLR3 agonist Poly I:C, TLR-4 agonist LPS and TLR9 agonist CpG induce protection against HIV-Vpr induced apoptosis in THP1 cells and primary human monocytes.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from blood obtained from healthy donors and were subjected to automacs negative selection to isolate monocytes. Flow cytometry using FITC-labeled annexin-V/PI was performed to analyze apoptosis. Whole cell extracts or cytosolic and mitochondrial fractions of cells were prepared and analyzed by Western Blot technique.

Results: 1) Pretreatment of THP1 cells and primary human monocytes with TLR3, TLR4 and TLR9 agonists PolyI:C, LPS and CpG respectively protects these cells from HIV-Vpr induced apoptosis.
2) Blocking TNFα production using antibodies against TNF-R1 seems to completely reverse the protective effect of Poly I:C, LPS and CpG against HIV-Vpr induced apoptosis.
3) Pretreatment of THP-1 cells with LPS and TNFα prevents HIV-Vpr induced release mitochondrial apoptotic factors.

Conclusions: It is reasonable to conclude that monocytes of HIV-infected patients may develop a reduced propensity to undergo apoptosis at least in part due to the presence of microbial products present in chronically-infected HIV patients as well as due to TNFα that is present in the intracellular milieu following HIV infection or as a result of the inflammatory responses in the patients. Strategies based on suppression of TNFα production may be helpful in controlling HIV reservoir formation and broadly prevent infection with intracellular pathogens and associated inflammatory responses.

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AN INNOVATIVE APPROACH TO FACILITATING COMMUNITY ENGAGEMENT IN HIV HEALTHCARE AND RESEARCH THROUGH THE HAMILTON COMMUNITY HIV/AIDS ADVISORY RESEARCH GROUP (HCHARG)

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Plain Language Summary: An innovative approach to facilitating community engagement in HIV healthcare and research through the Hamilton Community HIV/AIDS Advisory Research Group (HCHARG).

Objective: HIV/AIDS is no longer considered a fatal disease but rather an episodic disability. Due to medical advances, people with HIV/AIDS (PHAs) are living longer. While more research focuses on their long-term health, input from community stakeholders (including PHAs), is often overlooked. Conversely, opportunities to participate in research projects that have direct health benefits may not be fully disseminated to stakeholders. Improving interprofessional collaboration through knowledge transfer and exchange with key stakeholders will aid research participation and potentially improve health outcomes.

Methods: The Hamilton Community HIV/AIDS Advisory Research Group (HCHARG) is comprised of community organizations, PHAs, clinical and research-based academia that focuses on research, community-based services, and improved health care through knowledge transfer and exchange (KTE). To this end an inaugural "Facilitating Engagement" conference was planned. Funding to support knowledge transfer and exchange was secured for this conference through both private and public sectors. The conference had interprofessional representation from all key stakeholders.

Results: The conference engaged stakeholders in the research process and raised awareness at the community level about HIV research taking place locally. The conference provided research updates, networking opportunities, open dialogue for new partnerships, as well as fostering a more multidisciplinary approach in the future.

Conclusions: HCHARG is an interprofessional collaboration that engages all stakeholders equally. HCHARG takes Knowledge Transfer and Exchange one step further by utilizing Knowledge Translation toaccelerate the knowledge cycle and transform knowledge into use. More effective health care and research engagement are desired outcomes.

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ENGAGING AND SUPPORTING THE INFORMATION NEEDS OF THE TORONTO HIV/AIDS COMMUNITY: THE FIRST 20 YEARS OF THE AIDS COMMITTEE OF TORONTO LIBRARY

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Plain Language Summary: The AIDS Committee of Toronto (ACT) Library supports the information needs of ACT service users, staff, and the broader HIV/AIDS community with one of the largest publicly accessible HIV/AIDS library collections in North America. To mark its first 20 years (1987-2007), the history of the Library was researched and the findings featured at an anniversary open house in September 2008. In addressing the ways the Library has engaged and provided services for the HIV/AIDS community over time, ACT will also have a better context for developing the Library's future identity and service delivery priorities in an evolving information management environment.

The Challenge: To research the development of the ACT Library's collection and services over the past 20 years in preparation for an anniversary open house.

Our Approach: The ACT board minutes, newsletters, and annual reports from 1983-2007 were reviewed for mentions of Library activities. A questionnaire requesting information on the accomplishments and challenges experienced by each librarian was distributed to eight former ACT librarians. The survey was completed by seven former librarians, as well as the two current librarians. Archival files in the library office were also consulted to verify facts. Research findings were used to complete a Library timeline, and to inform other historical displays created for the open house.

Key Findings: Themes that characterized the delivery of Library services included: the role of an information professional in a community-based organization, the engagement of HIV-positive people, the engagement of service providers, and the integration and growing importance of information technology. While the Library has sustained its core services of collecting and providing access to HIV/AIDS information throughout its history, there have been changes in the information requirements of the HIV/AIDS community as the understanding of HIV/AIDS has increased and the approaches to managing the epidemic have evolved.

Impact on Policy and Practice: An upcoming needs assessment will gauge the information needs of the Library's current user groups and help define the Library's direction as it moves forward. By understanding the Library's history, ACT will also be able to consider the rationale and intentions that form the basis of current services when envisioning their future as new information management concepts like knowledge transfer and exchange gain momentum in the HIV/AIDS community.

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ACKNOWLEDGING COMMUNITY KNOWLEDGE: FRONTLINE PERSPECTIVES ON EFFECTIVE HIV KNOWLEDGE BROKERING

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Plain Language Summary: Effective April 1, 2008 the Canadian AIDS Treatment Information Exchange (CATIE) took on an expanded mandate becoming the National HIV/AIDS Knowledge Exchange Broker for frontline organizations related to HIV prevention, care, treatment and support for people living with and vulnerable to HIV/AIDS. CATIE consulted with a wide variety of frontline community-based and national HIV/AIDS stakeholders in order to inform its new expanded mandate as Knowledge Broker (KB).

The Challenge: The goal of the consultations was to document the perspectives of local, regional and national community-based HIV/AIDS organizations with respect to their needs and expectations for CATIE's KB roles and Knowledge Exchange (KE) services. This data, along with a national survey, provided guidance to CATIE in its development of a national strategic plan for HIV/AIDS KE.

Our Approach: Between January and June 2008, CATIE conducted interviews with representatives from nine national HIV/AIDS NGOs and held discussions with 18 groups of frontline organizations (i.e., AIDS service organizations – ASOs). The consultation data were captured through detailed notes which were then transcribed and analyzed thematically.

Key Findings: National NGOs and frontline organizations described their vision for a KE network, emphasizing the need for "fewer gaps between what we know and what we do" and greater awareness and flow of knowledge and expertise. Consultation participants envisioned KE as serving a proactive role in matching knowledge users with producers, and facilitating KE activities on specific topics. Several strengths and opportunities were identified for the KE role, including: CATIE's established role in treatment KE, partnerships among national NGOs, and pre-existing KE mechanisms and forums. Barriers and challenges included concerns about increased workload, inadequate financial resources, meeting the full range of knowledge needs, and meaningful linkages between frontline service and HIV research. Frontline organizations expressed the need for an information hub which would allow them to find resources and experts in specific service areas and topics, and provided practical suggestions for ensuring cultural competence and appropriateness in KE activities. Researchers, pharmacists and nurses also provided useful perspectives on how best to bridge their knowledge and expertise with that of frontline ASOs.

Impact on Policy and Practice: The consultations yielded extensive useful guidance for CATIE as it develops its new role as KB. A key recommendation was for CATIE to develop tools and networking opportunities which would encourage documentation and sharing of best practices, including a proactive role in helping various HIV/AIDS stakeholders get the information that would help improve their work.

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COLLABORATION IN THE THIRD SECTOR; FROM CO-OPETITION TO IMPACT DRIVEN COOPERATION

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Plain Language Summary: The third sector has suffered from ineffective collaborations which have occurred at the superficial knowledge exchange level. Certain organizations and movements such as the HIV/AIDS groups have managed to break this mold and develop collaborations which share reserach, policy and resources. Furthermore these collaborations have been well funded. This paper explores the current situation and provides real and pragmatic solutions for moving the third sector forward.

The Challenge: Organizations compete against each other for funding, brand position and share of voice in an increasingly crowded third sector. Ease of entry to the sector means that many small organizations continually "pop up" to add to the cacophony of the message. Only through effective collaborations can these organizations survive.

Our Approach: The WI commissioned a series of four research projects within the NFP sector including a survey of 300 EDs. CBR projects were also included in which the WI studied three agencies involved in collaboration. Policy recommendations were developed in this context.

Key Findings:
1) We can't do business like this anymore; funding and reporting models must change
2) Funders must devote 10-15% of their grants to support collaborative networks
3) A Center for leadership in collaboration should be established using existing organizations
4) Organizations must move from competing to cooperating through specific initiatives

Impact on Policy and Practice:
1) Creates a new model for collaborative networks based on shared missions, goals and impact
2) Creates a solutions-based collaboration in which the collaboration is the winner
3) Cross fertilization occurs at an organizational level, not just scientific level
4) Collaboration becomes time dated; it has a goal with a beginning and an end

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SUPPORTING AIDS SERVICE ORGANIZATIONS' NEED FOR RESEARCH EVIDENCE: A RAPID RESPONSE SERVICE

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Plain Language Summary: To facilitate timely access to research evidence for ASOs, we have developed a Rapid Response Service that conducts targeted literature searches and develops fact sheets that highlight key take-home messages. To date, the service has made a positive impact by informing ASOs engaged in policy development and debate, program planning and applications/requests for program funding.

The Challenge: For research to have an impact on HIV policy and practice, it is essential to get relevant evidence into the hands of people who will use it. In a previous survey, we found that ASOs in Ontario did not have the capacity to acquire and assess research. To assist them, it is important to develop a rigorous mechanism that will give ASOs timely access to recent research findings.

Our Approach: To provide ASOs with research evidence on time-sensitive topics, the OHTN has developed a Rapid Response Service. Through this service, we identify relevant research evidence by locating existing summaries of systematic reviews (e.g., Database of Abstracts of Reviews of Effects -DARE), systematic reviews through targeted database searches (e.g., Cochrane Collaboration), primary literature (where no systematic reviews exist) and by contacting experts. We then develop a 1-2 page summary that outlines the take-home messages, factors that may impact the local applicability of the research (e.g., jurisdictions and populations studied) and a description of the evidence we used to develop the summary. The nature and extent of research evidence we can provide depends on the timeframe. If given 1-2 days, the OHTN can provide only existing summaries of systematic reviews, additional key systematic reviews (if available) and a listing of key primary research; if given 2-3 weeks, we can supplement this with information from key contacts, and develop a detailed fact sheet including quality assessments of relevant systematic reviews and more detailed assessment of the factors that may impact applicability.

Key Findings: Since launching the Rapid Response Service, we have responded to five requests from ASOs about 1) depo-progesterone and susceptibility to HIV; 2) cost-effectiveness and HIV prevention; 3) most effective models of needle exchange; 4) impact of depression on young mothers with HIV; and 5) crystal meth use and sexual risk among MSM

Impact on Policy and Practice: Based on these requests, the Rapid Response Service has already had a positive impact by helping inform ASOs engaged in policy development and debate, program planning and applications/requests for program funding.

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DOES PEER FACILITATION TRAINING EFFECTIVELY LEAD TO COMMUNITY AND INDIVIDUAL EMPOWERMENT: LESSONS LEARNED FROM THE AIDS BEREAVEMENT PROJECT OF ONTARIO.

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Plain Language Summary: In Ontario, the assumption that peer facilitation and capacity building leads to community and individual empowerment has not been sufficiently evaluated. In collaboration with community members, the AIDS Bereavement Project of Ontario (ABPO) identified the need for effective training for peer facilitators who would provide bereavement and multiple loss support.

Objective: One of the objectives of this initiative was to identify and evaluate Peer Facilitator Trainee capacities and skills learned, including: self-awareness, self-care, community building abilities and leadership.

Methods: Training retreats were held in two sessions, 16 and 18 participants respectively; their average age was 45 and 90% were HIV-positive, with an average of 15 years since diagnoses. Peer Facilitator Trainees represented a variety of geographic, social, cultural and sexual communities. Trainees self-completed evaluation forms, rating their peer facilitation skills, confidence in skills learned, tools provided and in participants' confidence in their own resources.

Results: Trainees rated ABPO's Peer Facilitation training as being "very successful in preparing them to do peer support in their local community"; 7.4/10, (where 10 was very prepared to do peer support in their local community) was the average rating in the fall training. In the following spring training, an average rating of 8.6/10 was reported.

1) 75% of all participants reported a high degree of confidence in communicating the Multiple Loss Journey to others, and they also felt confident in their ability to share the theory of grief and loss;
2) Participants expressed an increased level of confidence in their abilities to use appropriate language to describe their experiences and to effectively support others;
3) They also felt a higher ability to reinvest and find value in their own lives

Conclusions: This evaluation provides evidence that ABPO's Peer Facilitation Training model was successful in training Peer Facilitators to provide formal and informal peer support to others.

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NATIONAL SURVEY OF FRONT-LINE ORGANIZATIONS TO GUIDE STRATEGIC DIRECTIONS FOR CATIE: THE NEW NATIONAL HIV/AIDS KNOWLEDGE EXCHANGE BROKER

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Plain Language Summary: Effective April 1, 2008 the Canadian AIDS Treatment Information Exchange (CATIE) took on an expanded mandate as National HIV/AIDS Knowledge Exchange Broker for front-line organizations related to HIV prevention, care, treatment and support for people living with and vulnerable to HIV/AIDS. The results of a national survey will help to inform the development of strategic priorities for CATIE as it assumes its expanded mandate.

The Challenge: To collect quantitative data on the needs and priorities of front-line staff in order to help guide CATIE in developing the strategic priorities for its new mandate. This data augments information collected from consultations with national non-governmental organizations and community-based organizations.

Our Approach: In July 2008, a 15 minute quantitative on-line survey was launched on CATIE's website. Email and mail invitations to complete the survey were sent to members of numerous different national and regional agencies and networks.

Key Findings: Three hundred and twenty two people representing a diverse array of front line organizations completed the survey. Prevention and treatment information needs are high for front-line organizations and their ability to locate these quite low. Preferred mediums by which to receive information are: the web, print materials; in person conferences, workshops, skills building or meetings, and e-mail. Preferred sources of information are presentations, workshops, and skills building plain language materials; research summaries; and health promotion materials. The five topic areas with the highest reported need for information are: HIV prevention, legal issues, addictions, mental health, and stigma and discrimination. The top four activities identified for CATIE as a knowledge broker are the development of plain language HIV information resources, the creation of a comprehensive website, the dissemination of HIV research bulletins, and distribution of print materials produced by organizations across Canada.

Impact on Policy and Practice: The goal of the knowledge exchange broker is to strengthen the responses of front-line organizations involved in the delivery of prevention, diagnosis, care, treatment, and support to people living with, and at risk to, HIV/AIDS by incorporating an active and continuous exchange of HIV/AIDS-related knowledge. A national consultation was conducted in order to ensure the development of CATIE's new strategic priorities meet the needs of our stakeholders.

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INTERGRATING THE THERAPEUTIC USE OF ART FOR INDIVIDUALS LIVING WITH HIV/AIDS - CLINICAL REFLECTIONS FROM COMMUNITY-BASED RESEARCH/PHA ACCESS

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1-Casey House

Plain Language Summary: In 2007 Casey House, a specialty hospital, participated as co-investigators in a community-based research (CBR) project.
PHA ACCESS is a community-based research (CBR) project pilot-testing a model of community-hospital collaboration, knowledge exchange, and capacity building, aimed at increasing access of people living with HIV to mental health services by training and supporting AIDS service organization (ASO) workers in the provision of evidence-based (art, mindfulness and narrative) psychotherapies.
This poster will outline the experience of clinicians who participated in the art therapy stream of this project.

The Challenge: There is broad recognition of the need for intersectoral collaboration in addressing mental health issues for people living with HIV.
Our challenge was to implement, integrate and evaluate the therapeutic use of art in both the residential and community settings by providing inter-professional staff at Casey House training in art therapy techniques within the knowledge exchange framework provided by PHA ACCESS.

Our Approach: Casey House trainees participated in training and biweekly support in providing therapeutic art.
They utilized a manual based on art practice techniques designed for community staff and volunteers. The aim was not to train community staff to become art therapists, but to provide a structured and supervised way of using art in their work with clients.
All PHA ACCESS trainees who provided interventions, participated in in-depth interviews or focus groups to assess the training effectiveness and to provide recommendations for adapting interventions and training. To assess the client impact, process and outcome measures were administered to clients before, during and after the interventions; they too participated in in-depth interviews.

Key Findings: In preliminary findings the responses from clinicians and clients were largely positive. The poster will share the observations of clinical staff who participated in training and were supported to provide counseling in the therapeutic use of art. We will offer an overview of the use of structured training, the process of learning a new modality, and reflections on client interactions.

Impact on Policy and Practice: Impact includes increased access to training and care; increased capacity for CBR, psychotherapeutic services, and community-hospital cooperation.
In moving forward PHA ACCESS co-investigators plan to develop new projects and advocate for policies to strengthen community mental health services for PHA's.

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THE MEN'S BODY MAPPING PROJECT: STORYTELLING, ADVOCACY AND HIV KNOWLEDGE EXCHANGE THROUGH AN ART-BASED PROCESS

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Plain Language Summary: This presentation focuses on the knowledge translation and exchange (KTE) component of a body mapping project. During the fall of 2007 in Toronto, seven men living with HIV created life-size "maps" of their bodies through a facilitated process involving drawing, painting, group discussion, interviews and personal reflection. Traditional KTE activities focus on disseminating printed research texts. We describe an approach that involved artwork and personal narrative to communicate the experiences of long-term HIV/AIDS survivors to multiple audiences.

The Challenge: KTE strategies represent an important process by which health care providers and other stakeholders can become engaged in treatment decision-making activities, education and advocacy. The translations of biomedical and experiential ways of knowing require effective mediums for information delivery and dissemination. At the same time, the challenge is to ensure that knowledge transfer serves the purpose of raising awareness and bridging information gaps that may separate the knowledge and experiences of people living with HIV/AIDS (PHAs) from providers, those in their support networks, and/or members of the general public.

Our Approach: Research themes emerging from observation and interviews were drawn out to form personal narratives that accompanied the body maps. Various iterations of the maps facilitated diverse forms of public engagement through the development of a website and other media. These dissemination tools offered observers insight into the participants' biomedical, social, psychological, physical and policy-based experiences. Additionally, body mapping exhibits were displayed in numerous spaces, including an HIV clinic, a retail store, university venues and the Global Village at the 2008 International AIDS Conference in Mexico City.

Key Findings: The men's body mapping project has contributed to our understanding of arts-based KTE through the implementation of dissemination strategies directed at a wider public audience. Project participants also benefited from the individual and group body mapping experience, taking the opportunity to explore deep-rooted experiences of stigma and exclusion. As a result, many participants indicated their interest in meeting again to explore themes that emerged during their experience. In this sense, the body mapping process may serve as a resource for PHAs to reconnect with support networks and to re-commit to social engagement.

Impact on Policy and Practice: Partnering institutions adopted body mapping tools for treatment and information outreach and took part in discussion and exhibition of the maps. In addition to benefiting from these activities, participants received support from project partners through a number of offshoot activities that brought public recognition to their stories and images.

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Vulnerable Populations and the Determinants of Health

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HIV, DISABILITY AND HUMAN RIGHTS: OPPORTUNITIES PRESENTED BY THE UN CONVENTION ON THE RIGHTS OF PERSONS WITH DISABILITIES

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1-Canadian HIV/AIDS Legal Network; 2-Canadian Working Group on HIV and Rehabilitation; 3-Interagency Coalition on AIDS and Development

Plain Language Summary: Many links exist between HIV and (other) disabilities, and between HIV and disability rights advocacy. Is HIV or AIDS a disability, and how? Should the new UN Convention on the Rights of Persons with Disabilities extend to cover PHAs? We examined the current recognition of HIV/AIDS as a "disability" in anti-discrimination laws in Canada and other countries, as well as challenges, opportunities and strategies for collaborations between HIV and disability communities.

The Challenge: People with disabilities face many barriers, including discrimination in accessing HIV prevention, care, treatment and support. PHAs often live with other disabilities, and HIV and its treatments can cause other disabilities. Perceived or real HIV-positive status exposes people to human rights violations, as do other disabilities. Should HIV and disability groups collaborate to promote human rights, and how?

Our Approach: We undertook research to: identify links between HIV and other disabilities; explore opportunities and challenges for integrating disability issues into HIV/AIDS programs and services, and vice versa; consider perspectives on the value of recognizing PHAs as persons with disabilities under the Convention; identify opportunities to engage advocates.

Key Findings: While the Convention, not ratified by Canada, addresses many issues faced by PHAs, it neither explicitly includes nor excludes HIV. It states: "Persons with disabilities include those who have long-term physical, mental, intellectual or sensory impairments which in interaction with various barriers may hinder their full and effective participation in society on an equal basis with others." Some countries' anti-discrimination laws have recognized HIV as a 'disability', through explicit or indirect reference or through judicial interpretation. There are different interpretations for protection of rights of PHAs and different perspectives within legal, human rights, disability and HIV fields.

Impact on Policy and Practice: The Convention could provide a human rights tool for PHAs. Concerns about HIV stigma and the stigma of disability pose challenges for collaboration across movements, but collaboration could also be mutually beneficial, and is necessary for a more comprehensive, effective response to HIV/AIDS.

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SUSTAINING HEALTH SUSTAINING HOUSING: AN EVALUATION STUDY OF A FIFE HOUSE SUPPORTED HOUSING PROGRAM FOR PEOPLE LIVING WITH HIV/AIDS

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Plain Language Summary: Sustaining Health Sustaining Housing is an evaluation study of a supported housing program for people living with HIV/AIDS (PHAs). The evaluation aimed to investigate how people living with HIV, who have accessed the support services provided by Fife House at Jarvis Program viewed the impact of these services on their housing experiences and their overall health.

Objective: To study the impact of support services provided at the Jarvis Program on the lives of people living with HIV accessing support services.

Methods: Both quantitative administered questionnaires and focus groups were used to access information from current service users of the Jarvis program. Two peer research assistants (PRAs) were trained in quantitative survey data collection and focus group facilitation methods. Thirty five residents were recruited and surveyed by the PRAs for the quantitative study of which fifteen went on to participate in the focus groups. The evaluation aimed to collect information on socio-demographics, housing and sense of neighborhood and Fife House services and programs.

Results: Twenty six (74%) participants were in the age group of 40-54 years and 97% were male, 74% born in Canada, 11% identified as black/African and 11% as Aboriginal. Ontario Disability Support Programs were the main source of income and 43% had a college or higher degree. The concept of 'community' had a different meaning for residents as compared to the service providers. While residents may be connected by a common experience of HIV, it also seems to act as a barrier to integration. Focus groups reiterated the importance of the role of Fife House services in reducing isolation and providing a sense of security which impact health.

Conclusions: The provision of HIV related services at the housing program has positive impacts on the lives of people living with HIV who access these support services. The knowledge of availability of the services also enhances a sense of security for those not regularly accessing them. The need for Fife House to bridge the communication between residents and Toronto Community Housing Corporation (TCHC) was also indicated. Networking with other service providers and increased programming around employment reintegration, presence of a qualified counselor and strategic display of HIV/AIDS information in the premises to avoid further stigmatization of the building were identified as areas requiring further consideration in order to support the residents.

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THE MAZE OF DISABILITY INCOME SUPPORT PROGRAMS FOR PHAS - A BARRIER TO ACCESSING EMPLOYMENT

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Plain Language Summary: Research has associated low income with increased vulnerability and poorer health outcomes related to HIV/AIDS. In research undertaken by the Canadian Working Group on HIV and Rehabilitation (CWGHR) and other organizations, people living with HIV (PHAs) identified lack of interjurisdicational coordination/integration of policies/programs addressing HIV, disability income support and employment as barriers to income security and labour force participation. As income security and employment access are key determinants of health, addressing these challenges will contribute to improved quality of life. This session will present the findings of a review of current Canadian policies and programs and seek input from participants on the implications of these findings.

Objective: To Research current policy and program challenges and barriers to labour force participation in order to promote opportunities for optimal labour force participation for PHAs, with security/ continuity of needed health, income and other supports.

Methods: Phase I
• Review current Canadian federal/provincial/territorial disability income/benefit and employment policies and programs to highlight jurisdictional inconsistencies, incompatibilities, gaps or lack of coordination;
Phase II (pending)
• Consult with: relevant governments/departments, including Public Health Agency and Human Resources and Social Development, provincial HIV and disability programs;
• FPT-AIDS and disability committees and key provincial policy stakeholders to determine current level of integration of HIV and disability income/benefit systems within/between provinces and identify regional challenges and opportunities;

Guiding questions will be presented to the participants to engage their participation in next steps.

Results: There is significant variances in definitions, funding, service standards, policies, practices and governance, which are barriers to income security and labour force participation for PHAs. In 2005-06, although over $26B was spent by government and non-government bodies in direct income support benefits to individuals with disabilities, there was no overall coordination or oversight.

Conclusions: Research to date demonstrates the current lack of coordination and communication among HIV and disability income support policies, programs and jurisdictions and will inform strategies to promote greater coordination of programs and support for PHAs. A health economic analysis will be helpful in demonstrating costs/benefits of a more integrated model.

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HIV RISK BEHAVIOUR AND INTERNALIZED HOMOPHOBIA AMONG HIV-POSITIVE AND HIV-NEGATIVE MEN WHO HAVE SEX WITH MEN

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Plain Language Summary: Previous research has demonstrated inconsistent findings related to the association of internalized homophobia (IH) and engaging in risky sexual behaviours. The present study investigated the subtypes of IH, and found that only the moral/religious acceptability of being gay correlated with unprotected anal intercourse (UAI), for both HIV+ and HIV- men who have sex with men (MSM). These findings can potentially be applied in clinical settings, as well as for designing novel HIV prevention interventions for MSM.

Objective: The present study sought to explore the relationship between the subtypes of IH, psychological distress, and risky sex (i.e. UAI) among a sample of HIV- and HIV+ MSM.

Methods: 173 sexually active MSM that engaged in anal intercourse (86 HIV- and 87 HIV+) were recruited from the community in Toronto. Mean age (SD) of participants was 44.38 (10.28). Almost 60% of the sample reported engaging in UAI in the past six months. Participants completed a structured clinical interview (assessing current depression, anxiety, and social anxiety symptoms), and a computer-administered questionnaire assessing three subtypes of IH (public identification as being gay, social comfort with gay men, and the moral and religious acceptability of being gay), sexual behaviours, and current psychosocial distress.

Results: T-tests found no differences between HIV- and HIV+ MSM on the IH subtypes or on the number of times they engaged in UAI, and so they were collapsed together for further analyses. A multiple logistic regression was conducted with any UAI as the dependent variable and the subtypes of IH as the independent variables. Only the moral/religious subscale was associated with UAI (OR = 1.11, 95% CI = 1.02-1.21, p = .014). Another logistic regression was conducted with current psychosocial distress variables and the moral/religious subscale as independent variables. Again, only the moral/religious subscale was associated with UAI (OR = 1.11, 95% CI = 1.02-1.21, p = .014), even when controlling for psychosocial distress. Among participants who engaged in receptive anal intercourse (RAI; N = 145), and among those engaging in insertive anal intercourse (IAI; N = 145), logistic regressions revealed that the moral/religious subscale was associated with engaging in unprotected IAI (OR = 1.12, 95% CI = 1.02-1.23, p = .02), but not unprotected RAI.

Conclusions: The findings of the present study highlight the importance of IH and moral/religious beliefs, in relation to UAI. Future research should look into the extent and types of religious beliefs that affect engagement in UAI.

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SEX IS GOOD: AN INVESTIGATION INTO THE QUALITY OF LIFE AND SEXUAL PRACTICES AMONG INDIVIDUALS ON HAART IN BRITISH COLUMBIA

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Plain Language Summary: We measured the frequency of sexual activity in a cohort of individuals on highly active antiretroviral therapy and compared the demographic, quality of life and clinical/ health measures between those who were sexually active to those who abstained. Our findings suggest that sexually active individuals had better quality of life than those who abstained.

Objective: We measured the prevalence of sexual activity among a cohort of HIV+ individuals on HAART to identify quality of life measures and socio-demographic predictors by gender and sexual orientation.

Methods: Individuals enrolled in the longitudinal investigations into support and ancillary health services (LISA) cohort (N=457) answered questions about oral, anal or vaginal sexual intercourse and the HIV-targeted quality of life. Fifty five percent of participants (70% of gay and bisexual, 47% of heterosexual males and 49% of heterosexual women) indicated that they were sexually active in the six months prior to participating in the survey. Multivariate models were used to measure the associations.

Results: The study found that individuals who were sexually active performed better on most of the quality of life measures than those who abstained. Consistent with other research, multivariate analyses for the whole cohort showed that being sexually active was associated with being in a relationship (OR: 0.26 (CI: 0.15,0.43)), having better body image (OR: 0.82 (CI: 0.70,0.95)), and higher scores on sexual function(OR: 1.39 (CI: 1.22, 1.58)). Among gay and bisexual men, being sexually active was also associated with higher life satisfaction (OR: 1.36 (CI: 1.02, 1.82)). In heterosexual females, being sexually active was associated with being depressed and having less disclosure worries (OR: 1.28 (CI: 1.02, 1.61)).

Conclusions: We need to further engage with people on HAART, their service providers, and other relevant community organizations to ensure that "sex" is on the agenda, supported in ways that are healthy and appropriate to these different groups and creatively incorporated into long-term HIV management programs and strategies in order to maximize function and well being in individuals living with HIV.

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SLEEP IMPAIRMENT AND HEALTH-RELATED QUALITY OF LIFE IN INDIVIDUALS LIVING WITH HIV.

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Plain Language Summary: The present study examined the prevalence and severity of insomnia in persons living with HIV, as well as its impact on health-related quality of life.

Objective: To examine the prevalence of sleep impairment and clinically significant insomnia in People Living with HIV/AIDS (PLWHA), as well as examine the relationship between insomnia and health-related quality of life in among this population.

Methods: A sample of 81 HIV-positive outpatients from The Ottawa Hospital-General Campus were recruited as part of a larger psychological study. Patients completed the Sleep Impairment Index (SII) (Morin, 1993) and the Short-Form-12 Health Survey (SF-12) (Ware, 1998) questionnaires. Data was subsequently statistically analyzed to examine the relationship between sleep impairment and health-related quality of life.

Results: Results indicated that approximately 68% of the sample experienced sleep disturbance in the clinically significant range according to the SII. Furthermore, sleep disturbance was found to be related to decreased physical and mental well-being.

Conclusions: Sleep quality plays an important role in health-related quality of life among HIV-positive populations, and should be an incorporated factor to address within intervention programmes for improving physical and mental well-being, and HIV medication adherence.

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THE COMPOUNDED STIGMA EXPERIENCE OF PHAS CO-INFECTED WITH HEPATITIS C

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Plain Language Summary: Stigma is a negative, multidimensional construct that denies individuals' societal acceptance. People living with HIV/AIDS (PHAs) are often subjected to stigmatization, as are people living with Hepatitis C (HCV). Both HIV and HCV-related stigma is associated with feelings of social isolation and internalized shame, which contribute to fears of accessing health care services and community prevention, education, and support services. Given that stigma is a common experience related to both HIV and HCV, PHAs co-infected with HCV may be suffering from compounded stigma. This study examined the stigma experiences of 28 men and women living with HIV who are also co-infected with HCV. Four types of HIV and HCV stigma (i.e., fear of disclosure, shame, rejection, and negative public attitudes) were explored, and their relationship to a variety of coping strategies were investigated. Results indicated that PHAs co-infected with HCV experience stigma related to both HIV and HCV, suggesting that they suffer from "double stigma." Furthermore, PHAs who report higher levels of HIV and HCV stigma employ more maladaptive coping strategies (e.g., using substances to cope) when dealing with stressful events than those who report lower levels of stigma.

Objective: This study examined (1) the HIV and HCV–related stigma experiences of PHAs who are co-infected with HCV, and (2) the impact of HIV and HCV stigma on coping strategies.

Methods: Study participants included 28 PHAs co-infected with HCV recruited during their regular clinic visits at The Ottawa Hospital. As part of a larger study, participants completed a questionnaire package, which contained sociodemographic information, a coping inventory (Carver, 1997), a HIV Stigma scale (Wright et al. 2007), and a HCV Stigma Scale.

Results: Results indicated that PHAs co-infected with HCV experience various forms of stigma related to both HIV and HCV, including fear of HIV and HCV disclosure, shame, rejection, and negative public attitudes. Their reported stigma experiences suggest that these individuals suffer from "double stigma." In addition, higher levels of HIV and HCV stigma were significantly positively correlated with higher levels of maladaptive coping strategies (e.g., substance use, disengaging from social support networks) when dealing with stressful life events.

Conclusions: PHAs co-infected with HCV experience "double stigma" related to both their HIV and HCV illnesses. In addition, individuals suffering from higher levels of stigma employ more maladaptive coping styles when dealing with stress. Results suggest that tailored coping skills training for PHAs stigmatized by both HIV and HCV warrants consideration. The negative impact of compounded HIV/HCV stigma on the lives of PHAs demands further attention.

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OPERATION HAIRSPRAY 2- SPRAY THE WORD ABOUT HEALTH – A COMMUNITY PARTNERSHIP TO CONTINUE HIV/AIDS EDUCATION WITH AFRICAN AND CARIBBEAN COMMUNITIES

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Plain Language Summary: Operation Hairspray 2 – Spray the Word about Health builds upon Ottawa Public Health's successful pilot peer-led health promotion initiative, which engaged African and Caribbean hairdressers and barbers as a channel to reach people from countries where HIV is endemic.

Objective: This phase of the project has 4 key objectives;
1. To expand the model beyond salons and barber shops to enable the health promotion messages to reach a larger target audience;
2. To evaluate the impact that stigma and discrimination have on community development approaches to the delivery of prevention strategies;
3. Identify strategies that reach more men within the African and Caribbean communities;
4. Evaluate the impact of the prevention approach on the community members receiving the health promotion information

An understanding of the impact the prevention information and resources has had on community members is critical to ensuring the project is making a difference in the target communities

Methods: The project seeks to increase community capacity, increase access/reduce barriers to health information on STIs and HIV/AIDS prevention, identify and document strategies to engage and reach African and Caribbean men in HIV/AIDS prevention and evaluate the impact of the prevention approach of peer volunteers by asking community members who receive the information for feedback via a confidential survey.
Data collection tools include: training evaluation forms, satisfaction surveys, focus group of peer volunteers, conversation recording forms with specific questions related to discussions on stigma and discrimination

Results: Preliminary analysis of data collected at this stage of the project will be presented.

Conclusions: Preliminary conclusions at this stage of the project will be presented.

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HIV/AIDS AND MENTAL HEALTH: ACCESS, INTEGRATION, EDUCATION

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Plain Language Summary: In 2006 Casey House, an inner city specialty hospital, established *Mental Health and HIV/AIDS: The Series*, an educational program for health care providers. The impetus for the series came from a need identified by inter-professional staff for further education in mental health in order to provide informed care for clients living with the implications of HIV/AIDS and mental health concerns. This poster provides an overview of the program and reviews preliminary evaluation data.

The Challenge: The challenge was to develop an accessible inter-professional educational opportunity for care providers across local agencies, facilitating a forum for enhancing knowledge of mental health concerns, informed practice guidelines, resources, and treatment options to better address client concerns.

Our Approach: The approach to initiating the project was collaborative, drawing on the expertise of inter-professional clinicians at Casey House, St. Michael's Hospital, local ASOs, and the mental health community. Mental health specialists, associates working in the area of HIV/AIDS, and Casey House clinicians were invited to present workshops, seminars and reflections from their experience to create a forum for dialogue and explore skill building possibilities. Facilitated discussion assisted to integrate mental health knowledge, existing within the health system, with the concerns clinicians expressed for their clients living with HIV/AIDS. An agreement with The Ontario HIV Treatment Network has allowed for filming and potential webcasting of the seminars, with a goal of creating greater access, locally and globally. The series has been approved for continuing education credits through the Faculty of Medicine at the University of Toronto.

Key Findings: This free, accessible program has been received with sustained interest from health care providers, mental health professionals and ASOs. The ability to support knowledge exchange between mental health professionals and HIV/AIDS service professionals has led to valuable partnerships and facilitated a forum for inter-agency communication. The data from preliminary evaluation feedback has assisted to identify learning needs and provided insight and direction for future course content.

Impact on Policy and Practice: The impact includes increased access to inter-professional education, capacity building for frontline staff, and enhanced opportunities for knowledge exchange. There is a need for ongoing evaluation and further data collection to inform recommendations. However, initial participant feedback has reflected implications for practice including an increased awareness of the linkage between theory and practice through skill building seminars - for example, an increased awareness of the principles of suicide risk assessment and dialectical bevaioural therapy.

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A COMPARISON OF TREATMENT UPTAKE IN HIV PATIENTS THAT ARE CANADIAN-BORN AND THOSE BORN IN HIV ENDEMIC COUNTRIES.

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Plain Language Summary: To determine whether treatment inequalities exist between Canadian-born persons living with HIV and those born in HIV endemic countries, we compared mean CD4 counts at the time of initiation of highly active antiretroviral therapy (HAART). We found no significant differences between the two populations, although Canadian-born women had higher CD4 counts overall. For persons who have accessed the Ontario health care system, there are no significant treatment inequalities concerning prompt HAART initiation due to country of birth.

Objective: In the developed world, inequalities have been documented for the health care of persons living with HIV between racial groups and based on country of birth. No studies currently exist to outline antiretroviral treatment differences between Canadian-born and Endemic-born patients. Our study describes immunologic status (measured as CD4 count) at the time treatment-naïve patients initiate HAART.

Methods: We compared mean CD4 counts at the time of HAART initiation between Canadian-born and Endemic-born patients. A higher CD4 count indicates prompt treatment or earlier diagnosis. Data were retrieved from The Ontario HIV Treatment Network Cohort Study (OCS) for patients who began HAART since January 1, 1997. Characteristics of the Canadian-born and HIV Endemic-born participants were compared using t-tests, chi-square tests and the Mann-Whitney U. Linear regression was used to assess the association between the independent variables of age, gender, country of origin and language with CD4 count.

Results: 1321 patients were included in the analysis. 1229 were Canadian-born and 92 were Endemic-born; 1155 were male and 161 were female. The average overall CD4 count was 263cells/µl. There was no significant difference between Canadian-born and Endemic-born CD4 counts. There was a non-significant trend for Canadian-born women to begin treatment earlier than Endemic-born women. Although women overall had significantly higher CD4 counts than men, Endemic-born women did not begin treatment earlier than Endemic-born men. Preliminary analysis suggests that native language is a predictor of immunologic status at treatment initiation, with French speakers appearing to begin earlier.

Conclusions: Being born in Canada or in an HIV endemic country does not affect CD4 count at HAART initiation. However, the increased CD4 counts of women overall may not include Endemic-born women. This analysis includes only persons who have accessed the Ontario health care system and have consented to data collection by the OCS. Therefore, if treatment discrepancies exist, they would be found at the level of access to care (not measured by our study) rather than treatment quality (immunologic status at HAART initiation).

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TRAINING AND SUPPORTING PSYCHOLOGICAL CARE IN THE COMMUNITY FOR AFRICAN CANADIANS LIVING WITH HIV WITHIN A KNOWLEDGE EXCHANGE FRAME

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3- Faculty of Medicine, University of Toronto; 4-Africans in Partnership Against AIDS

Plain Language Summary: PHA ACCESS is a community-based research (CBR) project pilot-testing a model of community-hospital collaboration, knowledge exchange, and capacity building, aimed at increasing access of people living with HIV to mental health services by training and supporting AIDS service organization (ASO) workers in the provision of evidence-based (art, mindfulness and narrative) psychotherapies.

In this presentation we will reflect on themes emerging in our current assessment of our collaboration with a focus on the perspective of a co-investigator from Africans in Partnership Against AIDS (APAA). We'll offer insights about culture-related concerns related to knowledge translation and exchange from the data about our collaboration.

The Challenge: There is broad recognition of the need for intersectoral collaboration in addressing mental health issues for people living with HIV. The challenge is to develop models sensitive to the complexities of local strengths and needs within the context of systemic issues such as racism, able-ism, heterosexism and institutional power imbalances.

Our Approach: Our research seeks to assess and reflect on the effectiveness of the process of collaboration, training procedures and interventions. ASO staff and volunteers were provided with training and biweekly support in providing psychotherapeutic interventions. CBR and knowledge exchange are being used to support learning, program refinement, and future program development in Ontario. PHA ACCESS co-investigators (i.e., staff from seven ASOs, a university hospital HIV psychiatric clinic and community members) participated in focus groups to reflect on the collaborative process and model. Trainees who provided interventions participated in in-depth interviews or focus groups to assess the training effectiveness and to provide recommendations for adapting interventions and training. To assess client impact, process and outcome measures were administered to clients before, during and after the interventions; they too participated in in-depth interviews. For evaluation, we are using both qualitative thematic analysis and repeated measures tests and ANOVAs.

Key Findings: Drawing on the experience of an African-Canadian co-investigator in the study and on preliminary qualitative study findings, we identified the complexities of the inter-cultural knowledge exchange process in successfully learning, adapting and implementing a therapeutic writing modality. The CBR principles informing the project were essential in supporting this process.

Impact on Policy and Practice: Impact includes reduced barriers to care; increased capacity for CBR, psychotherapeutic services, and community-hospital cooperation. The team will discuss new projects, while advocating for policies providing stronger support for intersectoral knowledge exchange in building community mental health services for PHAs.

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LEARNING NEEDS OF TORONTO-AREA DESIGNATED MEDICAL PRACTITIONERS REGARDING HIV INFECTION AMONG NEWCOMERS TO CANADA

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Plain Language Summary: We conducted a needs assessment survey among physicians who routinely perform HIV testing among newcomers to Canada, to identify their learning needs. The results will be used to develop educational sessions for designated medical practitioners (DMPs) in the future that will ultimately benefit HIV-infected immigrants and refugees.

The Challenge: Since January 2002, Citizenship and Immigration Canada has mandated that HIV testing be routinely performed on all individuals aged 15 years or older wishing to immigrate to Canada. Testing is performed by DMPs who may have limited experience with these tests. Because HIV-infected immigrants and refugees in Canada may face unique challenges related to their newcomer status and medical condition, it is important that DMPs feel well prepared for performing HIV tests in a busy clinical setting.

Our Approach: In Spring/Summer 2008, a subcommittee of the Committee for Accessible AIDS Treatment (CAAT) conducted a needs assessment survey of DMPs in the Greater Toronto Area to determine their key learning needs and professional interests in relation to HIV/AIDS and immigration.

Key Findings: Of 30 mailed surveys, 18 responses (60%) were received. Most respondents reported performing over 25 HIV tests per week, of which <1% returned HIV seropositives. Learning topics of greatest interest to respondents included local service organizations available to HIV-infected immigrants and refugees, the Canadian immigrant and refugee acceptance systems, and updates on HIV management ("what your patients can expect after referral to an HIV physician"). No trends in learning needs related to the geographic origin of DMPs' patients were noted.

Impact on Policy and Practice: The key learning needs identified by this sample of Toronto-area DMPs included psychosocial, immigration policy and biomedical topics with practical implications for patient management. The findings will be used to develop educational sessions specifically targeted to this important group of physicians, and will benefit HIV-infected newcomers to Canada in the future.

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RISK BEHAVIOUR AMONG NON-TESTERS WHO THINK THEY ARE NOT AT RISK FOR HIV: RESULTS FROM THE EAST AFRICAN HEALTH STUDY IN TORONTO (EAST)

Kimberly Gray [1]; Liviana Calzavara [1,2]; Wangari Tharao [3]; Ashley Johns [1]; Ann Burchell [4]; Ted Myers [1,2]; Robert Remis [2]; Carol Swantee [5]; Catherine Chalin [2]
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Plain Language Summary: The East African Health Study in Toronto (EAST) was the first large-scale Canadian survey of HIV among people from African countries. Although Canadian immigration policy now requires HIV testing, many East Africans who arrived before 2002 have never tested. We looked at risk behaviour among participants who had never tested for HIV because they did not think they were at risk. We found that the sexual behaviour of many of these participants did not match with their perception of not being at risk for HIV.

Objective: To describe the risk behaviour of East Africans living in Toronto who have not tested for HIV because they do not think they are at risk.

Methods: During 2004-2006, we conducted 456 surveys with persons from five East African (Ethiopian, Kenyan, Somali, Tanzanian, and Ugandan) communities in the Greater Toronto Area. Participants were recruited through member lists from community organizations and recruitment outreach activities. Univariate and bivariate analyses were used to characterize risk behaviour of participants who reported that they had never tested for HIV due to low perceived risk.

Results: 22% (101) of 456 participants reported never testing for HIV. 79% (80/101) said they did not test because they did not think they were at risk. Of these, 65% (52/80) have had sex, and more men than women reported having had sex (88% v 55%, p= 0.005). Of those who had sex, 35% (18/52) had 2-4 lifetime sexual partners and 29% (15/52) had 5+ partners. In the previous year, 17% (9/52) had 2+ partners. Six of those reported they had concurrent sexual relationships, one of whom reported her regular partner also had concurrent sex. Of the participants who had multiple partners and/or their partner had a concurrent sexual relationship in the previous year, 50% (6/12) reported inconsistent condom use.

Conclusions: Our results suggest a disconnect between reported risk behaviour and the perceived need for HIV testing in this population. Although the majority of non-testers felt they did not need to be tested because they were not at risk, over 40% reported two or more lifetime sexual partners. Inconsistent condom use among persons with multiple and/or concurrent partnerships is concerning due to the potential for HIV transmission. These findings are critical for informing testing campaigns and prevention programs.

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HEALTH AND DEMOGRAPHIC CORRELATES OF STIGMA TOWARDS PEOPLE LIVING WITH HIV/AIDS: A META-ANALYSIS

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Plain Language Summary: HIV stigma has persisted for over 25 years and may negatively impact the health, quality of life and well-being of people living with HIV. Previous studies have used diverse samples and multiple measurement instruments to examine demographic and health correlates of HIV stigma, highlighting the importance of synthesizing findings across different studies to gain a better understanding of these associations.

Objective: To examine demographic, physical and mental health correlates of HIV stigma among people living with HIV.

Methods: A quantitative meta-analysis was conducted of 24 peer reviewed journal articles published since 2000 that examined correlates of HIV stigma with people living with HIV (PLHIV). Specifically, we used meta-analysis and quantitative methodologies to study the levels and direction of association between HIV stigma and a range of demographic, social, physical and health characteristics. Studies were reviewed and a quantitative synthesis of their results was carried out via the calculation of standardized effect sizes. Heterogeneity of reported results was also assessed and examined.

Results: Our review revealed substantial variability in the ways researchers measure participants' HIV related stigma as well as their physical, emotional and mental health. The association between positive mental health indicators and HIV stigma was negative and statistically significant ($p<0.0005$). The association between negative mental health indicators and HIV stigma was positive and statistically significant ($p<0.005$). High stigma level was consistently and significantly associated with low social support ($r=-0.369$, $p<0.0005$), poor physical health ($r=-0.324$, $p<0.0005$), poor mental health ($r=-0.402$, $p<0.0005$), younger age ($r=-0.066$, $p<0.05$), and lower income ($r=-0.172$, $p<0.005$). These correlations, based on data from over 5, 600 individuals living with HIV, were of a medium size, which would be recognized in daily life.

Conclusions: Health and mental health professionals working with individuals and families impacted by HIV could benefit from an enhanced understanding of correlates of HIV stigma, which could inform assessments, interventions and treatment plans. PLHIV could be screened for mental health issues and treatment of such issues integrated into their clinical management. The association between HIV stigma and physical health has potential implications for treatment, care and support for people at different stages of HIV. Support groups and other sources of social support are essential to reduce stigma. AIDS Service Organizations are encouraged to integrate findings into HIV stigma interventions and social support programs. Additionally, HIV stigma scales should be developed and validated, so that future studies using them are able to report findings that are operationally and conceptually consistent.

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Vulnerable Populations and the Determinants of Health

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HIV RELATED STIGMA AND DEPRESSION EXPERIENCED BY MEN AND WOMEN LIVING WITH HIV

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Plain Language Summary: HIV-related stigma is a societal label that is negative and discrediting, and often contributes to PHAs feeling judged, marginalized, and socially isolated. HIV-stigma is multi-faceted and may be experienced in different contexts. The present study aims to examine how 95 PHAs experience different types of HIV-related stigma, including: 1) stigma related to HIV disclosure, (2) HIV negative self-image (e.g. shame) (3) negative public attitudes towards HIV, and (4) personalized rejection due to HIV. Negative public attitudes towards HIV may become internalized as a negative self-evaluation and may affect one's mental wellbeing (e.g., depression). Thus, a goal of this study is to understand how HIV stigma and depression may be related in PHAs. A second goal is to explore whether there are any gender differences in how HIV-related stigma is experienced. A clearer understanding how HIV stigma and depression affect men and women would help to inform the development of more tailored interventions to help address the effects of HIV-related stigma on self-esteem and depression among PHAs.

Objective: To examine multiple dimension of HIV related stigma, depression, and gender issues among PHAs.

Methods: Study participants included of a sample of 95 PHAs who were recruited during
their regular HIV hospital clinic visits. As part of a larger psychological study, PHAs were invited to completed a questionnaire package consisting of socio-demographic information, a validated HIV Stigma Scale (Wright et al. 2007), and a validated measure of Depression (CES-D) (Radloff et al., 1977). Data were analyzed using quantitative statistical techniques.

Results: Results indicated that PHAs experienced multiple forms of HIV related stigma. Types of HIV stigma included stigma related to: (1) HIV disclosure, (2) negative self-image, (3) negative public attitudes about HIV, and (4) personalized rejection due to HIV. High levels of HIV stigma were significantly associated with high level of depressed mood. As well, both men and women experienced all forms of HIV stigma; however, gender differences in HIV stigma have implications for further study.

Conclusions: Many dimensions of HIV stigma were experienced by PHAs. PHAs who reported feeling stigmatized also endorsed significant symptoms of depression. Both men and women PHAs struggle with HIV stigma, and gender differences suggest different experiences of stigma. The debilitating impact of HIV-related stigma needs to be more fully acknowledged. Tailored interventions need to be developed to help reduce the negative impact of HIV stigma on the lives of PHAs.

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CELL BASED SYSTEMS FOR HIGH THROUGHPUT SCREENING OF FACTORS REGULATING HIV-1 GENE EXPRESSION

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Plain Language Summary: Due to its limited size, replication of HIV-1 is highly dependent upon host factors to carry out many of the metabolic processes required for assembly of new virions. Identifying host factors that play critical roles in HIV replication and determining their mechanism of action would allow the development of new strategies to inhibit HIV growth that would supplement existing treatment strategies.

The Challenge: The challenge is to develop tools that permit rapid analysis of host factors for their effect on HIV gene expression.

Our Approach: Following integration into the host genome, HIV-1 initiates transcription to generate new virions. At this step, successful viral replication is critically dependent upon controlled processing of the 9kb transcript into over 30 viral mRNAs mediated by host cell factors. To investigate the role of specific factors that affect post-integration events and assess their mechanism of action, we have established two cell based assays that allow tightly regulated expression of viral proteins. The first uses an integrated copy of a replication defective form of HIV-1 in which the protease and reverse transcription reading frames have been replaced with GFP and point mutations inactivating the Rev reading frame. Induction of HIV-1 structural gene expression (GagGFP, Env) is provided by expression in trans of Rev fused to the hormone binding domain of the glucocorticoid receptor. As a result, expression of the viral structural proteins is dependent upon addition of dexamethasone to the medium. For the second system, we have generated cell lines that express a replication defective form of HIV-1 (due to deletion of the RT and IN reading frames) under the regulation of tetracycline-induced promoter.

Key Findings: Analyses to date have confirmed that the two cell-based are functioning as required; providing very tight regulation of HIV gene expression. Initial experiments have demonstrated that the system can be used in a high throughout manner using both overexpression and shRNA-based gene silencing to identify factors involved in regulating HIV gene expression. Preliminary results of initial screens for new host factors impacting viral protein expression will be presented.

Impact on Policy and Practice: Identifying host proteins essential for HIV replication will facilitate the development of new treatment strategies to control HIV-1. Targeting these factors has the advantage over existing therapeutic targets given that they are not subject to rapid evolution. Hence, development of resistant HIV strains should prove more difficult and provide more robust and long term treatment strategies than currently exist.

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COMPREHENSIVE CROSS-CLADE ELIMINATION OF HIV-1 AND HIV-2 INFECTED PRIMARY CD4+ T CELLS BY LINE-1 RETROTRANSPOSABLE ELEMENT SPECIFIC T CELLS

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Plain Language Summary: One of the greatest challenges in developing an effective HIV vaccine has been the ability of HIV to rapidly alter itself in order to hide from immune responses. We have observed that a protein called "L1-p150" can be found in HIV infected but not in uninfected cells, and therefore represents a surrogate marker of HIV infected cells. This protein is not part of HIV itself, but the presence of HIV causes it to be expressed. Unlike HIV, L1-p150 cannot rapidly change to escape immune responses, and therefore may represent a stable target for immune responses aimed at eliminating HIV infected cells. We have identified a population of 'killer T cells' in an HIV infected individual who has naturally controlled their virus for more than 10 years without antiretroviral therapy. These T cells were found to kill diverse strains of HIV isolated from around the world when tested in cell culture. This finding is unprecedented as immune responses which directly target HIV only recognize a limited diversity of HIV viruses. These observations lead us to speculate that developing vaccines which train T cells to recognize L1-p150 on HIV-infected cells, rather than recognizing HIV itself, may represent a novel strategy by which to overcome the ability of HIV to change and thereby hide from immune responses.

Objective: LINE-1 (L1) retrotransposable elements comprise ~17% of the human genome. Intact L1 elements encode a 40kDa RNA chaperone protein (p40) and a 150kDa enzymatic protein (p150). Expression of these proteins has been observed in malignant tissues but is largely absent from healthy tissue. We have observed that HIV-1 infections result in expression of L1. We hypothesized that this would stimulate a L1-specific cellular immune response capable of recognizing HIV-1-infected cells presenting MHC-bound L1 epitopes.

Methods: L1 protein expression was examined in HIV-1-infected versus uninfected primary CD4+ T cells by western blot. L1 peptides were selected based on predicted immunogenicity. HIV-1-infected individuals were screened for L1-specific T cell responses by IFN-gamma ELISPOT. L1, HIV-Gag, and CMV-specific CD8+ T clones were established, and tested for their ability to recognize and eliminate autologous targets infected with a panel of HIV-1 and HIV-2.

Results: L1-p150 expression was observed in HIV-1-infected, but not uninfected primary CD4+ T cells. L1-specific CD8+ T cell responses were detected in a subset of HIV-1-infected individuals. CD8+ T cell clones to three L1 epitopes were derived from three elite controllers. These clones were not cross-reactive with HIV-1 peptides, but responded to autologous HIV-1-infected targets by producing cytokine and degranulating. L1-specific clones comprehensively recognized primary isolates representing HIV-1 clades A-G as well as HIV-2. These clones specifically eliminated HIV-1-infected autologous targets, and potently suppressed virus replication.

Conclusions: The cellular immune response to HIV-1 infection is vital to immunological control. However, it is an assumption that this response is entirely directed against HIV-1 antigens. Here we demonstrate an HIV-1 antigen-independent cellular immune response that specifically suppresses HIV-1 replication in a MHC-restricted manner. This has implications for studying mechanisms of natural control and resistance. Targeting stable, genome encoded L1 antigens presents a way to circumvent the variability of HIV-1 antigens in novel vaccine and immunotherapeutic strategies.

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DEFINING THE CHANNEL ASSEMBLY AND DRUG INTERACTIONS OF HIV-1 VPU

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Plain Language Summary: Due to the increased emergence of HIV strains exhibiting resistance to available drugs, there is a pressing need to identify and characterize new targets for antiviral drug development. The HIV-1 accessory protein Vpu plays an important role in release of virus particles from host cells. This activity is mediated by the transmembrane domain of Vpu, either through direct interaction with host cell proteins involved in tethering new virus particle to the cell, or as a result of Vpu cation channel activity in infected cells. It has been shown that amiloride-based drugs are able to inhibit Vpu channel activity and prevent virus release. As the first step towards design of new antiviral compounds targeting Vpu, we are investigating the molecular basis for channel formation and drug interactions with this protein.

Objective: Our recent solid state nuclear magnetic resonance (NMR) studies have provided the first experimental models of the Vpu channel structure, which we are testing through site-directed mutagenesis. Using our model as a starting point, we are characterizing the mechanisms through which amiloride-based compounds bind to and inhibit Vpu. In tandem, we are developing new, high-throughput assays for channel activity, to allow rapid screening of potential inhibitors.

Methods: Starting with an initial structural model for the channel formed by Vpu, we have used site directed mutagenesis to identify key determinants of channel assembly. NMR has been used to investigate proposed models of drug binding to the Vpu ion channel. New assays based on fluorescent dye-release from liposomes by Vpu channel formation have been developed for screening of mutants and drug-protein interactions.

Results: Key residues responsible for Vpu channel assembly have been identified, and we are in the process of identifying those essential for cation conductance. NMR experiments on Vpu peptides containing 13C and 15N labeling at sites proposed to interact with HMA suggest that literature models for drug interaction with Vpu are incorrect. Combined with characterization of HMA-lipid interactions by NMR, our data currently support a model in which amiloride-based drugs alter the overall orientation and dynamics of Vpu, rather than acting as specific channel blockers.

Conclusions: We have produced a refined model for the ion channel formed by HIV-1 Vpu. Initial studies of drug-binding suggest that rather than obstructing the channel, amiloride-based compounds may instead alter the protein-protein associations of Vpu. The implications for antiviral drug design targeting Vpu will be discussed.

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HIV AND VPR-MEDIATED MODULATION OF CD14, TLR4 AND GLUCOCORTICOID RECEPTOR EXPRESSION

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Plain Language Summary: Infection with HIV decreases the ability of the immune system to respond to and clear HIV, as well as other secondary pathogens. Many pathogens activate the immune response through receptor recognition of molecules like LPS. We are investigating key communication molecules of early infection to determine the effect of HIV on their expression. The goal of this project is to outline new potential therapeutic targets to improve the health and longevity of people with HIV infection.

Objective: To determine the effect of HIV infection on the expression of upstream LPS signaling receptors CD14 and TLR4, and specifically the effect of HIV-protein-Vpr on these receptors. To determine if the LPS response in monocytes or peripheral blood mononuclear cells (PBMC) is affected by HIV-Vpr and to further determine if any of these effects are mediated by the anti-inflammatory glucocorticoid receptor (GR).

Methods: PBMCs were mock infected or in vitro infected with a dual tropic strain HIVCS204. In parallel, an HIV-Vpr-retrovirus was constructed to express intracellular full-length Vpr peptide. PBMCs and monocytes isolated by negative bead selection were each infected with the Vpr-retrovirus or the negative control PLXIN-retrovirus. The monocyte gated-population was analyzed by flow cytometry for expression of the upstream LPS signaling receptors TLR4 and CD14 as well as GR expression. GR signaling was blocked by the addition of the inhibitor Ru486 to determine the effect of GR on TLR4 and CD14 expression.

Results: HIV and Vpr decrease LPS induced TLR4 expression following LPS stimulation. This effect is prevented by RU486, therefore Vpr mediates this affect through glucocorticoid receptor signaling. In addition, PBMCs infected with HIV resulted in an increase in CD14 expression. Vpr expressing cells stimulated with LPS had a higher CD14 expression than uninfected LPS stimulated PBMCs or monocytes. PBMC infection with HIV showed no altered GR expression whereas an increase in LPS induced GR expression was found in isolated Vpr expressing monocytes.

Conclusions: These results demonstrate that HIV and Vpr affect the early innate immune response to secondary infection. Characterizing the cellular mechanisms by which HIV inhibits the LPS response will lead to a better understanding of how cell-mediated immune responses are inhibited by HIV infection and have the potential to lead to the development of novel immune based therapies.

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HUMAN MACROPHAGES ARE RESISTANT TO HIV-VPR INDUCED APOPTOSIS

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Plain Language Summary: Macrophages are cells of the innate immune system that have a defensive role against foreign pathogens. They represent a major reservoir during HIV infection, because although infected, they survive and resist antiviral therapy. Vpr (viral protein R) is an HIV protein, known for its ability to kill various cell types, including macrophage precursors (monocytic cells). We report here that macrophages are resistant to Vpr induced cell death, although they originate from Vpr sensitive cells. How macrophages become resistant to cell death throughout differentiation from monocytes is of major importance in understanding how viral reservoirs are being established during the infection and how they can be eliminated by therapy.

Objective: This project looks at the effect of Vpr on the viability of human monocyte derived macrophages (MDMs) and of macrophages derived from the promonocytic cell line THP1. We wanted to see if differentiation towards a macrophage phenotype induces changes in susceptibility to Vpr apoptosis, given the fact that monocytic cells are sensitive to Vpr cell death.

Methods: Monocytes were isolated by adherence from PBMCs and cultivated in the presence of M-CSF (macrophage colony stimulating factor) for six days, to generate macrophages. MDMs were stimulated with various concentrations of synthetic Vpr peptide for 24h, after which apoptosis was measured by intracellular propidium iodide staining. The expression level of various antiapoptotic proteins was evaluated by Western blot.

Results: Both MDMs and THP1 derived macrophages were resistant to Vpr apoptosis, compared to monocytes and THP1 cells respectively. The apoptotic effect in monocytes and THP1 cells was associated with the downregulation of antiapoptotic proteins Bcl2 and cIAP1. In macrophages Vpr induced no change in the levels of Bcl2 and cIAP1, but decreased the expression level of other two antiapoptotic proteins, XIAP and cIAP2, with no effect on cells' viability, suggesting that Bcl2 and cIAP1 may be responsible for the protective effect against Vpr induced apoptosis.

Conclusions: Eliminating viral reservoirs is the major obstacle in curing the disease, because of the inability of therapy to eradicate the virus from these cells. This is the first report about macrophage resistance to Vpr induced apoptosis. This result is particularly intriguing, as the originating cells (monocytes) are sensitive to Vpr effect, but they seem to lose this responsiveness as they differentiate into macrophages. Although the exact mechanisms are currently being investigated, this research provides insight into the possible explanations for viral reservoirs persistence and may contribute to the establishment of new therapeutic approaches.

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INHIBITION OF HIV-1 REPLICATION THROUGH THE USE OF MODIFIED U1SNRNAS

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Plain Language Summary: The rapid evolutionary rate of HIV-1 has lead to the emergence of multi-drug resistant variants, emphasizing the need for novel inhibitory methods. One such method could be based upon inhibiting viral gene expression through disruption of HIV-1 RNA processing. A means of accomplishing this goal is through use of modified U1snRNA that target highly conserved regions of HIV-1. We have demonstrated such U1 derivatives can be used to yield a dramatic (>95%) suppression of HIV gene expression and are currently testing the potential of this approach in virus challenge assays.

Objective: To determine which of the identified conserved regions of the HIV-1 terminal exon is capable of inhibiting HIV-1 replication when targeted by the modified U1snRNA by preventing viral 3'end formation. To establish a suitable method of administering these modified U1snRNA constructs as a possible HIV-1 therapeutic.

Methods: To determine the possible HIV-1 regions capable of inhibiting HIV-1 replication when targeted by the modified U1snRNA, multiple sequences were tested. The complementary ten nucleotide sequences were inserted in the 5' end of the U1snRNA and tested by determining the HIV-1 protein expression levels when cotransfected with HIV-1 virus. Human cell lines stably expressing the modified U1 constructs were either transiently transfected with HIV-1 provirus or infected with HIV-1. Viral protein production was assayed by Western blot. To verify that the effects were specific to HIV-1 and to minimize any off target effects, the modified U1snRNA were further modified to abolish their original ability to form spliceosome assembly complexes. Other techniques include viral challenge assays, Northern blotting, RNA protection assays, Alkaline Phosphatase assay, and Chloramphenicol Acetyl Transferase assay.

Results: Several sequences of the tested constructs displayed substantial HIV-1 protein inhibition when inserted in the U1snRNA construct. Our studies indicate that these modified U1 constructs can be used synergistically to further inhibit the viral protein expression. Spliceosome deficient U1 constructs containing a rearranged protein snRNP composition have been shown to retain complete HIV-1 viral inhibitory property, while other spliceosome deficient U1 constructs lost all HIV-1 inhibition. Stably expressing modified U1 constructs in HeLa and Jurkat cell lines have shown inhibition to a similar extent when challenged transiently.

The production of stably expressing modified U1 constructs in stem cells has substantial therapeutic potential. By creating a stem cell that differentiates into all mature cell lineages affected by HIV-1 infections, one could effectively halt viral progression. Once mature, they are subjected to an HIV-1 viral challenge to determine if the cells were capable of retaining viral inhibitory properties of the modified U1 constructs throughout the developmental process. Preliminary results of the viral challenge indicate an 80% inhibition of HIV-1 virion production when compared to wild-type cells.

Conclusions: We have determined several sequences in HIV-1 that when targeted by the modified U1snRNA inhibit viral structural protein expression by as much as 95%. Inhibition was maintained when the modified U1snRNA was further modified to lose spliceosome initiating ability making it a strong candidate as a therapeutic agent for HIV-1. Human HSC cells stably expressing modified U1 constructs have an unaltered developmental progression into mature T-cells, and the resultant T-cells are capable of inhibiting HIV-1 progression by as much as 80%.

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INTERACTIONS OF HIV-1 PROTEASE INHIBITORS WITH THE OATP2B1 INFLUX TRANSPORTER IN CACO-2 CELLS

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Plain Language Summary: Interactions of commonly used antiretroviral drugs, including many PIs, NRTIs, and NNRTIs, with intestinal drug uptake transporter OATP2B1 were examined in a human intestinal epithelium model, Caco-2 cell line system, and MDCKII/OATP2B1 transporter expression system. Although, atazanavir and ritonavir were not transported by OATP2B1, they were potent inhibitors of this transporter, along with lopinavir, tipranavir, and nelfinavir. Hence, interactions of PIs with OATP2B1 could lead to important pharmacokinetic drug-drug interactions between antiretrovirals.

Objective: OATP2B1 is a multispecific drug uptake transporter, highly expressed at the apical membrane of intestinal epithelium and other tissues, and implicated in the absorption of many orally administered drugs. At present, limited information is available on the mechanism of intestinal absorption of HIV-1 protease inhibitors (PIs). Interactions of PIs with intestinal uptake transporters, such as OATPs, could further elucidate the bioavailability and complex drug-drug interactions associated with PI-based therapy. This study examines the ability of PIs to act as substrates and/or inhibitors of OATP2B1.

Methods: OATP2B1 mRNA and protein expression was evaluated by RT-PCR and immunoblotting, respectively. OATP2B1 activity was assessed through time-dependent uptake of an established OATP substrate [3H]estrone-3-sulfate (E3S) and transport inhibition by standard inhibitors. Similarly, OATP2B1-mediated uptake of [3H]atazanavir or [3H]ritonavir was evaluated. The effect of antiretroviral drugs on OATP2B1 activity was assessed through comparing the uptake of [3H]E3S in the absence or presence of each drug at varying concentrations and evaluating the corresponding IC50 values.

Results: Caco-2 and MDCKII/OATP2B1 cells highly expressed OATP2B1 and the uptake of [3H]E3S was time-dependent, saturable, and susceptible to inhibition by standard inhibitors. OATP2B1-mediated transport of E3S had comparable transport kinetics in Caco-2 and MDCKII/OATP2B1 cells, with KM values 11μM and 16μM, respectively. PIs potently inhibited OATP2B1, with most effective inhibition observed for lopinavir, tipranavir, and nelfinavir – IC50 values of 0.72μM, 0.88μM, and 0.67μM in MDCKII/OAPT2B1 cells. Atazanavir and ritonavir also potently inhibited OATP2B1 (IC50 values 2.16μM and 3.88μM), but were not transported by OATP2B1, with no significant difference in their uptake by OATP2B1-overexpressing and wild type MDCKII cells. Preliminary data suggests that darunavir is a competitive OATP2B1 inhibitor (IC50=26.3μM; KI=24μM); however, a direct assessment of darunavir transport by OATP2B1 is required.

Conclusions: Although, atazanavir and ritonavir are not OATP2B1 substrates, they are potent inhibitors of this system with IC50 values within the therapeutic concentration range. Since OATP2B1 exhibits an increasing number of drug substrates, including statins, alterations of its function by PIs could result in clinically important drug-drug interactions.

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MOLECULAR CHARACTERIZATION OF THE HIV TAT PROTEIN AND ITS INTERACTIONS WITH CELLULAR PROTEINS IN DOWN REGULATING CD127 ON CD8 T CELLS

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Plain Language Summary: We have previously shown soluble HIV Tat protein down regulates expression of the interleukin (IL)-7 receptor alpha chain (CD127) on the surface of CD8 T-cells leading to impaired cell proliferation and perforin synthesis. We have also shown that once taken up by the cell, Tat interacts directly with the cytosolic tail of CD127 at the inner leaflet of the plasma membrane and directs the receptor for internalization and proteasomal degradation. The exact nature of this interaction between Tat and CD127 remains unclear. The purpose of this study is to determine which domain(s) of Tat is essential for CD127 down regulation. Using a histidine-tagged (6xHis) Tat protein, we have generated a series of Tat mutations each lacking one of the six protein domains. These proteins will be purified over nickel columns followed by HPLC. To date, we have produced and partially purified full-length his-tagged Tat and demonstrated its ability to down regulate CD127

Objective: To identify which domain(s) of the HIV Tat protein is necessary for down regulation of CD127 from the surface of CD8 T cells.

Methods: The pTatC6H-1 plasmid, obtained from the NIH AIDS Reagent Program, was used to generate mutants each lacking one of Tat's six functional domains. Full length his-tagged Tat was purified by Ni-TED chromatography followed by HPLC. Purified Tat protein (10 ug/ml) was then incubated with CD8 T-cells isolated from healthy volunteers and CD127 surface expression was analyzed by flow cytometry.

Results: His-Tat protein was produced in E. coli and purified by Ni-TED chromatography. This single-step purification method provided partially pure Tat protein at high yield (up to 2.5 mg per 600 ml culture). A single 37 kDa protein consistently co-purified with Tat. In spite of this, His-Tat was able to down regulate CD127 on the surface of CD8 T cells. At this stage, His-Tat is being further purified by HPLC. His-Tat mutants lacking each domain of the protein have been cloned and expressed in E. coli and will be used to identify which parts of Tat are necessary for CD127 down regulation.

Conclusions: Partially purified recombinant His-Tat protein is biologically active and able to down regulate CD127 on CD8 T-cells. By deleting each domain from Tat, we plan to isolate the region of this protein essential for this biological activity.

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REGULATION OF P-GLYCOPROTEIN (P-GP) IN HUMAN BRAIN MICROVESSEL ENDOTHELIAL CELLS (HBMVEC) BY THE HIV-1 ENVELOPE GLYCOPROTEIN-120 (GP-120)

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Plain Language Summary: P-glycoprotein (P-gp), an ATP-binding cassette (ABC) membrane transporter is known to be involved in the extrusion of antiretroviral compounds at the blood-brain barrier (BBB). HIV-1 viral envelope protein gp-120 permits HIV-1 infection through its interaction with the chemokine receptors (CXCR4 and CCR5). Our laboratory has previously demonstrated that HIV-1 gp-120 can trigger an inflammatory response in cultured rat astrocytes leading to a down-regulation of P-gp and up-regulation of MRP1. In addition, human brain microvessel endothelial cells (hBMVEC) have been shown to respond to HIV-1 gp120 triggering which leads to changes in the tightness of the endothelial cell junctions at the BBB. We hypothesized that treatment with HIV-1 gp-120 will lead to changes in the expression of P-gp in hCMEC/D3s cell system.

Objective:
1) To characterize the hCMEC/D3 (immortalized hBMVEC cell line) for the expression of P-gp and the chemokine receptors CXCR4 and CCR5
2) To determine if acute exposure (4hrs) of hCMEC/D3 cells to HIV-1 gp120 leads to changes in the protein expression of P-glycoprotein

Methods: hCMEC/D3 was used as a cell-culture system and was originally derived from hBMVECs and has been well characterized for maintaining BBB properties. Cells were characterized for endogenous expression of chemokine receptors (CXCR4, CCR5) and drug efflux transporters (P-gp, MRP1). Cells were cultured and treated with HIV-1 gp120 at various concentrations (0.83 – 1000pM) for 4 hours.
Cells lysates were analyzed by immunoblotting to determine expression (CCR5, CXCR4, efflux transporters) as well as changes in expression.

Results: Immunoblot analysis of hCMEC/D3 cells has shown expression of P-gp and the chemokine receptors CXCR4 and CCR5. Treatment of hCMEC/D3 cells with HIV-1 gp120 for four hours led to a concentration-dependent increase in P-gp expression when compared to untreated hCMEC/D3 cells.

Conclusions: In this present study we have shown that HIV-1 gp120 can increase the expression of P-glycoprotein in a dose-dependent manner in an in vitro model of the BBB . This suggests that HIV-1 gp120 may be involved in altering antiretroviral drug distribution through the BBB even with acute exposure. Further work is needed to explain the mechanisms by which HIV-1 gp120 induces the expression of P-glycoprotein.

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REGULATION OF P-GLYCOPROTEIN EXPRESSION BY THE VIRAL ENVELOPE PROTEIN GP120 AND PROINFLAMMATORY CYTOKINES IN HUMAN GLIAL CELLS

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Plain Language Summary: P-glycoprotein (P-gp) is an efflux pump that exports anti-HIV drugs and reduces the bioavailability of antiretroviral drugs at several sites including the brain. Previously, we demonstrated that gp120 induces pro-inflammatory cytokine secretion (TNF-α and IL-6) and reduces P-gp protein expression in primary cultures of rat astrocytes, a cellular reservoir of HIV-1 virus. In this study, we have established the role of gp120 and the involvement of chemokine receptors in cytokine secretion in human fetal astrocytes. We have also shown the modulation of P-gp expression in response to gp120 and cytokines. Our data show that gp120 induced cytokine secretion is mediated by CCR5 receptor and P-gp protein expression is altered in response to both gp120 and cytokine treatment. This study recognizes possible mechanisms of cytokine secretion from astrocytes and also implies how drug distribution can be influenced by circulating viral proteins and cytokines.

Objective: Previously our laboratory has shown that gp120 induces cytokine secretion in primary cultures of rat astrocytes by interacting with CCR5 receptor. In addition, reduced expression of P-gp protein has been observed due to gp120 or cytokine treatment (IL-6). However, whether P-gp is regulated in a similar way in human astrocytes is unknown at this stage. Our aim is to understand the regulation of P-gp by gp120 and pro-inflammatory cytokines in human astrocytes.

Methods: Primary cultures of human fetal astrocytes were treated with gp120 (1.0nM), for 6 and 24 hours in the presence or absence of CXCR4 and CCR5 neutralizing antibodies (1mg/ml). TNF-α and IL-6 secretion in response to gp120 were measured using ELISA analysis. Astrocytes were also treated with 0.5ng/ml and 10 ng/ml concentrations of TNF-α or IL-6 for the desired time (6h and 24h). Immunoblot analysis was subsequently used to determine the protein expression of CXCR4, CCR5 and P-gp. Functional assay with [3H]digoxin was performed to determine P-gp activity in gp120 treated cells.

Results: Immunoblot analysis confirmed the presence of CXCR4 and CCR5 receptors in human fetal astrocytes. However, pretreatment of the cells with only CCR5 neutralizing antibody attenuated the TNF-α and IL-6 secretion. Treatment with gp120 reduced the protein expression and increased cellular accumulation of [3H]digoxin. IL-6 treatment decreased P-gp protein expression whereas the cytokine TNF-α increased its protein expression.

Conclusions: Our data show that interaction of gp120 with CXCR4 and CCR5 receptors are necessary for cytokine secretion and both gp120 and cytokine treatment can modulate P-gp protein expression in astrocytes.

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T-CELL CROSS-REACTIVE RECOGNITION OF HLA-A2-RESTRICTED HIV-GAG: SLYNTVATL AND HCV-NS5B: ALYDVVSKL EPITOPES

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Plain Language Summary: Hepatitis C virus (HCV)-related liver disease progresses faster in individuals co-infected with Human Immunodeficiency Virus-1 (HIV-1); however the underlying immunologic mechanisms are yet to be elucidated. Several lines of evidence signify the extent of T-cell degeneracy and the role of molecular mimicry on provoking an immune response. Cross-reactivity between HCV-and influenza-specific T-cells and an association with the severity of the clinical course of HCV disease has been previously demonstrated, which may potentially apply to other viral infections including HIV-1.

Objective: To identify if HIV-specific T-cells recognize heterologous HCV epitopes and if this recognition alters the immuno-pathological profile of HCV infection in HCV/HIV-1 co-infected individuals.

Methods: A detailed search for amino acid sequence homology between HCV and HIV-1 proteome was conducted using Basic Local Alignment Search Tool (BLAST) from NCBI database. Using IFN-g ELISPOT, 21 HLA-A2+, HIV-1 mono-infected individuals were screened for responses to both HIV:SL9 and HCV:AL9 peptides. Staining of PBMCs with tetrameric HLA-class-I complexes of either SL9 or AL9 peptides was performed. Tetramer stained cells were washed and stimulated with each peptide followed by intracellular staining for IFN-g and CD107-a.

Results: We identified a relatively high degree of amino acid sequence similarity between HLA-A2-restricted epitopes HIV-1 (HXB2) gag: 77-85 (SLYNTVATL: SL9) and HCV (H77) NS5b:2594-2602 (ALYDVVSKL: AL9). Of the screened HIV-infected individuals, 5 subjects showed significant response to both peptides. PBMCs from these individuals were used for tetramer analysis. Among the examined responders, three individuals showed CD8+ T-cells distinctly double-stained for both tetramers. Flow cytometry was conducted for expression analysis of IFN-α and the degranulation marker CD107-a on PBMCs stained with SL9 tetramer and stimulated with either SL9 or AL9 peptides. Tetramer positive cells from both stimulated groups showed responses significantly larger than background. However, responses from these cells to cross-reactive AL9 peptide were much weaker compared to those from SL9 peptide stimulation. Further analysis of antigen-specific expansion is required to confirm the cross-reactive recognition of this HCV epitope by HIV-specific CD8+ T-cells.

Conclusions: Our preliminary findings indicate a potential T-cell cross-recognition between HIV-1 derived HLA-A2 restricted SLYNTVATL and HCV derived HLA-A2 restricted ALYDVVSKL epitopes. This degeneracy of HIV-specific T-cells may play a role in the underlying immunological mechanisms related to pathological profile of HCV/HIV-1 co-infection and variable clinical outcomes influenced by different CD8 T-cell repertoire.

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EXTRACELLULAR HIV-1 TAT STIMULATES STAT3 PHOSPHORYLATION IN CD8 T CELLS THROUGH INDUCTION OF A SOLUBLE FACTOR

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Plain Language Summary: During the course of HIV infection, CD8 T cells become progressively dysfunctional and ultimately fail to respond to antigen stimulation. Dysregulation of cytokines during HIV infection could play a role in CD8 T cell dysfunction. HIV Tat protein is secreted into the extracellular environment by infected CD4 cells and is taken up by neighbouring uninfected cells. We show here that CD8 T cells incubated with Tat protein have increased phosphorylation of STAT3 after a period of 48-72 hrs.

Objective: We hypothesize that Tat induces production and release of immune cytokines from CD8 T cells which in an autocrine fashion induce STAT3 phosphorylation.

Methods: Peripheral blood mononuclear cells were isolated by Ficoll-Paque density centrifugation from healthy donors. CD8 T cells were isolated using magnetic bead separation and incubated with Tat protein for 24-72 hours. CD8 T cells were stained for intracellular phospho-STAT3 and analyzed by flow cytometry.

Results: CD8 T cells incubated with soluble Tat protein demonstrate a delayed increase in STAT3 phosphorylation. Whereas IL-10 induces STAT3 phosphorylation in CD8 T cells within 15 minutes, STAT3 phosphorylation in the presence of Tat did not appear until 48-72h incubation. Tat treated cells that were washed every 24h in media containing Tat had no phosphorylated STAT3, suggesting Tat induces a secreted factor that must accumulate in the media to have an affect. Interestingly, phosphorylation of STAT3 in the presence of Tat was completely blocked by cyclohexamide and Brefeldin A supporting the idea that Tat induces expression and secretion of a secondary factor required for STAT3 phosphorylation. We have identified several candidate cytokines and are presently investigating their role in STAT3 phosphorylation in CD8 T cells.

Conclusions: Soluble Tat protein appears to induce the synthesis and secretion of a secondary cytokine in CD8 T cells which in an autocrine manner induces phosphorylation of STAT3. The biological impact of STAT3 phosphorylation in these cells is currently under investigation.

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UPREGULATION OF THE EFFLUX DRUG TRANSPORTER, P-GLYCOPROTEIN (P-GP), BY HIV PROTEASE INHIBITORS (PIS), IN A HUMAN BRAIN MICROVESSEL ENDOTHELIAL CELL LINE

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Plain Language Summary: Atazanavir is currently recommended in ritonavir boosted and unboosted HAART regimens for the treatment of HIV-1 infection. However, little information is known on the effect of atazanavir on drug efflux transporters (i.e., P-gp) expression at the blood-brain barrier (BBB). Previous data have shown the inductive effect of other PIs, in particular ritonavir, on the expression of drug efflux transporters. In addition, many PIs have been shown to be ligands of the nuclear receptor, Pregnane X receptor (PXR), a known regulator of P-gp. Our data suggest that both atazanavir and ritonavir induce P-gp expression and function in an in vitro human BBB model. We hypothesize that the inductive properties of atazanavir on drug efflux transporter expression are mediated through the activity of PXR. Since several PIs are known substrates of P-gp, this may further contribute to limit and restrict CNS penetration of antiretroviral drugs in the brain.

Objective: To characterize, in vitro, the inductive properties of atazanavir and ritonavir on hPXR activation and the involvement of hPXR on the regulation of P-gp expression in human brain microvessel endothelial cells, hCMEC/D3.

Methods: Expression of P-gp and hPXR was determined by western blot analysis and immunocytochemistry. Cell viability was assessed in the presence of several ligands applying an MTT assay. To examine functional activity, accumulation of the fluorescent P-gp probe, Rhodamine-6G (R-6G), was assessed in control and treated cells with or without P-gp inhibitor, PSC-833.

Results: We observed that P-gp and hPXR are expressed and localized in hCMEC/D3 cells. Treatment of hCMEC/D3 cells for 72h with atazanavir or ritonavir or rifampin (1-10uM) led to a two-fold increase in P-gp expression and a two-fold reduction in the cellular accumulation of rhodamine-6G. Treatment of hCMEC/D3 cells for 72H with a potent hPXR ligand, SR12813, (1-10uM) resulted in an approximately 6-fold increase in P-gp expression. Treatment of hCMEC/D3 cells for 72H with SR12813 or atazanavir or ritonavir in the presence of hPXR inhibitor ketoconazole seems to attenuate ligand-induced upregulation of P-gp caused by atazanavir, ritonavir and SR12813.

Conclusions: Exposure of atazanavir or ritonavir at clinical therapeutic concentrations resulted in an upregulation of P-gp expression and function in a human brain microvessel endothelial cell line, representative of the BBB. The role of PXR in regulating P-gp expression at the BBB is presently investigated in our laboratory. The inductive properties of PIs on P-gp may contribute further to limit CNS penetration of antiretroviral drugs. (Supported by CIHR)

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DISTRIBUTING JUST HEALTHCARE: AN IMPETUS DERIVED FROM THE HIV/AIDS PANDEMIC

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Plain Language Summary: The right to health and health as a human right are popular terms when addressing the prevailing deficiencies in the distribution of healthcare. The problem presents itself when these arguments are furthered without precise explication and application of the term "rights", as these arguments rely solely on the intuitive nature of the premise to support the conclusion. Daniels argues; "most people who assert a right to health or healthcare offer no particular theoretical account of its foundations – its grounds or its justifications – or its limits. They simply hope that if we all acknowledge such a right, we will unite behind the desired reform."

The Challenge: The challenge is to provide a rights based argument that establishes "the normative foundations for providing [universal] access to healthcare," as health inequalities unjustly limit liberty and are therefore especially morally problematic. Evidence to support a right to healthcare will be derived from an examination of the AIDS pandemic to highlight deficiencies in the distribution of healthcare. This project will provide the necessary philosophical investigation and explication of the term "rights," a necessary preface for specifying the scope and limits of justified rights claims.

Our Approach: This project will contain a literature synthesis of distributive justice and justice in healthcare materials. This project will employ Rawls's "reflective equilibrium" as a guide in finding principles that are strong enough to support a right to healthcare on a global scale. This project will examine the social determinants of health and investigate the social arrangements that simultaneously propel infections and vulnerable populations. This project will offer a quantitative study of the economic factors that underpin the spread of AIDS and elucidate the relationship between AIDS and inequality. This project will be guided by principles of distributive and comparative justice.

Key Findings: If health is a right then there are consequent duties imposed upon citizens and non-citizens alike. AIDS disproportionately affects the marginalized and a commitment to (global) justice means acknowledging these duties on a national and international level. The proper distribution of healthcare, guided by principles of distributive and comparative justice, can achieve lasting ends towards justice in healthcare.

Impact on Policy and Practice: Our commitment to justice must be reflected in policy. This project advocates redistributive social policy that secures healthcare globally. Comparatively speaking, industrialized nations, who are in a greater (economic) position to contribute to healthcare globally without unduly burdening their own citizens, incur more responsibility than other nations.

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INTERNATIONAL MEDICAL STUDENTS' HIV TREATMENT KNOWLEDGE AND HIV ATTITUDES – IS MEDICAL EDUCATION DOING ENOUGH ?

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Plain Language Summary: All over the world, medical students are often involved in the treatment people living with HIV/AIDS (PLWHAs). Greater knowledge about HIV is often associated with lower levels of HIV stigma. In the context of HIV health care, improved HIV knowledge and less HIV stigma ultimately translates to better quality care. Few studies have systematically examined and compared HIV knowledge gaps and HIV attitudes among medical students from both developing and developed world contexts. This study is the first to examine 133 international medical students' HIV training experiences, HIV treatment knowledge levels and HIV attitude/stigma levels. Results indicated that medical students with HIV training had fewer gaps in HIV knowledge and relatively low levels of HIV stigma. These findings support the need to advocate for consistent and comprehensive HIV/AIDS curriculum in medical schools around the world.

Objective: To date, few studies have systematically examined the relationship between medical students' HIV training experiences, HIV treatment knowledge, and HIV attitudes/stigma levels from an international perspective. This is the first study designed to assess how medical students' HIV training relates to their HIV treatment knowledge levels and HIV attitudes/stigma levels using psychometrically validated questionnaires.

Methods: Data collection for this study was carried out during a major international medical students' conference designed to unite globally minded medical student ambassadors. Study participants included 133 medical students from X countries. Participants completed an anonymous 15 minute questionnaire package assessing socio demographic information, HIV training experience, and validated tools assessing HIV treatment knowledge and HIV attitudes.

Results: Study participants (N=133) consisted of an even ratio of male to female medical students. Most participants (87%) had received some previous HIV training. HIV treatment knowledge scores were significantly higher in those with HIV training (75% correct) compared to those without HIV training (66% correct, $p<.05$). Lower HIV treatment knowledge and higher HIV stigma/attitude correlated significantly ($R=-.408$). Comfort with condom distribution was positively correlated with levels of HIV knowledge and inversely correlated with levels of HIV stigma.

Conclusions: Globally minded medical students with HIV training demonstrate greater HIV treatment knowledge than those without training, however, gaps in knowledge still exist across both groups. HIV attitudes/stigma levels are lower among medical students who are more knowledgeable about HIV, but negative attitudes still persist among some.
Findings across different countries around the world will be discussed as well as implications for advocating for more standardized and comprehensive medical school curriculum in HIV/AIDS.

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"CAN YOU CHANGE YOUR PROJECT TITLE?": LEARNING FROM THE KEY INFORMANTS OF A HIV RESEARCH PROJECT

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Plain Language Summary: Movement of people in this globalized world has generated challenges and possibilities concerning public health in host countries. In Canada, however, it is not yet clear how immigration processes have shaped newcomers' perceptions about, experiences with and capacity to respond to various health risks including HIV risk. Funded by the Canadian Institutes of Health Research (CIHR), three researchers from three disciplines of McMaster University are currently conducting an empirical study on the vulnerability to HIV of (mainland) Chinese and Indian immigrant communities in Canada. This paper presents some preliminary results of the qualitative individual interviews with 12 key informants from the mainland Chinese communities in Toronto and Hamilton. Specifically, it identifies the specific sub-groups that may be vulnerable to HIV infection, participant recruitment strategies, possible challenges at the later stages of the research project, and some "new" issues meriting further examination. These interviews also suggest some difficulties to identify "appropriate" key informants in a relatively newer Chinese sub-community (as compared to Cantonese-speaking sub-community, for example) that is not yet well resourced. It is concluded that, in a community in which HIV/AIDS is not well understood and highly stigmatized, conducting interviews with the "insiders" as key informants are not only necessary for developing culturally sensitive research strategies but also crucial in ensuring the relevance of this research project.

Objective: The overall objective of this research project is to explore the impacts of immigration processes (e.g., settlement and international travel) on the vulnerability to HIV of Chinese and Indian immigrant communities in Canada. The objective of the interviews with key informants from mainland Chinese communities is to seek a range of "insider" information that will be helpful in refining the design of the proposed study.

Methods: The data used in this paper were collected through qualitative individual interviews with 12 key informants from the mainland Chinese communities in Toronto and Hamilton.

Results: The preliminary results of data analysis identify the specific sub-groups that may be vulnerable to HIV infection, participant recruitment strategies, possible challenges at the later stages of this research project, and some "new" issues meriting further examination. The results also suggest some difficulties to identify "appropriate" key informants in a relatively newer Chinese sub-community (as compared to Cantonese-speaking sub-community, for example) that is not yet well resourced.

Conclusions: In a community in which HIV/AIDS is not well understood and highly stigmatized, conducting interviews with the key informants are not only necessary for developing culturally sensitive research strategies but also crucial in ensuring the relevance of this research project.

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AN HIV/AIDS EXPO FOR HIGH SCHOOL STUDENTS: LESSONS LEARNED FROM A COLLABORATIVE VENTURE

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Plain Language Summary: December 1 of each year marks World AIDS Day. The purpose of the Expo is to educate youth about HIV/AIDS and to inspire involvement among youth in the fight against HIV/AIDS at home and abroad. The broad-ranging impact of HIV/AIDS were emphasized at the Expo through a variety of topics including stigma & discrimination, safer sex, global issues and scientific research. Students participated in activities including yoga and a "create a video" contest. They also viewed presentations, workshops and demonstrations by over 30 agencies ranging from local volunteer initiatives to international agencies such as Doctors Without Borders.

Objectives:
1. The benefits of using an Expo as a learning tool
2. The value of collaborating with community agencies
3. Lessons learned, both positive and negative, from holding a health focused Expo

Methods: Introduction: Who we are (The Middlesex-London Health Unit, The AIDS Committee of London, The Thames Valley District School Board) and what roles we had in planning the Expo

Planning:

- Why acknowledge World AIDS Day with the teen population? Sexual health education is not consistent and misinformation and misconceptions about HIV/AIDS are not uncommon in this age group.
- Why did we choose the format of an Expo? The Thames Valley District School Board has 30 secondary schools and we wanted to reach as many students as possible but we had limited resources.
- How did we choose the presenters and displays? Using the expertise of the planning committee and the social determinants of health helped us identify community agencies including those that one might not immediately associate with HIV/AIDS.
- Who was invited to attend the event? Collaborating with the school board was essential. We also examined the curriculum and invited teachers and students from a wide range of classes.
- How did we make this event an active rather than a passive learning experience? Using research on the effectiveness of learning from health fairs we developed a worksheet for the teachers to use with their students during the Expo.

Results: We had more than 45 displays and presentations at the Expo and over 650 students and teachers actively engaging in the event. We are now planning this year's Expo and will share with the audience the lessons we learned from our initial venture.

Conclusions: The many agencies and presenters that were involved with this event provided a tremendous opportunity for our students to see the work that is going on in our community and how many different ways there are to get involved in understanding the impact of HIV/AIDS and preventing its spread. The diversity of this event gives students a global perspective of the disease while at the same time helping to establish a web of support and education with their community.

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ASO411 – AN ONLINE TOOL FOR ACCESSING UP-TO-DATE INFORMATION ABOUT HIV/AIDS-RELATED SERVICES AND PROGRAMS IN ONTARIO, CANADA

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Plain Language Summary: A new online search tool – ASO411 – was developed to provide up-to-date information about HIV/AIDS-related services and programs for people living with HIV/AIDS (PHAs) and service providers in Ontario, Canada. ASO411 was developed as a result of a collaborative effort between various HIV/AIDS organizations in Toronto.

The Challenge: In Ontario, Canada, people affected by, at risk for, or living with HIV/AIDS require up-to-date information about HIV/AIDS-related services and programs available in their area, while service providers require this information to make referrals.

Our Approach: Consultations conducted by the Toronto HIV/AIDS Community Planning Initiative (TCPI) from 2005-2006 revealed that, among people living with HIV/AIDS (PHAs) and service providers, lack of information about available services hampered accessibility. In response, TCPI recommended the development of an accessible, coordinated HIV/AIDS service information system (TCPI Plan March 2007). The Information and Access Working Group of TCPI was tasked with this specific initiative. After reviewing various existing information tools, the Working Group decided to partner with the Ontario HIV Treatment Network (OHTN) and expanded the scope of their "ASO411" project to fulfill TCPI's request. The new online search tool – ASO411 – has been created and is available online at www.aso411.ca, and provides up-to-date information on the location, services offered, and target populations of HIV/AIDS-related services in Ontario.

Key Findings: Preliminary feedback from other organizations has indicated that this type of resource can be invaluable for providing access to information for both service users and service providers. To maintain this usefulness, the Working Group will continually maintain and update ASO411, promote the tool to various communities of users, and expand access in multiple languages. PHA involvement into the Working Group will be promoted. Ongoing evaluation will continue to assess the usefulness of the tool among service users and providers, and recommend strategies to promote awareness in the appropriate communities.

Impact on Policy and Practice: This tool will facilitate access to services, but by tracking the services most often sought, it will also help document demand for various services. Where gaps may exist, the information gathered from the tool will support future planning efforts.

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ADAPTING TO HIV: A PROPOSAL FOR A COMPREHENSIVE TASK-MODEL APPROACH

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Plain Language Summary: With the decline in the morbidity and mortality associated with HIV infection, a primary consequence of this evolution is that, rather than prepare to die, individuals diagnosed with HIV are encouraged to learn how to adapt over the long term. We believe that it is crucial to gain an in-depth understanding of how this process of adjustment unfold. We do propose a comprehensive task-based model that provides an understanding of this specific process of adaptation.

The Challenge: While the task-based approach to adaptation presents us with an interesting theoretical foundation, one is still faced with the challenge of unifying the various existing models. Though they each promote different versions of task-based adaptation, each researcher – or set of researchers – offers particular points of view, none of which are mutually exclusive. Each model embodies a set of strengths that would prove highly enriching if unified into a comprehensive and coherent framework.

Our Approach: This presentation proposes a task-model based on the empirical foundations previously laid out by Moos and Tsu [1977], Cohen and Lazarus [1979], Corr [2002] and Samson [2007]. We intend to propose a task-based framework that integrates these four different models.

Key Findings: Task-based models provide a holistic perspective of the individual that encompasses the medical, emotional and psychosocial components of illness. Furthermore, this approach situates the individual at the center of the process
of adaptation.

Impact on Policy and Practice: A comprehensive understanding of the process of adaptation may help guide diagnosed patients, family members and their relatives through the many uncertainties they face and help them find a way to stabilize the sudden disruption they have experienced. Furthermore, medical staff may be better equipped to understand their patients' efforts to adapt. An in-depth look at adaptation processes could also provide administrative staff and policy makers with a broader view of the psychosocial ramifications and the implications of chronic illness.

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IMPLEMENTING AN INTER-PROFESSIONAL MENTORSHIP PROGRAMME TO BUILD CAPACITY AMONG REHABILITATION PROFESSIONALS AND PEOPLE LIVING WITH HIV IN ONTARIO.

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Plain Language Summary: We describe an inter-professional mentorship programme aimed at advancing HIV rehabilitation care and practice for people living with HIV in Ontario. The programme includes 3 rehabilitation professionals (physiotherapist, occupational therapist and speech-language pathologist) and 3 people living with HIV as mentors who will address clinical cases and questions from clinicians interested in the area of HIV care and practice.

The Challenge: People living with HIV (PHAs) experience a high prevalence of impairments, activity limitations and participation restrictions. Rehabilitation professionals have a role in addressing disablement issues for PHAs. Eighty-six percent of rehabilitation professional respondents to a national survey felt their profession is important to HIV care, however only 19% agreed they possessed adequate knowledge to provide rehabilitation services. Hence, there is a need to build capacity among rehabilitation professionals to better address the disablement challenges of PHAs.

Our Approach: Our overall goal is to develop, implement and evaluate a six month mentorship programme to increase the capacity of rehabilitation professionals to better address the needs of PHAs in Ontario. Specifically we plan to: 1) describe changes in knowledge, attitudes and practices of rehabilitation professional participants, 2) identify strengths and challenges associated with the programme, 3) identify key elements of HIV mentorship that promotes knowledge translation, and 4) determine satisfaction of the mentorship process among participants.

We recruited 6 mentors (3 rehabilitation professionals and 3 PHAs with expertise in HIV and rehabilitation). Recruitment of 12 rehabilitation professionals from across central south-western Ontario to participate as "mentees" in the six month programme is underway. Participants will meet for a face-to-face introductory workshop providing inter-professional HIV education, followed by five monthly teleconference/videoconference meetings. Participants will collaborate on case-based learning with opportunities to connect informally throughout. We will document changes in knowledge, attitudes and practices through reflective journals, pre and post mentorship surveys, interviews and focus group discussions.

Key Findings: We are in the implementation phase of the programme. Flexibility is important to accommodate varying schedules and meet the fluctuating needs of PHAs. Early education about the programme to employers is needed for clinicians to obtain support for investing time in mentorship. Overall findings will be based on evaluating changes in knowledge, attitudes and practices.

Impact on Policy and Practice: We propose an inter-professional rehabilitation mentorship programme to facilitate learning to increase capacity of rehabilitation professionals in HIV care. Lessons learned will help to inform future directions for ongoing mentorship initiatives that may include other health professionals and provinces to enhance rehabilitation care for PHAs.

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QUALITATIVE ASSESSMENT OF PAIN, PAIN-RELATED TREATMENT NEEDS AND BARRIERS TO CARE AMONG INDIVIDUALS LIVING WITH HIV – PHASE 1: HIV FOCUS GROUP

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Plain Language Summary:
A focus group made up of people living with HIV (PHAs) was conducted to learn about their experiences with pain and their opinions regarding the pain treatment needs and treatment preferences of PHAs. The focus group was conducted at the AIDS Committee of Ottawa and was the first phase of an OHTN funded pain needs assessment. The data gathered from the focus group was analyzed using thematic analyses. Results revealed six themes that were most relevant to the pain experiences of PHAs. Themes included frustration with the medical system and feelings that pain needs were not properly addressed. Participants felt that drug addiction stigma could be a barrier to proper pain treatment. They also felt resigned to their pain and the resulting lifestyle limitations. PHAs were unaware of treatment options but were interested in trying any kind of treatment. Group based pain management programs were of interest; however, there was concern about stigma related to HIV in group settings

Objective: The objectives were: a) to assess and document personal experiences with pain and the effects of pain on quality of life among PHAs, and b) to examine the barriers to pain treatment and the willingness to explore different pain related treatment options. Participants were also asked to evaluate a pain needs assessment questionnaire package that was to be used in Phase 2 of the study.

Methods: A 3 hour focus group composed of eleven PHAs and one individual in HIV support services was conducted. Focus group data was transcribed and then analyzed using thematic analyses. Four coders read the transcript individually and then worked as a group to determine themes.

Results: Six themes emerged from the thematic analysis. The themes were: 1) Doctors Disregarding Pain 2) Frustration with the System 3) Lack of Treatment Options 4) Drug Addiction Stigma 5) Pain as a Lifestyle 6) Group-Based Pain Management As a Treatment Option.

Conclusions: There is a feeling among PHAs that pain is not adequately addressed by the medical system, that pain negatively impacts all areas of life (mood, sleep, stress), and that treatment to alleviate pain is unavailable or non-existent. PHA's are willing to "try anything" and group based pain management is a desirable option; however, HIV-related stigma when participating in group programs may be problematic. Further research to examine appropriate treatment options and education regarding helpful pain management strategies is needed.

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DIVERSE COMMUNITY REACTIONS TO AN HIV VACCINE STUDY SHUT DOWN: IMPLICATIONS FOR FUTURE TRIALS

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Plain Language Summary: Clinical trials involving tens of thousands of volunteers over time are essential to the development of safe and efficacious HIV vaccines. The recent shutdown of an international HIV vaccine trial, however, raises significant challenges for future trials. We explored, in-depth, perspectives of individuals from diverse vulnerable communities in Toronto on the aftermath of the HIV vaccine trial shutdown and implications for future HIV vaccine development.

Objective: To assess the impact of the recent shutdown of the STEP Study HIV vaccine trial on community perceptions of HIV vaccine research and willingness to participate in future trials.

Methods: A qualitative investigation was designed and implemented in partnership between University of Toronto and community-based organizations in Toronto. We conducted 9 focus groups (n=72) with individuals recruited from diverse communities: African and Caribbean black women (2), MSM (2), female sex workers (1), injection drug/crack using men and women (2), and Aboriginal men and women (2). Three groups were HIV-positives and six HIV-negatives. Focus groups were digitally recorded and transcribed. Narrative thematic analysis was conducted using NVivo software.

Results: Participants' (n=72) mean age was 39.5 years (range 21-66); 60% (n=43) were women, 40% (n=29) men. Themes regarding negative fallout from the HIV vaccine study shutdown included: 1) perception that certain groups (i.e. sex workers) were too vulnerable for trial participation; 2) fear of vaccine related side effects; 3) concern that people will increase high-risk behavior due to a false sense of security; 4) discouragement from future trial participation, and, 5) people living with HIV expressed concerns regarding potential vaccine interactions with anti-retroviral medication. Support for future HIV vaccine trials also emerged in beliefs that 1) we can't give up hope; 2) human trials are necessary for scientific development; and, 3) participation of high-risk groups in HIV vaccine research is essential. Lessons learned and community recommendations included the importance of information dissemination about past trials, more rigorous informed consent processes, and mental health and substance use assessments for potential trial participants.

Conclusions: Despite negative fall-out from the recent STEP study HIV vaccine trial, diverse communities articulated the importance of continued HIV vaccine research and involvement of populations at elevated risk for HIV (i.e. sex workers, MSM). Ongoing community engagement in HIV vaccine research and clear dissemination of past trial results, as well as individualized trial-related counseling and mental health and substance use screening for potential participants may promote informed participation and reduce vulnerability of future HIV vaccine trial volunteers.

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IMPLEMENTING RESPONDENT DRIVEN SAMPLING: LESSONS LEARNED

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Plain Language Summary: This paper reports on the use of respondent driven sampling (RDS) as a recruitment methodology to sample women and men who inject drugs in Ottawa. The major objectives of our study were to collect data, via interviews and dried blood samples, to identify and characterize potential distinct networks of injection drug users (IDUs) and determine routes by which HIV and hepatitis C (HCV) are being transmitted. This information will be used to identify HIV and HCV infection clusters and strains, confirm social network data, and provide a basis for primary and secondary prevention interventions.

The Challenge: Implementing RDS uncovered a variety of logistical challenges. RDS is similar to snowball sampling as it involves peer, chain referral sampling, but has a built in mathematical system that calculates selection probabilities. Participants recruit their peers and the research team tracks who recruited whom to create a resulting model that enables researchers to provide population estimates and measure the precision of their estimates. RDS is particularly suited to research with groups that are small, inaccessible, and marginalized.

Our Approach: We began by recruiting a group of 8 first generation "seed" participants, who were referred by local service providers. The seeds were selected based on their perceived 'connectedness' within the community and represented a diversified cross-section of the IDU population in Ottawa. Once interviewed, each participant was given 3 recruitment cards to pass on to their injection drug using peers.

Key Findings: Seven of the 8 selected seeds participated. The two largest individual networks produced contained 126 and 253 members, representing 93% of the overall sample. Two seeds produced between 10-15 participants and three seeds produced 0 participants. RDS proved to be very time-efficient, with over 400 participants recruited in four months. Logistical challenges encountered were: variability in seed productivity, participant interest outweighing project capacity, attempted repeaters, and recruitment cards as currency. Identifying connected seeds, stressing the importance of peer referral and talking to participants about their experiences in the study, helped identify logistical challenges in a timely manner.

Impact on Policy and Practice: The added utility of applying this methodology apart from its direct relevance to the research question of characterizing social networks is that we will arrive at HCV and HIV prevalence rates that will have greater generalisability or external validity as they will have been derived from IDUs beyond those accessible at the more usual recruitment sites. In addition, through applying RDS, the research process may also have a prevention intervention effect in that IDUs who present for interview may well be those that are unaware of, or previously have not accessed, the range of harm reduction resources available in our city.

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Mixed Methods, Models and Questions

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IS HIV VACCINE TRIAL PARTICIPATION ASSOCIATED WITH INCREASES IN RISK BEHAVIOURS?

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Plain Language Summary: Social-behavioural research is a vital companion to HIV vaccine trials. This study explored trends in risk behaviour over time among participants in an HIV vaccine trial in Toronto. We found most participants did not increase their risk behaviours over time. Ongoing monitoring of volunteers in HIV vaccine trials is important to ensure safe and ethically conducted HIV vaccine research.

Objective: To examine trends in risk behaviours over time among participants enrolled in a Phase-IIb HIV-1 vaccine trial.

Methods: Volunteers enrolled in a prophylactic HIV vaccine trial were invited to participate in a longitudinal socio-behavioural study. Trial selection criteria were: 18-45 years of age; HIV-1 seronegative men or women; >=2 sexual partners or unprotected sex in past 6 months. Participants completed confidential, self-administered baseline, 6- and 12- month follow-up questionnaires addressing demographics, motivations for trial enrolment, vaccine efficacy belief, and risk behaviours. We assessed trends in risk behaviours over time and associations between risk behaviour trends and sociodemographics, baseline beliefs and motivations, respectively, utilizing chi-squares.

Results: Participants' (n=30) were all male, mean age=38.9 years; average monthly income=$2900. Most (70%) had some college/university education; 80% were employed. From baseline to 12 months, 40% (n=12) reported the same number of sexual partners at each time period, 13% (n=4) reported fewer partners, 13% (n=4) reported more partners, and 33% (n=10) displayed no trend. Regarding condom use for anal sex with a primary partner, 47% (n=14) didn't change condom use over time, 17% (n=5) used condoms less, 10% (n=3) used condoms more, and 27% (n=8) displayed no trend. Importantly, 31% (n=9) improved condom use with casual partners over time, 55% (n=16) maintained condom use, 7% (n=2) decreased condom use and 7% (n=2) displayed no trend. Most (70%; n=21) indicated no change over 12 months in condom use during last anal sex. Trends in risk behaviour were not significantly associated with participant demographics, vaccine efficacy belief (i.e., that the test vaccine would be effective) or protection motivation (i.e., joining the trial to gain protection against HIV infection).

Conclusions: HIV vaccine trial participation was not associated with increased sexual risk behaviours over time. Continued caution is warranted to minimize risks to HIV vaccine trial volunteers, but trial involvement and risk behaviour counselling appear to be effective in preventing risk behaviour increases. Continued socio-behavioural research in tandem with HIV vaccine trials can help sustain momentum on the road to a safe and efficacious HIV vaccine.

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DOES THE RATIFICATION OF HUMAN RIGHTS TREATIES IMPACT POPULATION HEALTH?

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Plain Language Summary: Human rights treaties serve to indicate state commitment to human rights. There is some doubt, however, as to whether these binding state documents improve the lives of citizens. We aimed to determine if human rights treaty ratification is associated with improved health and social indicators. After controlling for economic and geographic heterogeneity, we were unable to demonstrate significant differences in either health or social indicators between ratifying states and non-ratifying states for all the human rights treaties. Established market economy states were found to have consistently improved health compared to less wealthy settings, but ratification of human rights documents shows no association with health and social indicators. These results suggest the need for more stringent requirements of states for treaty ratification, improved accountability mechanisms to monitor compliance of states with treaty obligations, and financial assistance to support the realization of the right to health.

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HIV INFECTED REFUGEES: ART THERAPY AND ITS AFFECT ON CD4 COUNTS AT 3 AND 6 MONTHS

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Plain Language Summary: This study is a retrospective chart review from records obtained at the Dekalb County Board of Health.
The objectives are:
1. To determine the number of HIV-infected refugees arriving in Dekalb County from 2004 to 2005
2. To determine initial CD4 at time of arrival
3. To determine 3 and 6 month change in #2
4. To determine those who went on Anti-Retroviral Therapy

Objective: To determine if CD4 cell counts are affected by travel and antiretroviral therapy (ART) in HIV infected refugees

Methods: This study was a retrospective chart review conducted at a HIV refugee clinic from January 2004 to December 2005. Patient factors recorded included: age, sex, race, country of origin, date of arrival, initial CD4 count and those at 3 and 6 months and the initiation of ART. The patients were also placed into categories based on whether or not their CD4 counts were greater or less than 200. The initiation of ART was compared to the initial CD4 counts and those at 3 and 6 month visits. Variables were compared by T-test and chi-square analysis

Results: 42 patients had HIV/AIDS upon arrival, 14 were excluded secondary to lack of follow-up and information about CD4 counts; 73% were female, 58% were black, mean age was 40.5, mean initial CD4 count upon arrival was 483.7 and 54% of the people were started on ARTs initially. 75% of the patients with initial CD4 counts less than 200 were started on antiretroviral therapy versus 50% of those with CD4 counts greater than 200 who were started on antiretroviral therapy. Of the 14 patients who were initially started on ARTs, 71% had an increase their CD4 counts at 3 months and 64% had an increase at 6 months. Although there was an increase at both intervals there was not a greater increase at 6 months than 3 months. This could be a factor of compliance as well as stress due to environmental changes.

Conclusions: Our study shows CD4 cell counts are increased with the use of ART.

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INCARCERATION AMONG OTHER FACTORS IS A PREDICTOR OF GETTING TESTED FOR HIV DRUG RESISTANCE IN A COHORT OF HIV-POSITIVE PEOPLE

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Plain Language Summary: Resistance testing has been promoted as part of routine clinical practice in HIV/AIDS treatment and care. This procedure is fundamental to HIV/AIDS management as antiretroviral resistance has been repeatedly implicated in incomplete viral suppression. It is thus important to know who is being tested as well as to understand the trends in the likelihood of getting tested.

The Challenge: The study objective was to determine the clinical and socio-demographic predictors of having been tested for HIV drug resistance in a cohort of HIV-positive persons.

Our Approach: A cohort of 426 HIV-positive persons in British Columbia who were antiretroviral-naïve prior to initiating HAART was studied. We conducted survey-based interviews to gather information on socio-demographic parameters and behaviour. Clinical data was assessed through linkages to laboratory records. Bivariable and multivariable analyses were performed to assess any potential association between the explanatory variables and having been tested for resistance. While controlling for other prognostic factors in the model, we tested the strength of the association between having been tested for HIV drug resistance with adherence and viral suppression status as the main explanatory variables of interest.

Key Findings: Almost one-fifth of the study's participants had not been tested for resistance. Persons with adherence levels ≥ 95% (AOR: 0.41, CI: 0.21 – 0.78) and those with virologically suppressed viral loads (AOR: 0.42, CI: 0.22 – 0.81) were less likely to have been tested for resistance. A history of incarceration was strongly associated with the probability of having been tested for HIV drug resistance. The length of time on therapy and being male showed a tendency of being associated with having been previously tested.

Impact on Policy and Practice: As expected, resistance testing was guided mostly by clinical factors and factors, such as high adherence, which may influence the clinical variables. The fact that persons with a history of incarceration were more likely to be tested supports policies geared at ensuring continuity in treatment for persons in jail. To fully ascertain the influence of incarceration on the likelihood of getting tested, future research should specifically target people who were already on antiretroviral drugs before entering jail. More effort should be made to encourage the practise of routine HIV resistance testing for HIV/AIDS persons since the procedure is critical in maximising therapeutic options.

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MYCOBACTERIUM AVIUM COMPLEX INFECTION IN THE HAART ERA

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Plain Language Summary: Infection with mycobacterium avium complex (MAC) in the context of HIV infection usually occurs in patients with very low CD4 counts (<50/mm3) who are not treated with, or who are failing, highly-active anti-retroviral therapy (HAART). Invasive disease from MAC may also occur during the initial period after the start of HAART (immune reconstitution) in patients with previous unrecognized infection. We present here a case of invasive MAC infection in an HIV-positive patient stable on three years of HAART therapy with a CD4 count of 556/mm3 and a completely suppressed viral load (HIV RNA < 50 copies/ml). A review of the literature pertaining to the changing face of MAC infection in HIV-positive patients during the HAART era will follow. We suggest consideration of MAC infection in HIV-positive patients in the correct clinical context regardless of CD4 count.

Objective: To describe the changing epidemiology of MAC infection in HIV-positive patients during the HAART era.

Methods: A clinical case will be presented to illustrate the theme of the changing epidemiology of MAC infection in HIV-positive patients during the HAART era. A systematic review of the relevant literature including published case reports and abstracts will be presented.

Results: A 51 year-old male HIV-positive patient who had been stable on HAART for three years, with a completely suppressed viral load (<50 copies/ml) and a CD4 count of 556/mm3, presented with right upper quadrant pain. Intra-abdominal collections were found beneath the liver capsule and posterior to the gallbladder. Multiple cavitating lesions were present in the left lung. MAC was isolated from cultures of the lung lesions which showed the characteristic pathology. The patient has been initiated on anti-mycobacterial antibiotic therapy.
MAC infection has rarely been described in HIV-positive patients with adequate and durable immunological and virological responses to HAART. This contrasts with the accepted understanding of MAC infection as an AIDS-defining disease in patients with very low CD4 counts, either in the absence of or failure of HAART or as a manifestation of an immune-reconstitution syndrome.

Conclusions: Invasive infection with mycobacterium avium complex may occur in HIV-positive patients even in the context of durable immunological and virological response to HAART therapy and should be considered in the correct clinical context regardless of CD4 count.
Further research is required to characterize host susceptibility factors for invasive mycobacterial disease and their relationship to infection with HIV.

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SMOKING DATA AND SMOKING PREVALENCE IN THE OHTN COHORT STUDY

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Plain Language Summary: PHAs (people living with HIV/AIDS) are living longer and facing more chronic diseases than before, including smoking related diseases. In the OHTN cohort study (OCS), we found 60-70% of PHAs smoked. These smoking rates were three times higher than that in the general Ontario population and highlighted the need for improved smoking cessation.

The Challenge: Smoking data was not well captured in the OCS, which would inevitably reduce data utility and bias smoking related results.

Our Approach: We treated missing smoking data as unknown. We replaced yearly unknown data by carrying the nearest known data backwards first, and then carrying forwards. We validated OCS smoking data by reviewing 33 (30%) randomly selected medical charts at SIS clinic in Hamilton.

Key Findings: Of 3236 patients, 2812 (87%) were men and 2547 (79%) were white. At baseline, mean (SD) age was 40.4 (9.3) years old. 654 (20%) died during follow up. Originally 70% of yearly smoking data was unknown from 1988 to 2007. After imputation 41% of smoking data was still unknown. 88% of 269 smoking status changes represented quitting, initiations, or relapse after imputation. While only 7% of 2613 changes were meaningful before imputation. By excluding unknown data, the range of smoking prevalence decreased by 10% after imputation, and the overall smoking prevalence decreased: the rate ratio (RR) was 0.92, 95% CI (confidence interval) was 0.90 to 0.94. The smoking prevalence fluctuated between 69% and 71% between 1995 and 2000, and then steadily decreased to 62% in 2007. In Ontario general population, the smoking prevalence steadily decreased from 23% in 1999 to 18.2% in 2007 with yearly decrease of 0.8% (95% CI: -1.2% to -0.4%), which overlapped with that of 1.3% (95% CI: -1.5% to -1.1%) in OCS. However the smoking prevalence in PHAs was constantly higher: RR was 3.1 (95% CI: 3.0 to 3.2) in 1999 and 3.4 (95% CI: 3.2 to 3.6) in 2007 respectively. For those 33 records we reviewed at SIS clinic, raw agreement was 85%. Weighted kappa was 91% (95% CI: 64% to 119%).

Impact on Policy and Practice: Imputation improved the quality of smoking data in OCS because the data was more stable and meaningful after imputation, and the overall smoking prevalence was somewhat lower. Smoking prevalence in PHAs was three times higher, which would lead to more smoking related diseases. When highly active anti-retroviral therapy makes HIV infection a manageable chronic disease, healthy life style including smoking cessation is becoming more important for PHAs.

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CLINICAL AND IMMUNOLOGICAL OUTCOMES OF A NATIONAL PAEDIATRIC COHORT RECEIVING COMBINATION ANTIRETROVIRAL THERAPY IN UGANDA

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Plain Language Summary: Access to combination antiretroviral therapy (cART) among children remains limited worldwide, with only 115,500 (15%) of those in clinical need receiving cART. Few studies have examined paediatric cART outcomes in resource-limited settings and in large regional networks. We evaluated the clinical and immunological outcomes of a national cohort of children receiving cART in Uganda. The 770 children in our cohort demonstrated reduced mortality and good clinical adherence. Orphans appear to have reduced access to cART, as they presented for treatment at older ages and with poorer immunological status, compared to non-orphans. Our study demonstrates that children in this low resource setting respond well to cART, and that special efforts must be taken to ensure orphans receive timely access to HIV treatment and care.

Objective: We aimed to evaluate clinical and immunological outcomes of paediatric cART patients enrolled in The AIDS Support Organization (TASO) Uganda national HIV/AIDS program.

Methods: We conducted an observational study of paediatric patients (<14 years) enrolled in 10 clinics across Uganda for which TASO has data
We extracted patient demographic, immunological and clinical outcomes from TASO's database regarding age, sex, cART regimen, CD4 and WHO stage at initiation, tuberculosis (TB), mortality and adherence. Outcomes were analyzed using Pearson's rank-order correlations, Wilcoxon's rank sum tests, Cox proportional hazard model and survivor functions.

Results: Of the total 770 HIV children on cART, median age was 9 years (Interquartile range [IQR], 5-13) and median follow-up time was 377 (IQR 173-624) days. 751 (97.5%), initiated on non-nucleoside reverse transcriptase inhibitor based regimens. 365 (47.5%), initiated cART with severe immune suppression (CD4%<15). Of the 18 (2.3%) children who died, mortality was associated with lower CD4% at initiation (B coefficient -0.144, SE 0.06, P=0.02). Of the total, 229 (30%) were single or double-orphans and more likely to initiate cART at an older age (mean age 9.25 vs 8.35, P=0.02), and have a lower CD4 cell count (median 268 vs 422, P=<0.0001) and CD4% (median 12.8 vs 15.5, P=0.02) at initiation. Pulmonary TB was present in 43 (5.6%) patients at initiation and 21 (2.3%) post-cART. Almost all patients (94.9%) demonstrated >95% adherence.

Conclusions: Children on cART in Uganda demonstrate positive clinical outcomes. However, additional support is required to ensure timely cART access among orphans and young children.

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Epidemiological Aspects of HIV

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IS CIRCUMCISION ASSOCIATED WITH HIV STATUS AMONG ONTARIO MEN WHO HAVE SEX WITH MEN (MSM)?

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Plain Language Summary: Research shows circumcision to be associated with reduced risk of HIV acquisition in heterosexual men. Factors associated with circumcision have not been studied. The role of circumcision in the HIV status of MSM in Canada is less understood. Our analysis suggests there are socio-demographic characteristics that are associated with circumcision. An understanding of these associations is important to consider when assessing the interplay between circumcision and HIV risk.

Objective: This analysis describes socio-demographic correlates of circumcision status among a venue-based community-sample of MSM and examines the association between circumcision and HIV status.

Methods: Men (n=5,080) self-completed a questionnaire and provided an optional saliva specimen for HIV testing. Multivariate logistic regressions were used to identify factors associated with circumcision; and describe the association between circumcision and HIV status when controlling for socio-demographic variables.

Results: Among the 3,558 men who provided sufficient saliva for HIV testing and answered the question on circumcision, 65.5% were circumcised. Results showed that circumcised men were more likely to live in South Ontario vs. Toronto (OR:1.46, 95%CI: 1.21-1.75), be born in Canada vs. outside (OR:2.25, 95%CI: 1.65-3.07), be age 25-39 (OR:1.81, 95%CI:1.43-2.30), age 40-59 vs. <25 (OR:2.12, 95%CI:1.50-3.02), and have college (OR:1.25, 95%CI:1.03-1.51) or higher education (OR:1.43, 95%CI:1.09-1.89) vs. high school or less. Men who spoke English were more likely to report being circumcised. Asians were more likely to be circumcised vs. Caucasians (OR: 1.89, 95%CI: 1.29-2.77), while Aboriginals were less likely (OR: 0.52, 95%CI: 0.33-0.84). Circumcision was not associated with HIV status in the analysis among those reporting only insertive anal intercourse in the past 3 months.

Conclusions: In this sample, a respondent's circumcision status did not correlate with HIV status. This finding confirms Templeton et al's (2006) assertion that the role of male circumcision in HIV acquisition among MSM remains unclear. The high rate of circumcision and lack of association with HIV infection provides evidence that circumcision as a mode of HIV prevention may have a limited impact for this population. However, additional study is warranted because of the limitation of the measures used.

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ISSUES IN PROVIDING HEPATITIS C TESTING AND SUPPORT IN PRIMARY CARE SETTINGS

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Plain Language Summary: Injection drug use is a major risk factor for both HIV and Hepatitis C (HCV) infection in Ontario, and there are many issues in common for access to appropriate testing and care for both diseases. This qualitative study was done to understand the experiences and concerns of primary care physicians about doing hepatitis C testing and treatment, as well as more general issues in providing care for patients who inject drugs. It provides insights into these issues and possible service models to address them.

The Challenge: One component in improving access to testing and treatment for persons living with Hepatitis C is to achieve a better understanding of the barriers and issues in providing such services from the point of view of primary care physicians. This study undertook a preliminary examination of their perspective.

Our Approach: A convenience sample of 14 physicians was recruited primarily through personal contacts and snowball techniques. A series of open-ended questions explored their experience with HCV testing and care, as well as barriers and facilitators to providing care for drug using patients. Interviews were tape-recorded and thematic analysis carried out. One physician was an internal medicine specialist, the rest were primary care providers. Twelve worked in downtown Toronto while two worked primarily in rural areas. Two were female, all but one did their medical training in Canada. Length of time in practice ranged from 3-30 years.

Key Findings: Several issues were identified with respect to HCV testing of patients, particularly need for open communication about risk, and difficulty doing follow-up antigen tests (needed to confirm chronic infection) after initial positive antibody tests. With respect to care and treatment, specialist support was identified as crucial, and specific models of care were identified. Physicians treating MSM identified a lack of treatment and support for patients with problematic methamphetamine use as an obstacle to HCV treatment and care. Physicians treating street-involved drug injectors at inner city clinics identified needs related to housing, nutrition, mental health, case management and addiction treatment as key issues for care and treatment. Some clinics had developed relationships with specialists who provided consultation and support, and primary care physicians identified their needs from such relationships to facilitate HCV care and treatment for their patients. Needs for care providers including nurses, counsellors, and outreach workers were also identified. One clinic offered a model of peer education and support regarding HCV particularly useful in developing treatment readiness and in supporting patients through treatment.

Impact on Policy and Practice: This study identified a number of barriers to HCV testing, treatment and support, and also provided information on models of care and potentially helpful policy and programming approaches. It will initially be used to provide policy makers and advocates with information to inform their work in improving access to primary care for HCV infected persons in Ontario.

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HIV ANTIVIRAL DRUG RESISTANCE: PATIENT COMPREHENSION AND IMPLICATIONS FOR TREATMENT SUCCESS

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Plain Language Summary: Patient understanding of antiretroviral drug resistance is important in comprehending the role of adherence in achieving positive clinical outcomes. The development of resistance is a major barrier to maintaining virological suppression, the overall goal of HAART. The results of this analysis indicate that patient knowledge of HIV resistance is greater in patients who discuss medications with a physician and have medication teaching sessions with a pharmacist.

Objective: To assess and characterize knowledge about HIV resistance in HIV+ persons on HAART and to identify potential intervention areas for improvement of HIV resistance knowledge among patients.

Methods: The longitudinal Investigation into Supportive and Ancillary health services (LISA) cohort is a prospective study of HIV+ persons on antiretroviral (ARV) care. Recruitment was done through the Drug Treatment Program (DTP) at the British Columbia Centre for Excellence in HIV/AIDS. An interviewer administered survey collected data on demographics, physician-patient relationship, quality of life and other socio-demographic variables. Resistance knowledge was determined based on a three-part definition. Clinical markers, including CD4, viral load and adherence were collected through the DTP database. Categorical variables were compared using Fisher's Exact Test and continuous variables using the Wilcoxon Rank–Sum Test. Logistic regression was performed for the unadjusted bivariate and the adjusted multivariate analysis.

Results: The LISA cohort contains 457 participants as of July 2008. Less than 4% of respondents could correctly define HIV resistance and 20% reported not discussing resistance with a physician. The adjusted model indicates being younger [OR =0.97,95%CI (0.95-0.99)], high school education or greater [OR=1.64,95%CI(1.07-2.51)], discussing medication with physicians [OR=3.67, 95%CI(1.76-7.64)], high provider trust [OR=1.02,95%CI(1.01-1.03)], having a teaching session with a pharmacist [OR=2.14,95%CI(1.41-3.24)] and having dependent children [OR=3.94,95%CI(1.05-14.73)] were predictive of a correct or partial HIV resistance definition. The probability of correctly defining HIV resistance increased from 15.8% to 63.9% if respondents had both discussed HIV medication with a physician and had a private teaching session with a pharmacist.

Conclusions: Personal contact with a physician about HIV medications and a pharmacist teaching sessions appear significant in a patient's ability to understand HIV resistance and the implications it holds for treatment. Increasing time spent discussing medications with patients at both the physician and pharmacist levels may be an area of focus for future interventions for improving patient knowledge of HIV resistance.

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INTEGRATED HIV SERVICE DELIVERY MODEL FOR AFRICAN AND CARIBBEAN WOMEN - 10 YEARS IN THE MAKING

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Plain Language Summary: African and Caribbean women are now an integral component of the HIV/AIDS epidemic in Canada, particularly in Ontario. Service delivery has evolved in the last 10 years but still continues to be located primarily within AIDS Service Organizations (ASOs). Meanwhile, organizations which deliver services for more immediate needs treat HIV/AIDS as a peripheral issue, removed from the realities of women's lives. Women's Health in Women's Hands CHC, an organizations working with Black women and women of colour across the GTA has developed and refined a service delivery model that integrates HIV/AIDS services into broader health service(s) targeted to African and Caribbean women and is in the process of extend model to reach Latin American and South Asian women in Toronto.

Objective: To highlight processes used to develop an integrated HIV/AIDS service delivery model, its components and flexibility for adaptation within a variety of settings.

Methods: Data to identify needs, gaps and service delivery issues was obtained through: Literature Review; examination of existing models to determine the flexibility for adaptation to local context(s); in-depth interviews with 21 key informants (service providers, researchers and policy makers); focus groups with 36 women from target populations.
Above data was analyzed and used to develop a service delivery model. Staff was trained to support model integration and delivery within a broader health framework.

Results: An anti-oppression framework which recognizes multiple locations of women as transnational citizens and their struggles on the margins of society within a developed country context was developed to ground model. Six 6 areas of specialization were identified and integrated within broader health services: HIV education, prevention and outreach; Treatment, support and care for HIV+ women; Resource acquisition/development; Knowledge creation, translation and exchange; Capacity/skills development; Advocacy/networking/partnership building. The six areas have been populated with specific projects and activities tailored to the needs of African and Caribbean women living with and at risk of contracting HIV.

Conclusions: HIV/AIDS service provision for African and Caribbean women and other immigrant/refugee women of colour must be expanded to meet needs of a growing epidemic. Integration of HIV/AIDS services into organizations/programs/services that deal with more immediate issues provides a mechanism for expanding services to reach maximum numbers of women. Flexibility and adaptability of the proposed model makes it ideal for integration into varieties of settings/contexts.

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NATIONAL REPORT CARDS TO INFLUENCE POLICY, TRACK PROGRESS AND ENSURE ACCOUNTABILITY FOR WOMEN AND HIV

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Plain Language Summary: Blueprint for Action on Women and Girls and HIV/AIDS created and evaluated a "Report Card" for Canada focusing on: legal/ethical/human rights; stigma/discrimination; diagnosis and treatment; prevention, care and support, and a Backgrounder to support its use. These tools aim to encourage dialogue and action to change policies/programs to improve the lives of women with and affected by HIV. To draw attention to the activities of the Canadian government, the tools were released during AIDS 2006, and were distributed among PHA's, communities affected, policy makers, service providers and researchers. Follow up included contact with key stakeholders to secure policy commitments and monitor progress on issues related to women and HIV.

The Challenge: Women in Canada, representing diverse cultural backgrounds and experiences, are largely absent from the HIV/AIDS research agenda and policy-making. Women often lack access to testing, are under-diagnosed and are diagnosed late. This is exacerbated by all forms of discrimination against women.

Our Approach: As women with HIV and as women working to address HIV, we see a need tools to encourage dialogue and action to change policies and programs to improve the lives of women with and affected by HIV. By surveying key leaders in the HIV and those working with women with and affected by HIV, we created a Report Card on Canada's response to HIV for women and girls, to be used as an advocacy and media tool. We also conducted an extensive literature search to inform a background document.

Key Findings: A coordinated, cross sector response is required to foster effective knowledge exchange related to HIV/AIDS and women. Partnerships among women's, sexual and reproductive rights, human rights and HIV groups are required to address the complex issues facing women with HIV/AIDS. Advocacy tools should be created and disseminated via these partnerships. Limitations to the 2006 Report Card include the lack of 'instructions', the lack of accessible background information and the lack of population-specific information, which were addressed in the 2008 Report Card. These tools, when developed by women with and affected by HIV, are useful in raising awareness and encouraging action among some key stakeholders.

Impact on Policy and Practice: Tools developed by affected communities, such as the Report Card and Backgrounder, can be effective in encouraging action in Canada, and they have potential implications for women in other settings: groups in Nicaragua, Norway, Zimbabwe and Rwanda have plans to develop their own national report cards with the support of Blueprint.

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EFFECTIVE RECRUITMENT STRATEGIES FOR HIV+ WOMEN IN A PROVINCE-WIDE CROSS-SECTIONAL RESEARCH STUDY

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Plain Language Summary: Women, along with other minority groups, have historically been under-represented in HIV research. This under-representation threatens the generalizability of studies. One reason for the under-representation is that typical recruitment strategies for this population may be ineffectual and different ones are required. We highlight successful recruitment strategies implemented while carrying out a province-wide cross-sectional study involving HIV-positive women of childbearing age (18-52 years). Participants were recruited from AIDS Service Organizations, Community Health Centres and HIV Clinics and completed a survey identifying their pregnancy desires and needs.

The Challenge: To address recruitment barriers and identify successful recruitment strategies for HIV-positive women throughout project execution.

Our Approach: We foresaw the potential recruitment barriers and addressed them by instituting population-specific recruitment strategies. The barriers and strategies were identified by the research team and Community Advisory Board/Project Advisory Committee (CAB/PAC) members.

Key Findings: The recruitment barriers included the sensitive nature of the topic, trust of and communication with research personnel including language, confidentiality and stigma issues, transportation difficulties including cost, time constraints and child care. The recruitment strategies implemented include: 1) acknowledging the sensitive nature of the topic; 2) approaching candidates at group events as women like to meet in groups; 3) approaching candidates during pre-scheduled health care visits; 4) commuting to the candidate's home to allow a familiar and confidential environment (sometimes long distances); 5) having HIV-positive female peers conduct group survey administration sessions; 6) offering a comfortable non-HIV affiliated environment; 7) offering flexibility study appointments; 8) debriefing after survey completion and offering a pre-approved list of counseling services; and 9) having friends recommend the survey to other peers. Other helpful strategies included monthly newsletters, CAB/PAC meetings and financial reimbursement (for child care and transportation).

Impact on Policy and Practice: It is important to address recruitment barriers for HIV-positive women taking part in research. The most important issue identified for recruiting HIV-positive women was trust. For recruitment to be successful there needs to be a strong rapport between study personnel and participants. This rapport is facilitated by having study personnel from similar cultural backgrounds or who are peer HIV-positive women. Furthermore, enrolling from a site with trusted staff was useful. Study personnel should be flexible, skilled, and empathetic. In combination with the other recruitment strategies, effective recruitment of HIV-positive women can be achieved. The use of population-specific recruitment strategies is important to ensure generalizability of study findings to minority groups such as women.

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LEARNING FROM CHALLENGES IN A QUALITATIVE STUDY OF FERTILITY EXPERIENCES IN SERODISCORDANT COUPLES (MALE HIV-POSITIVE, FEMALE HIV-NEGATIVE).

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Plain Language Summary: We present findings of the challenges encountered while conducting a qualitative study using interviews of serodiscordant couples (male HIV-positive, female HIV-negative) to determine their experiences undergoing fertility assessment and/or treatment. These obstacles, including long distances, telephone consent issues, funding shortfalls, logistics of interviewing couples together, and particularly the sensitive nature of the research, proved to be barriers in the research process.

The Challenge: To determine barriers that were identified through conducting the project, methods helpful in overcoming them and making recommendations to help the efficacy and success of future projects.

Our Approach: We identified factors that played the largest barriers to the study in order to recommend solutions. These barriers included issues inherent to the study design (e.g. logistics of interviewing couples together), problems not considered initially (e.g. approval for telephone consent due to long distances), and problems encountered that were specific to this study (e.g. highly sensitive topic, coordinating the schedules of the interviewer, the male and female partners, disclosure and confidentiality issues).

Key Findings: The sensitive nature of this research, the busy schedules of participants and the distances needed to travel were challenges that had a cumulative effect on the success of study completion. The number of potential participants, already small to begin with, was further limited by logistical difficulties of time and distance (secondary to limited availability of fertility services for serodiscordant couples), as well as confidentiality issues (e.g. difficulty in contacting participants). Strategies to overcome these barriers include conducting interviews during evenings and weekends, offering financial compensation for traveling or childcare, adding research personnel located in closer proximity to clusters of participants and greatly acknowledging the sensitive topic being researched.

Impact on Policy and Practice: In future studies, it would be helpful to contact potential participants prospectively about: convenient times/dates to contact them and whether researchers are permitted to leave voicemail messages. The sensitive nature of our research study (participants have often not shared their HIV status and/or plans to conceive with others) raised a significant barrier and it was critical for the researchers to appreciate and acknowledge. Other techniques as listed above could be used to overcome the barriers. Despite these challenges, we believe the information is very important in both documenting the experience of the couples, as well as helping other couples in similar situations and their healthcare providers, to become aware of the resources available to them.

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SAFER SEX NEGOTIATION AMONG UNIVERSITY STUDENTS: AN ANALYSIS THROUGH THE LENSE OF GENDER

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Plain Language Summary: HIV prevention and safer sex negotiation were examined among Canadian university undergraduates. Focus groups were conducted with 20 female and 9 male undergraduate students to investigate their perception of risk for HIV, safer sex practices, sexual negotiation skills, and attitudes towards condom use. Thematic analysis of the data revealed that HIV was not a primary concern for participants, and that they evaluated their personal risk for HIV as being very low. This was despite the fact that they were sexually active with multiple heterosexual partners, and were not consistently using condoms. Women were much more likely to insist upon condom use during sexual activity, but their motivation for condom use was to prevent pregnancy.

The Challenge: The challenge of the research was to identify the concerns of Canadian university undergraduates about their sexual behaviour. How could we identify their beliefs about HIV transmission and their personal risk perception for HIV? How did their risk perception for HIV modify their sexual behaviour? What could we learn from the research that would inform HIV prevention programs at Canadian universities?

Our Approach: We recorded participants responses during focus groups sessions, transcribed the comments verbatim, and used the qualitative approach of thematic analyses to understand the results.

Key Findings: University undergraduates exhibited excellent knowledge about HIV, but deemed themselves at low risk. When condoms were used, it was for prevention of pregnancy, rather than for prevention of HIV transmission or the transmission of other sexually transmitted infections (STIs). Women were much more likely than men to insist upon condom use during sexual activity, but did so for the primary motivation of preventing pregnancy, and only secondarily for STI protection. Only women indicated that they would refuse sexual activity without the use of condoms, while men, even if they reported a preference for protected sex, would still engage in sex without condoms.

Impact on Policy and Practice: Results of this study suggested that the emphasis for HIV education and prevention with heterosexually-identified university undergraduates needs to be on increasing personal risk perception for HIV. University students need to be more aware of the risks involved in serial monogamy, and how that unprotected sexual practice increases their risk for exposure to HIV and other STIs. The risk of transmission of a variety of STIs need to be emphasized, and the exclusive focus of the risk of pregnancy needs to be broadened.

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STRESSORS AND WAYS OF COPING FOR WOMEN LIVING WITH HIV IN TORONTO AND HAMILTON

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Plain Language Summary: Excessive and sustained stress is physically and mentally unhealthy for people living with HIV. Stress can also quicken the progression of HIV to AIDS and prompt unhealthy behavior including decreased adherence to ARV medication. Women living with HIV are particularly vulnerable to stress. Given the social, political, historical and economic context in which they live, their exposure and vulnerability to stressful situations is particularly substantial and different from their male counterparts. It is therefore important to understand the stressful experiences faced by women living with HIV and the coping strategies they adopt.

Objective: The objective of this study is to qualitatively examine the stressors identified to be most recent and challenging by women living with HIV in Hamilton and Toronto. A secondary objective is to analyze the coping strategies adopted by these women within the context of the stressors to which they are responding.

Methods: Eight women living with HIV in Hamilton and Toronto who are currently participating in the wHEALTH study were asked to describe their most recent and challenging stressful experience during the wHEALTH baseline interview. Six consented. Each of these descriptions were analyzed using qualitative content analysis and NVIVO. These women were also asked to complete the Ways of Coping Questionnaire. This data was then analyzed according to the Ways of Coping Questionnaire Manual.

Results: Child-related problems and housing problems were the two key themes which arose from the stressor narratives. Child-related problems included conflict with child; desire to have a child and maternal disclosure of HIV status. Housing related problems involved mould and excessive noise. Four sub themes were also identified. These were, namely: partner-related problems, culturally appropriate services related to children, illness of other and of self. Each participant used a variety of coping strategies to address their stressor. The most common coping strategy used was seeking social support even when stressors were analyzed separately according to their main themes

Conclusions: When a sample of women living with HIV in Toronto and Hamilton were asked to describe their most recent and challenging experience, they spoke either of child-related problems or housing issues. Though these women used a variety of coping strategies, one of the main strategies used was seeking social support. These findings support the need for more targeted programs to help mothers (and women of childbearing age) living with HIV as well as the promotion of support-related services (i.e. case management and support groups) provided by local community-based AIDS organizations in order to alleviate the stress faced by these women.

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Women, Youth and HIV

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THE wHEALTH INTERVENTION PROJECT FOR WOMEN LIVING WITH HIV/AIDS

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Plain Language Summary: The Women's HIV Empowerment Through Life Tools for Health Project (wHEALTH) is a community-based research project (CBR) studying how peer case management affects the quality of life of HIV-positive women. The intervention works with participants to identify and utilize strengths and resources to address life challenges and will be compared to support programs offered by Voices of Positive Women. Peer case managers who understand the challenges faced by HIV-positive women will deliver the intervention. wHEALTH is guided by a multi-stakeholder research team who value CBR principles including equitable collaboration and capacity building.

The Challenge: HIV-positive women face not only a chronic illness and complex medical demands, but also extensive social challenges, including access to health care and community services, financial assistance, and social support. The risk for depression is significantly elevated in HIV infection and is associated with poor social support and quality of life. The HIV/AIDS paradigm shift from acute illness to chronic disease coupled with persisting stigma has enhanced the generation of multi-disciplinary care networks, including case management, to address the complex needs of PHAs.

Our Approach: This study will determine whether six-months of strength-based case management improves the quality of life of HIV-positive women. Secondary aims are to understand how a response to wHEALTH is associated with socio-demographic characteristics, psychological adjustment, coping and social support compared to services offered by Voices. 176 women will be randomized to receive either the wHEALTH intervention or the control condition. Outcome measures will be assessed at baseline, six and nine months. Qualitative data of women's experiences in wHEALTH will complement survey data. Recruitment commenced in June 2008.

Key Findings: wHEALTH Manual - A manual was developed to complement the case manager training and includes a wHEALTH delivery guide and worksheets for sessions with participants; Recruitment of peer case managers - Four HIV-positive women were hired and trained in the delivery of strength-based case management. One woman is based in Hamilton at McMaster University and three women are based in Toronto at Voices; Study recruitment - Recruitment and data collection are underway. 66 and 110 women will be recruited from the Hamilton and Toronto areas, respectively.

Impact on Policy and Practice: This project will provide evidence for developing innovative and culturally relevant support services for HIV-positive women. This intervention may identify effective ways to link HIV-positive women to community services, reduce social isolation, improve access to and retention in care and highlight how the social determinants of health impact health-related quality of life.

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DEVELOPMENT OF PSYCHOSOCIAL ASSESSMENT GUIDELINES FOR DETERMINING STRENGTHS AND NEEDS OF WOMEN WITH HIV AND THEIR FAMILIES DURING PREVENTION OF MOTHER TO CHILD TRANSMISSION (PMTCT) TREATMENT

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Plain Language Summary: During and after pregnancy, there are many possible stresses women with HIV go through that prevent their babies from getting HIV. Four HIV social workers from Canada and Kenya made a list of stressors based on their work with women and their families in this situation. We also reviewed over 450 studies but did not find any of which list the many possible stressors. We plan to ask women in Canada and Kenya about their problems and what helps them. Working with women, we will write guidelines which can be used by women, their families and counselors for use in support programming in low and high-income countries.

The Challenge: HIV-positive women going through PMTCT treatment, and their families, cope with complex psychosocial issues during and after pregnancy. As HIV counselors, we see a need for evidence-based psychosocial assessment guidelines to:
1) identify maternal/ family strengths, concerns and priorities;
2) provide information on psychosocial issues, raising awareness of "normal" concerns;
3) improve counseling with clients; and
4) develop support programs

Our Approach: Four HIV social workers providing counseling in Kenya and Canada developed a practice-based outline of psychosocial issues using the following headings: Mother and Infant Health in PMTCT Treatment; Stigma, Disclosure Decision; Mother's Mental Health and Well-Being; Father's Mental Health and Well-Being; Couple Relationships; Family HIV Issues; Income/Employment/Poverty/Health Care Costs; Migration/Resettlement; Social and Spiritual Support.
An interprofessional HIV team conducted an extensive literature review, examining peer reviewed publications and secondary literature and is developing a research plan.

Key Findings: There is very limited literature specific to HIV psychosocial issues during PMTCT. The main issues identified are: maternal depression, coping with stigma and disclosure decisions, concerns about infant HIV status and infant feeding. We did not find any evidence-based psychosocial assessment guidelines or published studies exploring the range of issues identified in our emerging guidelines. Gaps in the literature include the immensity of maternal stress and complex, multiple issues for women and their families. Using focus group methodology, our research team plans to refine, pilot and evaluate our assessment guidelines.

Impact on Policy and Practice: Our evidence-based guidelines will be widely applicable, internationally, for: 1) policy and program development and awareness-raising; 2) counseling and self-help programs for women going through PMTCT treatment and their families

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STREETLIVES ARTWORK: ARTS-INFORMED HARM REDUCTION WITH STREET INVOLVED YOUTH IN THUNDER BAY

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Plain Language Summary: Artwork/Streetlives is a community based, arts-informed, ethnography, which addressed the results of the 2005 Street Youth Drug Questionnaire in Thunder Bay. Nine street involved participant researchers were supported by a research team. They used art and story to come to specific conclusions, and to act on the risks specific to street involved youth in Thunder Bay.

The Challenge: To demonstrate visually though art making, the risks specific to street involved youth in Thunder Bay, and to use this process as a way of coming to specific actions that will positively impact the lives of participants and their peers.

Our Approach: Our approach was to gather a representative group of Street involved youth. This group included currently or formerly street involved youth 16-26, from Thunder Bay, Ontario. These included 7 Aboriginal participants, 5 male and 5 female, 3 queer, 4 parents, 5 IDUs, all used street drugs, 3 people who have done sex work, all have experienced unstable housing. We met once per week for seven months to make art and move through phases of rapport building, data collection, data analysis, and action.

Key Findings: 1. That street involved youth are particularly vulnerable to the social services and law enforcement systems. They wish to be better understood and treated more respectfully, and they would like to use their art as a teaching tool with these populations.
2. That meeting weekly to do art, and being involved in presenting their work was both gratifying and therapeutic, and that they did not want to stop meeting on Wednesday nights.
3. That the risk of losing children is both a source of increased vulnerability, and a barrier to treatment, and they wanted to do some further work on how treatment can be provided in ways that do not involve their children being in the custody of child protection.
4. That their art also contained strong prevention messages that they could have learned from as younger people, and as such they wished to use their art as an educative tool with young people.

Impact on Policy and Practice: This project will have significant impact on the practice of law enforcement and social work in Thunder Bay, through education by participant researchers. This project will work to impact treatment policy and practice for IDUs who are parents.

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HIV POSITIVE ADOLESCENTS' PERSPECTIVES ON SEXUAL HEALTH AND DISCLOSURE ISSUES AND NEEDS: A MIXED METHODS APPROACH

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Plain Language Summary: This poster presentation will provide information on doctoral research to be conducted using a mixed qualitative and quantitative approach to explore the sexual health concerns and disclosure needs of perinatally infected HIV positive adolescents and to explore, for comparative purposes, the sexual health concerns and disclosure needs of a group of age-matched adolescents with type 1 diabetes, as well as the sexual health concerns and needs of a comparison group of age-matched adolescents without a chronic illness. Clarification of sexual health needs and available and needed but unavailable support services will be explored. Since minimal research has focused upon the sexual development needs of HIV+ adolescents in Canada, little is known about their sexual health issues and needs.

Objective: The objectives of my PhD research are to: 1) Obtain the perspectives of perinatally infected HIV+ adolescents, a comparison group of age matched adolescents with type 1 diabetes, and a comparison group of age-matched adolescents without a chronic illness, concerning sexual health and disclosure needs; and 2) Determine available and needed but unavailable support services. The purpose of the comparison groups is to determine which perceived needs of HIV+ adolescents are similar to those of other chronically ill adolescents, or all adolescents in general, and which are distinctive to the group of perinatally infected HIV+ adolescents.

Methods: In this study, 20 HIV+ adolescents infected perinatally, 14-17 years of age and 20 age-matched adolescents with type 1 diabetes will be recruited from The Hospital for Sick Children patient population, and 20 age-matched adolescents without a chronic illness will be recruited through family physicians in Toronto to participate in in-depth semi-structured interviews. Following the qualitative interviews, participants will be asked to complete a questionnaire to determine what services are available to them and what services are needed to help support their sexual health concerns and disclosure needs. NVivo, a qualitative computer software program will facilitate data analysis. Statistical analysis of the questionnaires will be conducted using SPSS.

Results: This poster presentation will address: the purpose of the study, theoretical framework, study design, data collection, and analysis strategies to be used in the proposed doctoral research.

Conclusions: This research is intended to enhance our ability to create and implement education, support, and prevention programs tailored specifically to the sexual health and disclosure needs of adolescents, as well as minimize the risk of HIV transmission. This research may also provide direction for research exploring the concerns and needs of HIV infected adolescents in endemic infection populations.

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HIV RISK & HIV TESTING BEHAVIOURS AMONG SOUTH ASIAN CANADIAN YOUNG ADULTS: THE ROLE OF SOCIAL CONTEXT AND INDIVIDUAL-LEVEL VARIABLES

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Plain Language Summary: The current study examined correlates of HIV risk and testing behaviours among South Asian young adults. Findings suggest that less religiosity and more positive emotions about sexuality were associated with unprotected sex and being sexually active.

Objective: It is important to examine HIV risk factors among under-examined ethnic groups such as the growing South Asian population. Researchers emphasize the importance of examining both social context variables (e.g., religion) and individual-level variables (e.g., HIV knowledge) when examining health behaviours in ethnocultural groups. This study examined social context and individual level correlates of three HIV-related behaviours in a sample of South Asian young adults.

Methods: 106 South Asian undergraduate students completed self-report measures including demographic variables, other social context variables, (e.g., religiosity and acculturation) and individual-level variables including, HIV-testing attitudes, AIDS self-relevance (i.e. the extent to which AIDS is perceived to be relevant), erotophilia (i.e. the tendency to respond positively to sexual stimuli), and HIV knowledge. Participants also reported if they had 1) ever engaged in vaginal intercourse, 2) engaged in unprotected vaginal intercourse (UVI) in the past six months, and 3) ever had an HIV test.

Results: 28% of participants had engaged in vaginal intercourse, 11.3% had UVI in the past six months and 11.3% had been tested for HIV. Among sexually active participants, 40% engaged in UVI and 13.3% had been tested for HIV. Multiple regression analyses revealed that only higher erotophilia was uniquely associated with a having engaged in any vaginal intercourse and UVI ($p = .001$; $p = .03$). Further, when we controlled for erotophilia, the association between religiosity and vaginal intercourse was significantly reduced, suggesting that erotophilia partially mediates this relationship. Similarly, the relationship between religiosity and UVI was eliminated when we controlled for erotophilia, suggesting that erotophilia completely mediates this relationship. For HIV testing behaviour, having positive attitudes towards HIV testing was uniquely associated with increased likelihood of being tested ($p = .03$).

Conclusions: Results highlight the importance of considering both social context and individual level variables when examining HIV risk among South Asians. Clinicians and prevention workers treating South Asian young adults should attend to the potential influence of religiosity and erotophilia on HIV-related behaviours. They should also be aware that although South Asians may engage in sexual intercourse at a later age, those who are sexually active are equally likely to engage in risky sex (i.e., UVI) compared to mixed ethnicity samples (Rotermann, 2005).

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TRAINING YOUTH IN RESEARCH TECHNIQUES: PERFORMING A LITERATURE REVIEW

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Plain Language Summary: We present the methodology used to train youths (age <18) to participate in research as literature review writers. A four-component process was implemented to train youth to conduct literature reviews that included initial background reading, library training sessions, community organization visits and writing and analysis, all under the supervision of a graduate student.

The Challenge: As the importance of community-based research is becoming increasingly recognized, innovative methods for increasing community capacity to conduct research are constantly needed. When working with groups such as youth, specific strategies need to be developed to ensure effective capacity building. This project's objectives were to train youth interested in sexual health peer education in the production of literature reviews.

Our Approach: As part of a project entitled, "Building capacity to conduct community-based research on evaluating youth sexual health peer education," two youths (aged <18) were hired for a four-week period in the summer and trained to conduct two literature reviews. A postgraduate student was also hired from York University to supervise and train the youths. This process was divided into four phases: 1) background reading of a series of identified articles; 2) training workshops on developing research techniques hosted by the University of Toronto's Robarts Library and then the application of these skills to search for relevant articles; 3) visits to a variety of local community organizations to enhance the youths' understanding of HIV and sexual health services; 4) critical analysis of the existing literature, a more thorough search based on identified gaps and the writing and revision of the literature reviews.

Key Findings: Two literature reviews were developed to examine: 1) levels of sexual health education among Canadian youth and their attitudes concerning HIV and people living with HIV and 2) sexual health peer education programs and methods of evaluation. The literature reviews were written in language that was more accessible to both community agencies working with youth and youth themselves.

The youth involved in this project gained valuable skills including library search strategies, critical appraisal of research and academic writing and referencing techniques. In addition, youth also were able to gain experience in working with and learning about community organizations.

Impact on Policy and Practice: This project demonstrates that youth can be trained in research techniques and can contribute greatly to the research process. As community-based research becomes increasingly popular in the field of HIV and sexual health, age should not be a factor that excludes community members from meaningful participation in research.

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CREATING HOPE: A PSYCHOSOCIAL INTERVENTION FOR YOUNG CHILDREN INFECTED AND AFFECTED BY HIV/AIDS

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Plain Language Summary: Conducting research with children infected and affected by HIV/AIDS aged three to five, their caregivers, and their intervention providers reveal areas that make psychosocial interventions successful. Young children infected and affected, who rarely receive this type of health care are benefited psychosocially when intervention programs include:
1) combining social services with childcare
2) implicit ecological perspectives of staff, and their knowledge of HIV-related variables
3) positive relationship development throughout the intervention program

These, combined with additional recommendations developed through analysis, validate the need for psychosocial intervention, and enable insight into best-practice approaches for serving this young population of children infected and affected by HIV/AIDS.

The Challenge: To understand what makes a successful psychosocial intervention program for children aged three to five, who are infected and affected by HIV/AIDS, according to children, their caregivers, intervention providers, and the researcher.

Our Approach: An ethnographic study of an intervention program in the southern United States was conducted in an attempt to understand what makes psychosocial intervention successful for children infected and affected, from the perspective of the children, their caregivers, and their intervention providers. Interviews and observations with all three groups took place over a three week period. Results were analyzed from an ecological and rights-based perspective.

Key Findings: Qualitative analysis suggests that combining social services with a childcare program, the implicit ecological perspective of staff and their knowledge of HIV-related variables, and the development of positive relationships are essential components of a successful psychosocial intervention program. Recommendations for effective practices are made, and future research needs are discussed.

Impact on Policy and Practice: This study reveals findings from the voices of children, their family members, and service providers, in addition to an educated researcher. This validates the rights of the child and may encourage the participation of young people when developing health care policies.

The lack of psychosocial research and services available to this population of children, under the age of six, suggests its rarity and reveals the void of information known about it, thus adding to the importance of this study. Findings show successful components of psychosocial intervention for young children infected and affected by HIV/AIDS, which may shape the policy and practice of current services for this young population, and provide a model for future programs in Canada.

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