Monday, November 3, 2003 11:30 a.m.

Local and Global Issues

LG1-1

ACCESS TO HIV TREATMENT IN RUSSIA: BARRIERS AND OPPORTUNITIES

William Flanagan, Queen's University.

Track/Theme: Sociobehavioural/Local and Global Issues.

Plain Language Summary: This paper examines available evidence on the number of people with HIV in Russia who require treatment (over 20,000 and a figure that will rapidly increase in the near future) and compares that to the estimated number of those receiving treatment (no more than 2000). The paper examines the various barriers to treatment in Russia, including cost, lack of political will, stigma, and a poorly developed capacity to treat. The paper then considers the various opportunities that may be available to Russia to increase access to treatment, including increased capacity to negotiate price reductions, efforts to increase domestic production or import generics, and efforts to build the political will to address Russia's treatment needs.

Objectives: To examine the barriers to treatment in Russia and to explore options to increase access to treatment.

Methods: Methods include a series of interviews conducted in Moscow in July 2004 with leading policy makers, domestic and foreign pharmaceutical companies in Russia, leading Russian NGO's, UNAIDS and WHO representatives in Moscow, and Russian government officials, with a view to identifying key barriers to treatment and key opportunuties to increase access. Methods also include an analysis of measures taken in other resource poor settings to increase access to treatment, particularly Brazil, with a view to assessing the extent to which these measures may be of use in Russia.

Results: Russia faces a number of severe barriers to treatment, not all of which are economic. Other barriers include a lack of political will, a poor capacity to plan for treatment needs, a weak capacity to negotiate appropriate price reductions, a lack of interest in domestic production on the part of both government and industry, and a weakly developed NGO sector with limited capacity to press for policy change.

Conclusions: Russia will soon face an exploding need for HIV treatment and is currently poorly equipped to face this challenge. Nonetheless, Russia has the basic infrastructure to treat people with HIV, including a functioning public health system and domestic pharmaceutical capacity, that could be enhanced to provide treatment to many thousands of Russians. Russia can also learn from other resource-poor settings, notably Brazil, to assist in the development of low cost strategies to increase access to treatment.

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LG1-2

STIGMA OF INJECTION DRUG USE AND ITS ROLE IN FUELING HIV AND HEPATITIS C EPIDEMICS IN RUSSIA: AN URGENT NEED FOR LEADERSHIP AND RESOURCES

Liviana Calzavara HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto and Department of Public Health Sciences; Alexy Yakovlev, Botkin Hospital, St. Petersburg, Russia; Tatiana Nikitina, Provincial AIDS Centre, Kaliningrad, Russia; Galina Volkova, Marina Michalchenko, Vinay Saldahna, Canada AIDS Russia Project (CARP), St. Petersburg, Russia; Victoria Orekhovsky, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto.

Track/Theme: EpidemiologySociobehavioural/Prevention and EducationLocal and Global Issues.

Objectives: Russia has the highest rate of HIV transmission in the world. Over 90% of the new infections are among the estimated 2 million IDU. A research project was initiated to understand the causes of the escalating HIV and HCV epidemics, and identify how to halt the spread, and improve prevention and care.

Methods: Focus groups and questionnaires were used to collect data from 63 male and female IDUs. Participants were recruited through service organizations, health care centres, and word-of-mouth.

Results: Mean age was 25 years. 49% were females, 21% were divorced or separated, 52% were unemployed, 48% reported being infected with HIV, and 56% with HCV. Mean age first injected was 18 years (range = 12-46). Heroin was the most commonly used drug (93%). Over 70% injected 6+ times/week, 73% shared needles, and 85% shared with 2 or more people. Needle exchanges were uncommon and use was limited by fear of arrest or disclosure. 33% had been arrested for drug-use. Methadone programs were illegal and existing treatment programs limited. Over 70% reported 2 or more partners in the last year, and 66% never or rarely used condoms. Only 19% of those infected with HIV/HCV/STI always used condoms, and 69% shared needles. Fear of stigma and discrimination lead to low disclosure of infections and IDU. IDUs stressed the importance of educating youth, medical professionals, police and the general public about drug use; providing effective treatments and harm-reduction; and enforcing laws (drug-trafficking, rights of individuals).

Conclusions: The transition from communism to a market economy and the globalization of the drug market have resulted in dramatic increases in the number of IDU and associated negative consequences. Action is urgently needed but is hindered by the failure to understand the seriousness of the IDU problem, by the lack of resources available, and the existing punitive attitudes toward IDUs.

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ONLINE AND WIRED: USING THE INTERNET AS A TOOL FOR REACHING POSITIVE YOUTH

Sarah Flicker TeenNet, University of Toronto, Public Health Sciences; Alex McClelland, Positive Youth Outreach; Tiffany Veinot, CATIE; Stan Read, Eudice Goldberg, The Hospital for Sick Children; Harvey Skinner, U of T, Public Health Sciences.

Track/Theme: Sociobehavioural/Health Services and Access to CareCare and TreatmentPrevention and EducationLocal and Global Issues.

Plain Language Summary: We interviewed 37 HIV-positive youth (12-25) across Ontario and asked them about their experiences being young and positive. Specifically, we were interested in what could be done to better support them and their needs. Generally, we found that young people used the net with regularity. In fact, 92% of those interviewed, were on the web at least once a week. While few currently used the net for health information purposes, many expressed interest in more targeted, youth-friendly web based HIV resources. Nearly, all the youth we spoke to feel excited about the idea of website dedicated to positive youth in Canada, and have said that they would use such a Web site.

Objectives: Half of all new HIV infections occur among young people. As of June 30, 2002, more than 13,000 youth and young adults were documented to be living with HIV in Canada. Despite this alarming growth, there is a profound lack of resources for Canadian HIV-positive youth. This project aimed to talk with a diverse group of positive youth about their experiences and what can be done to better support them.

Methods: The Positive Youth Project uses a community-based participatory research model to address the needs of positive youth in Canada. A stakeholder group of HIV+ youth and supporting professionals collaboratively developed the research design, instruments and protocol. Thirty seven key informant interviews were conducted with a broad spectrum of HIV+ youth in Ontario. Interviews were taped and transcribed. A grounded theory interpretive approach guided analyses. Data were coded using Nudist qualitative software. The stakeholder group met regularly to generate themes emerging from the data and discuss their meaning, relevance and implications.

Results: The Internet has an unprecedented potential reach, it can: reach people isolated geographically or by stigma, facilitate repeat use of materials, be available at the time of need, be anonymous, be interactive and community-building, and it is available internationally. HIV Positive youth are online and are savvy web users. This is an opportunity to connect with young people and allow them to connect with each other.

Conclusions: The Internet has an unprecedented potential reach: it can reach people who are isolated geographically or by stigma, it can facilitate repeat use of materials, it is available at the time of need, it is anonymous, it is interactive and community-building, and it is available internationally. HIV Positive Youth are online and are savvy web users. This is an opportunity to connect with young people and allow them to connect with each other.

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LG1-4

WHAT GOOD IS MULTI-DISCIPLINARY RESEARCH ANYWAY?: THE POLARIS EXAMPLE

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Track/Theme: Clinical Epidemiology Sociobehavioural/Health Services and Access to CareCare and Treatment Prevention and Education Immunology and VirologyLocal and Global Issues.

Objectives: To describe the use of multidisciplinary research to guide future research and influence prevention, care and treatment.

Methods: Polaris is a longitudinal open-cohort study of recent seroconverters and HIV-negative controls in Ontario. Its objectives are to understand HIV transmission; the behavioural, psychological, economic and social impact of HIV; and the clinical course of early infection and therapy. Data sources include quantitative and qualitative interviews, medical-chart reviews, blood tests, and the HIV diagnostic-testing database.

Results: Polaris has contributed to our understanding of the HIV epidemic. It was the first Canadian study to identify an increased HIV-incidence among MSM in 1996 (Calzavara et al. AIDS 2002). These results contributed to increased community awareness and discussion about HIV (e.g. community forums/meetings, Ontario MSM Situation Report, media coverage), and the development of prevention programs (e.g. “Welcome to Condom Country”). Results highlighted the need for research to monitor the epidemic over time and what fuels it. The finding that delayed application of condoms pose as much risk for infection as unprotected receptive anal sex (Calzavara et al. American Journal of Epidemiology 2003) assists in refining messages and dispel myths about pre-ejaculate. Polaris is currently conducting an investigation on the biological mechanisms of HIV transmission in pre-ejaculate. Polaris also found that symptoms associated with primary infection are a significant reason for HIV testing and diagnosis. For some, symptoms are a more important motivator for testing than risk experiences. Better recognition of symptoms of primary infection by patients/physicians could lead to improved diagnosis of seroconversion, opportunities for early HAART, and prevention of transmission (Burchell et al. International Journal of STD & AIDS 2003).

Conclusions: The interdisciplinary and community-based approach used has made significant contributions to HIV knowledge and received international recognition. The study was recently adapted for use in Russia to better understand their HIV epidemic.

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Advances in HIV Replication

AHR-1

CONTROL OF HIV-1 ENV RNA PROCESSING AND TRANSPORT

Alan Cochrane University of Toronto; Kengo Asai, University of Toronto.

Track/Theme: Basic/Immunology and Virology.

Plain Language Summary: The expression of proteins (the building blocks of life) requires processing and transport of RNA. This study focusses on unique features of HIV-1 RNA processing and transport that may provide insight for novel therapeutics.

Objectives: The objective of this study is to examine the effect of ESS3 on RNA processing and transport of HIV-1 env RNA.

Methods: Methods used in this study include: RT-PCR RNAse Protection Assay Immunofluorescence In situ hybridization

Results: Analysis of the ESS3 within the terminal tat/rev exon demonstrates an inhibitory role on splicing, 3' end formation, and Rev-mediated transport.

Conclusions: The inhibition of cleavage and polyadenylation by ESS3 results in an inhibition of Rev-mediated transport of env RNA. Rev-mediated export can be rescued upon expression of Sam68, which increases 3'end formation of env RNA.

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AHR-2

GILA MONSTER-DERIVED PEPTIDE INHIBITS HIV-1 INFECTION

Payman B. Bokaei Canadian Blood Services; Xue-Zong Ma, University of Toronto; Darinka Sakac, Donald R.Branch, Canadian Blood Services.

Track/Theme: Basic/ Care and TreatmentImmunology and Virology

Plain Language Summary: Certain proteins that are on the surface of cells are called receptors. Two of these receptors called VPAC1 and VPAC2. They have different functions and sometime they act in opposite manner. Recently, it has been shown that VPAC1 helps HIV infection. In this study we have shown that VPAC2 can inhibit HIV infection. We used a peptide, which originally isolated from the Gila monster lizard, called helodermin. This peptide can preferentially stimulate VPAC2 receptor. Indeed, by VPAC2 stimulation HIV infection can be inhibited among different cells. This approach may lead to a novel strategy to prevent HIV/AIDS.

Objectives: Objective: The VPAC neuroendocrine receptors, VPAC1 and VPAC2, belong to the class 2 subfamily of seven transmembrane G protein-coupled receptors. Recent studies from our laboratory have shown that VPAC1 is a potent facilitator of HIV-1 infection; however there are no studies on VPAC2 for HIV/AIDS. Reports have shown VPAC2 to have opposite function to VPAC1 due to signaling differences. Thus, we hypothesized that VPAC2 may have an opposing effect to VPAC1 in HIV infection

Methods: Methods: Jurkat T cells expressing VPAC2, were treated with 5x10-5M helodermin prior to infection with HIV-1IIIB. Helodermin is a 32 amino acid peptide originally isolated from the Gila monster lizard (Heloderma horridum/suspectum). Helodermin acts as an agonist for VPAC2 stimulation. Productive HIV-1 infection was monitored by p24 ELISA over time of culture. The VPAC2 cDNA was cloned from human SupT-1 lymphoma cells and optimized for codon usage, based on that used by Rhodopsin, to insure maximum expression of the receptor. Hut78 cells, which do not expressVPAC2, were transiently transfected with optimized VPAC2 cDNA to over-express VPAC2

Results: Results: Helodermin inhibitory effect was dose dependent (100% inhibition at 5x10-4 and 50% at 5x10-5 M). In addition to pretreatment with helodermin, we found that helodermin was inhibitory for HIV-1 infection when cells were treated during the infection or treatment was post-HIV-1 infection. Thus helodermin treatment appears to inhibit initial as well as established HIV-1 infection, presumably through a signal transduced by VPAC2. Indeed, VPAC2-transfected Hut78 cells when treated with helodermin showed a 40% decrease in HIV-1 infection compared to cells transfected with empty vector or untransfected cells. Inhibition of HIV-1 infection by helodermin was shown to be independent of viral entry, cell growth, or apoptosis.

Conclusions: Conclusion: These results suggest that agonists that stimulate VPAC2 may act to inhibit HIV-1 infection and thus, could provide a novel therapeutic strategy to prevent HIV/AIDS.

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AHR-3

A NOVEL SOLUBLE MIMIC OF THE GLYCOLIPID, GLOBOTRIAOSYL CERAMIDE INHIBITS HIV INFECTION

Nicole Lund Canadian Blood Services; Donald Branch, Xue-Zhong Ma, Darinka Sakac, Canadian Blood Services; Murugespillai Mylvaganam, Davin Chark, Beth Binnington, Clifford Lingwood, Hospital for Sick Children; Jacques Fantini, Institut Méditerranéen de Recherche en Nutrition; Anu Puri, National Cancer Institute; Robert Blumenthal, National Cancer Institute.

Track/Theme: Basic/Care and Treatment /Immunology and Virology.

Plain Language Summary: Glyscosphingolipids (GSL) are lipid(fat)-sugar conjugates within the cell membrane, that are required for HIV infection. We have made soluble derivatives of several GSLs that are able to bind to an outer surface HIV protein called gp120. The modified GSL globotriaosylceramide, called adamantylGb3, inhibits HIV fusion and infection in the test tube, irrespective of the type of HIV. Other modified GSLs, adamantyl galactosyl ceramide and adamantly sulfogalactosyl ceramide, have not been able to inhibit HIV infection in the same way. AdamantylGb3 could therefore provide a basis for a new approach to treatment of HIV/AIDS.

Objectives: Previously, we found that a novel soluble analogue of the glycosphingolipid, globotriaosylceramide (Gb3), involved in HIV/host cell fusion, is a highly effective ligand for HIV gp120 in vitro. Additionally, this mimic, adamantylGb3, inhibits fusion and syncytium formation by HIV-1 and HIV-2. We also showed that adamantylGb3 inhibits HIV infection of Jurkat T-cells in vitro. We have now investigated the potential for adamantylGb3 and other glycosphingolipid analogues, namely adamantyl galactosyl ceramide (GC) and adamantyl sulfogalactosyl ceramide (SGC), to prevent T-cell- and Monocyte-tropic HIV-1 infection of primary cells in vitro.

Methods: Using Jurkat T-cells, we investigated the ability of adamantylGb3, adamantylGC and adamantylSGC to inhibit HIV-1IIIB infection in vitro. Peripheral blood-derived mononuclear cells (PBMCs) were isolated and used to determine if adamantylGb3 prevented infection with HIV-1IIIB (T-tropic) or HIV-1Ba-L (M-tropic). Similarly, adamantylGC and adamantylSGC were tested.

Results: Within the same dose range that syncytium formation was inhibited, adamantylGb3 blocked productive HIV-1IIIB infection in Jurkat and peripheral blood-derived T-cells. Similarly, HIV-1Ba-L infection of PBMCs was blocked. AdamantylGC and adamantylSGC inhibited HIV-1IIIB infection of Jurkat, but not primary cells. In fact, adamantylGC elicited an opposite effect, causing a dose-dependent increase in HIV infection of PBMCs, while adamantylSGC had no effect.

Conclusions: Our findings show that adamantylGb3 is a powerful inhibitor of T- and M-tropic HIV-1 infection in vitro, likely functioning at both HIV binding and membrane fusion. With primary cell HIV-1 infection, inhibition appears to be exclusive. In comparison, adamantylGC and adamantylSGC did not inhibit primary cell infection. The different outcome elicited by adamantylGC and adamantylSGC on Jurkat versus primary cell infection, may be due to the transformed nature of Jurkat T-cells. Thus, testing these analogues in primary cells is essential to understanding effects on HIV infection in a physiological setting. In conclusion, adamantylGb3 may prove an effective new strategy in treatment and prevention of HIV infection.

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AHR-4

STRUCTURE AND FUNCTION ANALYSIS OF HUMAN TRA2ALPHA AND TRA2BETA

Jodi Bubenik Dept. of Molecular and Medical Genetics, University of Toronto; Craig Platt, Tina Rajabian, Alan Cochrane, Dept. of Molecular and Medical Genetics, University of Toronto.

Track/Theme: Basic/Immunology and Virology.

Plain Language Summary: Rev plays an essential role in the the viral lifecycle in that it is required for production of the viral structural and enzymatic proteins.The correct processing of viral RNA is also a requirement for successful viral replication. Altering the state of the infected cell to make it unable to support either Rev function or viral RNA processing would inhibit progression of the viral lifecycle. It has been shown that host cell factors can affect Rev activity and RNA metabolism in different ways, including Tra2alpha and Tra2beta. If we can determine the mechanisms by which these human factors regulate Rev function and viral RNA processing, we can generate new ways to inhibit progression of the virus.

Objectives: To charaterize the Tra2alpha and Tra2beta domain requirements for RNA splicing, protein localization and protein shuttling.

Methods: RT-PCR was used to analyze the effect of the Tra2 proteins on splicing of the fibronectin gene. Immunofluorescence was performed on transfected human cell lines to determine localization of the proteins. Heterokaryon experiments followed by immunofluorescence were used to determine the shutlling capacity of the Tra2 proteins and their mutants.

Results: We demonstrate that either RS domain is required for association with nuclear speckles. Tra2a and Tra2ß are capable of shuttling between the nucleus and cytoplasm and either RS domain is sufficient to impart shuttling activity. Overexpression of Tra2a or Tra2ß was observed to promote exclusion of the alternative EDA exon in a fibronectin minigene system. This activity was found to be independent of exon splicing silencer and enhancer elements present within the EDA exon. Furthermore, the ability of the N-terminal mutant of Tra2a but not the C-terminal mutant of Tra2a to alter the inclusion ratio of the EDA exon indicates that the two RS domains of Tra2a are not functionally equivalent.

Conclusions: The two RS domains found in the Tra2 proteins are required for different functions of the protein.

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Return To Work And Employment Issues

RWEI-1

A LONGITUDINAL STUDY OF THE ROLE OF WORKPLACE FACTORS IN WORKER TURNOVER, RETENTION AND DEPLOYMENT

Robin Weir Investigator, CLEAR Unit, McMaster University; Alex Berry, Former Executive Director, AIDS Committee of London; Peter Hayes, Executive Director, AIDS Committee of London; Jacqueline Roberts, Joan Crook, Investigators, CLEAR Unit, McMaster University.

Track/Theme: Sociobehavioural/Health Services and Access to Care

Plain Language Summary: The changing face of HIV/AIDS work has had an impact on the focus and range of activities that CBAOs address. This beginning change has begun to affect the retention of, recruitment to and rewards for staff and volunteer employees. The shift in work emphasis from a more direct supportive role to a more distant role in terms of type of involvement may ultimately affect staff's sense of meaningful work.

Objectives: The purpose of the study was to attempt to capture some of the changes in CBAOs work, work assignments and work environment through answering the following study questions: 1) What work place factors were associated with volunteers and paid staff's satisfaction with their work; and 2) what types of activities characterized the role of volunteers and paid staff.

Methods: This was a cross-sectional longitudinal survey in which paid and volunteer workers took part in 2 telephone interviews in which a structured questionnaire was administered that assessed the social environment of the work setting, their specific and general work activities, their reason for working at CBAO, their styles of coping, their work satisfaction and length of employment. Comparisons of responses between time 1 and time 2 were calculated and multiple regression analyses were done to identify predictors of work life quality.

Results: Of the 77 voluntary and 10 paid workers who completed the measures at time 1, 46 of the volunteers and 8 of the paid workers completed the interview 1 year later at time 2. The findings indicate a positive relationship between the social dimension of work and work satisfaction. This very satisfied work force's expectations for their work were met and their motivation to remain at this CBA) were high on the relationship, personal growth and system aspects of work.

Conclusions: This study identifies the importance of the intraorganizational attributes that seem to characterize the capacity of this CBA, and the outcomes of retention and satisfaction with work. Further longitudinal studies are required to examine the factors that contribute to the stability of the staff and volunteers labor force and to the effectiveness and efficiency of service programs.

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RWEI-2

EMPLOYMENT STATUS IS ASSOCIATED WITH HEALTH-RELATED QUALITY OF LIFE IN HIV/AIDS

Sergio Rueda St. Michael's Hospital Mental Health Service and Inner City Health Research Unit; Sean B. Rourke, St. Michael's Hospital Mental Health Service and Inner City Health Research Unit.

Track/Theme: ClinicalEpidemiologySociobehavioural/Health Services and Access to CareCare and Treatment

Plain Language Summary: Lower health-related quality of life in HIV/AIDS is associated with unemployment, length of time out of the workforce, having more symptoms, advanced HIV disease, and neurocognitive impairment.

Objectives: The aim of the study is to evaluate the relationship between employment status and health-related quality of life (HRQOL) in HIV/AIDS.

Methods: A total of 210 adult participants (80% unemployed) completed questionnaires to assess HRQOL (MOS-HIV) and depression (Beck Depression Inventory). A structured interview was used to determine employment status, HIV disease markers (CD4 counts and HIV disease severity), and number of medical symptoms. Neurocognitive tests included: Digit Span (attention), CVLT (learning efficiency) and Symbol Digit Modalities (processing speed). Hierarchical linear regression analyses were employed to evaluate the contribution of employment status to the PCA-derived Mental and Physical Health Summary Scores of the MOS-HIV, after controlling for (a) demographics (age, ethnicity, education, and time off work), (b) HIV disease markers (CD4 counts and CDC-93), (c) symptomatology (depression and medical symptoms), and (d) neurocognitive function (attention, learning efficiency, and processing speed).

Results: In the final model, significant factors associated with HRQOL included: (1) Mental Health Summary Score: Total model R2 = 0.59; depression only significant predictor. (2) Physical Health Summary Score: Total model R2 = 0.42; R2 changes: demographics (0.10), HIV disease markers (0.07), symptomatology (0.17), neurocognitive function (0.03) and employment status (0.05).

Conclusions: Employment status is significantly associated with physical health dimensions of HRQOL over and above those effects attributable to demographic characteristics, HIV disease markers, symptomatology, and neurocognitive function. Prospective studies are needed to determine the direction of causality in the relationship between employment status and HRQOL.

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RWEI-3

PHAS AND RETURN-TO-WORK PROGRAMS: URGENT NEEDS, HIGH EXPECTATIONS AND MODEST OPPORTUNITIES

Winston Husbands, AIDS Committee of Toronto.

Track/Theme: Sociobehavioural/Care and Treatment.

Plain Language Summary: PHAS participating in a return-to-work program have a strong desire to become employed, but expect specific kinds of assistance to prepare them for employment. Participants benefit from the program in very practical ways, and also experience a high degree of emotional support. However, despite their high expectations and the support they receive in the program, relatively few participants move into the workforce and most continue to feel hampered by their income support programs. A more open process of program development can resolve this dilemma.

Objectives: To determine the extent to which a return-to-work program meets the needs and expectations of PHAs who want to re-enter the workforce.

Methods: The data are from a needs analysis of Employment Action (EA), a program of the AIDS Committee of Toronto (ACT) and Toronto People with AIDS Foundation (TPWAF). Data collection methods were (a) a survey of active and inactive EA clients, (b) focus groups with active and inactive clients, and (c) personal in-depth interviews.

Results: The majority of EA clients are men in their 30s or 40s with college or university education, who were employed for long periods prior to an HIV diagnosis, and whose income comes mainly from provincial income support programs. Within EA, they benefit from specific kinds of assistance to help them re-enter the workforce (e.g., help/advice writing a resume, advice on their income support programs, job search and interview skills, etc). However, few actually find jobs and most are unable to resolve return-to-work issues with their income support programs.

Conclusions: EA clients have high expectations. The program has either raised expectations or reached out to PHAs whose expectations are considerable. However, the program functions according to more modest objectives. ACT and TPWAF are attempting to resolve this contradiction with a more open process of program development.

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RWEI-4

DISABILITY AMONG PEOPLE LIVING WITH HIV IN BRITISH COLUMBIA: THE UNACKNOWLEDGED EPIDEMIC

Peter Williams, Canadian Working Group on HIV and Rehabilitation; M.Rusch, K. Chan, B. Hogg, B.C. Centre for Excellence in HIV/AIDS; S Nixon, University of Toronto; A. Schilder, P. Braitstein, B.C. Persons With AIDS Society/ B.C. Centre for Excellence in HIV/AIDS.

Track/Theme: ClinicalSociobehavioural/Care and TreatmentLocal and Global Issues

Plain Language Summary: This study of 762 people living with HIV (PHAs) in British Columbia (BC) looks at how much they experience impairments (symptoms), activity limitations (challenges in daily tasks), and participation restrictions (challenges with usual social roles) affect). The study indicates high levels of impairment, activity limitation and participation restriction among PHAs in BC, and that the rate of activity limitations is much higher among PHAs than the general population. This is one of the first attempts to quantify impairments and life challenges faced by people living with HIV.

Objectives: (1) To characterize the prevalence of impairments, activity limitations and participation restrictions among people living with HIV in British Columbia (BC) and (2) to compare levels of activity limitation with the general BC population.

Methods: In 2002, the BC Persons With AIDS (BCPWA) Society and BC Center for Excellence in HIV/AIDS surveyed people living with HIV in BC. Following the International Classification of Functioning, Disability and Health (WHO, 2001), data were collected regarding diagnoses, impairments (symptoms), activity limitations (challenges in daily tasks), and participation restrictions (challenges with usual social roles). Activity limitation questions on the 1999 National Population Health Survey were used to compare people living with HIV to the general BC population. Age standardized rates were calculated for the general population to determine standardized prevalence ratios (SPR) for activity limitation.

Results: 762 people living with HIV completed the survey. Mental health diagnoses were reported by 62.9% (N=479) of participants. At least one impairment was reported by 91.5% (N=697). Mental impairment was reported by 78.2%(N=596), sensory impairment by 71.9% (N=548), neuromuscular impairment by 49.5% (N=377), and systemic impairment by 81.0% (N=617) of participants. A total of 284 (37.3%) reported moderate/severe HIV-related pain. Activity limitation was reported by 80.6% (N=607). Six hundred ninety-nine (93.2%) reported some level of participation restriction. The SPR for activity limitations among male participants using rates of limitation among the general population of BC as the standard was 9.41 (8.39 – 10.55); the SPR for women was 9.86 (7.19 – 11.05).

Conclusions: Our work demonstrates high levels of impairment, activity limitation and participation restriction among people living with HIV in BC. Furthermore, the prevalence of activity limitations is much higher among people living with HIV than the general population. This is one of the first attempts to quantify impairments and life challenges faced by people living with HIV.

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Monday, November 3, 2003 1:30 pm

IDU Harm Reduction

LG2-1

PERSPECTIVES ON PARENTING FROM HIV+ MOTHERS AND FATHERS FROM SUB-SAHARA AFRICA AND THE WEST INDIES: EARLY FINDINGS

Beverley J. Antle, The Hospital for Sick Children; Shelane Donoghue, Simone Shindler, The Teresa Group.

Track/Theme: Sociobehavioural/ Health Services and Access to Care

Plain Language Summary: This project will highlight the experiences of mothers and fathers living with and affected by HIV who are from Sub-Sahara Africa or the West Indies, provide insight with respect to their priorities and concerns as parents living with HIV/AIDS in a new country and lead to the development of consumer-informed strategies to more effectively meet the unique needs of parents and children settling here from these countries.

Objectives: The overall project objectives are: 1. Learn about the experiences and concerns of parents living with HIV who have emigrated to Ontario from Sub-Sahara Africa and the West Indies with respect to family life and parenting in a new country 1.1. Illuminate the role of beliefs and customs of their home country/community in current daily routines and parenting practices in Canada 1.2. Learn about how these parents handled disclosure of HIV status, particularly with respect to their children 1.3. Provide insights into how service providers might more effectively meet the needs of these parents and their children

Methods: In this qualitative study, drawing on both grounded theory and participatory research methods, we plan to interview 25-30 mothers and fathers living with and affected by HIV/AIDS who have settled in Ontario from Sub-Sarhara Africa or the West Indies. Face to face interviews are currently being implemented. These interviews will be transcribed and analyzed using a constant comparison method frequently used in grounded-theory studies. Our research is guided by an advisory committee with service providers and consumers representing the communities in this study.

Results: We are in the early stage of data collection and plan to present early findings, focused on mothers and fathers' experiences as PHA's and parents, integration of parenting practices from their home country/community and decisions with respect to disclosure of their HIV status within their family and community here.

Conclusions: This presentation will provide researchers, service providers and PHA's with valuable preliminary findings on the experiences of individuals from HIV endemic countries, their priorities and struggles as parents living with and affected by HIV/AIDS and preferences with respect to service delivery

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LG2-2

THE SILENT VOICES OF THE HIV/AIDS EPIDEMIC: AFRICAN AND CARIBBEAN WOMEN

Senait Teclom, Women's Health in Women's Hands; Esther Tharao, Women's Health in Women's Hands and University of Toronto, Department of Public Health Science; Notisha Massaquoi, Women's Health in Women's Hands, and the Ontario Institute for Studies in Education, University of Toronto.

Track/Theme: Sociobehavioural/Local and Global Issues

Plain Language Summary: This abstract will present findings of a study done by Women's Health in Women's Hands with African and Caribbean women and their providers in Toronto. The purpose of the study was to examine factors that influence women's response to HIV/AIDS. Findings of the study will be presented.

Objectives: 1. To determine knowledge and level of awareness of HIV/AIDS and related services, service utilization and factors influencing access to HIV/AIDS information and services 2. Identify and document the type of HIV/AIDS services available and the role(s) played by target population in identified services 3. Identify and document the major issues/challenges/barriers faced by service providers working with target population

Methods: Data was collected through 2 focus groups with 21 women, including women living with HIV/AIDS, 45 in-depth interviews with key African and Caribbean women and HIV/AIDS service providers. The focus groups and in-depth interviews were audiotaped, transcribed, analyzed thematically using NVIVO, a qualitative data analysis computer program and shared with an advisory committee for further input and analysis.

Results: Results obtained indicate that: 1. Basic knowledge about HIV/AIDS and available services varied amongst the two groups of women and was dependent on awareness of HIV status - African women had more knowledge compared to Caribbean. 2. Gender related factors including lack of communication between partners, women's dependence on men, lack of power to negotiate condom use, lack of respect for women, changing gender roles were identified as key factors in maintaining women's silence even for women living with HIV. 3. Cultural and religious values, beliefs and practices, cultural and language barriers influence women's access to information and services, limiting their ability to cope with HIV or protect themselves from infection. Other identified factors included: Unemployment/underemployment, immigration, fear of HIV and its implications, quality of care provided, HIV/AIDS myths/stereotypes, racism and gender discrimination, confidentiality/disclosure issues, exclusion from decision making, development or delivery of services.

Conclusions: Most African and Caribbean women learn about HIV and related services after being diagnosed with HIV. Factors limiting access to HIV/AIDS information and services need to be understood within the broader context of culture, gender, religion, politics and socio-economic dimensions in order to mount effective responses. Only by understanding where women are coming from, their current location(s) and reasons why they are there can they effectively be guided or supported to move to the right location.

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LG2-3

COMBINING FORCES AND RESOURCES AGAINST HIV/AIDS IN SIEM REAP, CAMBODIA: A CLOSER LOOK AT A MULTI-SECTORAL, MULTI-TIER HEALTH RESPONSE

Sarath Kros, SIem Reap Provincial AIDS Office/SiRCHESI NGO, Sarath Kros, Siem Reap Provincial AIDS Office/SiRCHESI NGO; Bun Chemm Dy, Provincial Health Department, Siem Reap, Cambodia; Christina Klemm, Angkor Children's Hospital, Siem Reap; Pascal Revault, Le Meliner, ESTHER NGO; Uy Borany, ICU, Siem Reap Provincial Hospital; Savun Touch, Provincial AIDS Office, SIem Reap/SiRCHESI NGO; Maryan Chhit, Provincial Department of Health, Siem Reap, Cambodia/SirCHESI NGO; Mee Lian Wong, National University of Singapore; Ian Lubek, University of Guelph.

Track/Theme: BasicEpidemiologySociobehavioural/Health Services and Access to CareCare and TreatmentPrevention and EducationLocal and Global Issues.

Plain Language Summary: We describe the mutli-tier and multi-sector health service response to a dramatic HIV/AIDS pandemic in Siem Reap, Cambodia. Private and public hospitals and health centres, and clinics and laboratories, co-exist and compete, along with international and local NGOs, each with specific mandates related to HIV/AIDS. We describe how attempts are made to co-ordinate all these resources and combine energies and skills and several pitfalls, are described as well,– differential salaries may lead to “personnel poaching”; a “hybrid model” of sharing of personnel between public service and NGOs is described.

Objectives: Siem Reap, amidst its economic tourism boom, simultaneously confronts one of South-East Asia’s highest HIV/AIDS infection rates and requires increasing resources from national programs, NGOs and foundations. Opportunistic infections and high HIV-seropositive prevalence rates (8-45% according to risk group) prove deadly. A multi-sectoral, multi-tier health approach is employed.

Methods: Epidemiological and questionnaire data showed prevalence rates for HIV voluntary testing/counselling (2003) of 33% (married pregnant women and local men). The complex community infection “bridging” pattern was analyzed: sexual tourists, sex workers, “beer girls”, local men, wives, infants, and young vendors..

Results: Two specialized private hospitals build capacity by training local health professionals. The Public (Provincial) hospital, through inpatient services (Intensive Care Unit) and out-patient Health Centres, coping with low salaries, see migration to private sectror clinics, full or part-time. Local and international NGOs confront HIV/AIDS according to their mandates; one private hospital confronts mother-child transmission, the other copes with AIDS in infants and orphans. One NGO tries to “street-proof” youngsters propositioned by tourists and create prevention workshops designed for local conditions; annual government surveillance monitoring (serological/behavioural surveys) provide impoirtant data and several NGOs and government programs all promote “100% condom-use” programs, Home-Based Care, etc. .Anti-retrovirals (ARVT) are provided free by two NGOs , but to fewer than 500 outpatients from among 7-10,000 PLWHAs.

Conclusions: The current multi-tier health system involves public, private and NGO institutions. Together, they face the challenge of concretely co-ordinating continuum of care, prevention, and treatment. Meetings organized by Provincial AIDS Office and Provincial AIDS Committee, and annual mini-conferences organized by NGO “SiRCHESI” permit health-related organizations to share programs, initiatives, workshops, resources and partnership possibilities. Although NGOs or foundations sometimes lure health professionals away from public service, a “hybrid” partnership model of capacity-building was developed by SiRCHESI, whereby NGO and public sector personnel/programs are shared.

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LG2-4

AND THE BEER FLOWS ON..... MOBILIZING COMMUNITY PARTICIPATION IN HIV/AIDS PREVENTION, AND ENGAGING FOUNDATIONS, GOVERNMENT AND INTERNATIONAL CORPORATE RESPONSIBILITY FOR LONG-TERM HEALTH-SERVICE PROVISION IN CAMBODIA

Ian Lubek, University of Guelph; Sarath Kros, Savun Touch, Provincial AIDS Office, Siem Reap Province/ SiRCHESI NGO; Bun Chemm Dy, Provincial Health Department, Siem Reap, Cambodia; Mee Lian Wong, National University of Singapore; Meghan McCourt, Danielle Stevanov, Pam Traut, Kylie Tribble, Emily Candy, University of Guelph.

Track/Theme: Basic/Epidemiology/Sociobehavioural/Health Services and Access to Care/Care and Treatment/Prevention and Education/Local and Global Issues.

Plain Language Summary: Siem Reap Cambodia faces an increasing pandemic of HIV/AIDS, with HIV+ rates from 8-45% for certain community groups. We have successfully begun to mobilize community members to become peer-educators to teach their friends, family and neighbours about HIV/AIDS prevention. We have asked major employers such as the hotel industry to hire women into safer careers than the entertainment industry, where they are at greater risk for HIV /AIDS. About 20% of the “beer promotion women” selling international brands are HIV positive , die on the job and are quickly replaced with unschooled women from the countryside. The international beer companies are reluctant to take proactive prevention and treatment actions to keep them alive; perhaps consumers using www.fairtradebeer.com or www.ethicalbeer.com can help convince them.

Objectives: In the face of the volatile HIV/AIDS pandemic in Siem Reap, Cambodia (8-45% seropositive rates for different risk groups), multi-sectoral efforts mobilized community peer-educator training, and coordination intensified amongst government programs, local NGOs, and international foundations. After foundations support “start-up” programs, the underfunded public health system must be sustained long-term through active cooperation of major employers ---hotels, tourism.

Methods: A “hybrid model” of capacity-building developed,: foundation-supported NGOs share personnel with public-service agencies and transparently transfer innovations to the public sphere. In the private sector, hotels were invited to recruit more women; literacy/language-training by the NGO combines with on-the-job paid hotel apprenticeships, removing women from riskier entertainment-industry jobs (e.g., “beer promotion women”).. We prod globalized beer companies selling in Cambodia to take responsibility for the economic well-being, health and safety of their sales-force (currently about 20% HIV-positive: quickly replaceable as they die on the job).

Results: Community members were most active in preventing HIV/AIDS,:50 peer educators trained an additional 1400 hundred women in 12 months. While hotels seem favorable to providing safer careers for women, international beer companies are reluctant. Despite one company’s stated policy to supply anti-retrovirals for all its employees worldwide, Cambodian beer-promotion women are specifically excluded. Approximately $360 /per person annually is needed to keep their female sales-force alive. This represents 50% of the annual remuneration for women selling their brand of beer exclusively; but for the companies, their distributors and world-wide shareholders, it represents just 10 days of each woman’s beer sales (out of $13,000 annual sales).

Conclusions: What is needed to convince beer companies to assume greater social responsibility in combatting HIV/AIDS in Cambodia? A grass-roots internet-based consumer campaign (e.g., www.fairtradebeer.com, or www.ethicalbeer.com) might complement and reinforce the grass-roots community and local NGO efforts already ongoing in Cambodia.

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Monday, November 3, 2003 1:30 p.m.

International and Endemic Issues

IHR-1

PREVALENCE AND FACTORS RELATED TO PUBLIC INJECTING AMONG INJECTION DRUG USERS IN OTTAWA

Lynne Leonard, University of Ottawa; Christine Navarro, Nicholas Birkett, University of Ottawa; Geoffrey Dunkley, City of Ottawa Health Department; Connie Kristiansen, Carleton University; Robert Remis, University of Toronto.

Track/Theme: Epidemiology/Health Services and Access to Care.

Plain Language Summary: Among 506 injection drug users (IDUs) in Ottawa completing personal interviews between October 2002 and January 2003, 65% reported injecting in public places such as public washrooms, parking lots, streets, or alleys in the previous six months. Public injecting was significantly related to male gender, homelessness, early age at first injection, type of drug injected most often, injecting with used needles, increasing severity of addiction, injecting with more than six different people, and reporting male clients, while receiving most income from welfare had a protective effect. IDUs reported injecting in public places for reasons of convenience, immediacy, proximity to where they bought drugs, privacy, and safety. These results demonstrate that this high-risk practice is frequent among the most marginalised IDUs and indicates a need to examine innovative prevention initiatives such as safer injecting facilities at a local level.

Objectives: To determine the prevalence of public injecting among IDUs in Ottawa, characteristics and behaviours associated with this practice, and IDUs' reasons for injecting in public.

Methods: Between October 2002 and January 2003, 506 IDUs street-recruited consented to personal interviews. Univariate analysis determined factors associated with public injecting. Factors significant at p(0.05 were entered into a multivariate logistic regression model. Content analysis was performed for an open-ended question regarding reasons for injecting in locations other than an IDU's own home.

Results: Overall, 65% of participants reported injecting in any public place in the previous six months. Injecting in a public washroom (41%), parking lot/street/alley (34%), stairwell/doorway of a building (29%), and cars (28%) were reported. Public injecting was significantly related to male gender (AOR=2.33, 95% CI: 1.24, 4.42); homelessness (AOR=6.62, 95% CI: 3.79, 11.55); age at first injection ≤20 years (AOR=2.05, 95% CI: 1.29, 3.24); injecting most often with any opioid other than morphine (AOR=2.37, 95% CI: 1.01, 5.58); increasing severity of dependence score (AOR=1.09, 95% CI: 1.03, 1.16); injecting with used needles (AOR=3.12, 95% CI: 1.62, 6.00); injecting with ≥5 different people (AOR=2.36, 95% CI: 1.40, 3.98); and reporting male clients (AOR=2.83, 95% CI: 1.11, 7.24). Receiving most income from welfare was protective (AOR=0.48, 95% CI: 0.30, 0.76). Convenience, immediacy, proximity to point of sale, privacy, and safety were why IDUs injected in public locations.

Conclusions: Given the high prevalence and risks associated with public injecting, the potential impact of an innovative prevention initiative such as safer injecting facilities should be investigated at the local level.

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IHR-2

PATTERNS OF NEEDLE ACQUISITION: STOCKING UP, PLANNING AHEAD OR MAKING DO DAY TO DAY

Carol Strike, Centre for Addiction and Mental Health; Walter Cavalieri, Robert Bright, Ted Myers, Liviana Calzavara, Margaret Millson, University of Toronto.

Track/Theme: Sociobehavioural/Health Services and Access to CarePrevention and Education

Plain Language Summary: Using data from a large, qualitative study, we explore how injection drug users acquire and needles. We found that pharmacy sales and needle exchanges helped IDUs to stockpile sterile supplies and reduce injection related HIV risk. However, other IDUs were unable to stockpile sterile supplies because of fear of arrest, immediate circumstances of drug use and/or their living arrangements. To further reduce HIV transmission, advocacy efforts and programs for IDUs need to be broadened beyond needle exchange.

Objectives: To explore patterns of needle access, factors that influence patterns, and implications for HIV prevention.

Methods: Data from open-ended qualitative interviews (n=120) with IDU in Toronto analyzed using qualitative methods. Purposive sampling used to recruit a diverse sample in terms of age, gender, ethnicity, and area of residence.

Results: Public health programs and pharmacy sales of needles have reduced needle re-use and sharing and facilitated development of distinct, but not always mutually exclusive patterns of needle acquisition. IDUs who stockpile needles ()100) from needle exchanges are daily drug injectors with stable housing and inject indoors. IDUs who plan ahead with weekly needle supplies (10 to 50) tend to purchase needles from pharmacies or get needles from peer exchangers, have stable housing and inject indoors more than outdoors. Convenience of the exchange or pharmacy have assisted these IDUs to eliminate almost all re-use and sharing. Disorganized or situationally determined drug use or a deliberate decision lead others to obtain needles on a daily basis. Those who obtain only a daily supply are more likely to be sex trade workers, on parole or probation, homeless or in tenuous housing circumstances or to be closeted IDUs and to inject outdoors more than indoors. While community norms have created an expectation that IDUs use their own sterile equipment, those who obtain a daily supply of needles are more prone to re-use, share or borrow needles than other IDUs.

Conclusions: When conditions exist or can be created, even under primitive circumstances (e.g., squats), IDUs will maintain a stock of sterile equipment and avoid HIV sharing needles. However, the relationship between needle acquisition, needle re-use/sharing and housing point to the need to advocate more broadly on behalf of IDUs for appropriate housing and health (e.g., needle exchange and safe injection facilities) and social services.

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IHR-3

SUSTAINED REDUCTION IN DRUG-RELATED HIV RISK BEHAVIOURS TWELVE MONTHS AFTER ENROLMENT IN LOW THRESHOLD METHADONE PROGRAMS AT TWO ONTARIO NEEDLE EXCHANGES

Peggy Millson, HIV Social, Behavioural, and Epidemiological Studies Unit, University of Toronto; Laurel Challacombe, Ted Myers Sara Raftis , HIV Social, Behavioural and Epidemiological Studies Unit, University of Toronto; Carol Strike, Center for Addiction and Mental Health; Paul Villeneuve, University of Toronto; Benedikt Fischer, CAMH and Dept of Public Health Sciences, University of Toronto; Ron Shore, Street Health & KFL&A Health Unit, Kingston, ON; Shaun Hopkins, The Works, Toronto and Toronto Public Health; Mary Pearson, Queen's University.

Track/Theme: EpidemiologySociobehavioural/Health Services and Access to CarePrevention and Education.

Plain Language Summary: This study has demonstrated that illicit opiate users who enrol in needle exchange based low threshold methadone programs show significant declines in their use of heroin, other opiates, and cocaine, and in their HIV risk behaviours including needle sharing, sharing of drug paraphernalia, and attendance at shooting galleries. These changes are signficant by 6 months after enrolment, and are sustained at 12 months. This type of program should be widely available as an option for IDU who are not necessarily ready to abstain from illicit drug use, in order to reduce their risk for HIV infection and other drug related harms.

Objectives: To determine whether reductions in drug use and HIV risk behaviours seen six months after enrolment in low threshold methadone programs are sustained at 12 months.

Methods: All new enrollees entering two low threshold methadone programs in Ontario are invited to participate in a prospective cohort study, completing interviewer administered questionnaires at baseline and at six monthly follow-ups, whether continuing in the program or not. Programs accept clients' treatment goal choices, whether abstinence or continued drug use. Mean number of days using each drug in the past month at baseline, 6 and 12 months are compared using repeated measures Anova. Logistic regression is used to compare proportions using each drug and sharing needles at baseline, 6 and 12 months, with time as an independent variable.

Results: By Aug. 2003, 114 participants completed 12 months follow-up (81%): 61% male, 39% female. At 12 months there had been significant declines in needle sharing (p (0.05), sharing of drug paraphernalia, and injection in shooting galleries, as well as in the proportion of participants using heroin, other opiates, cocaine, amphetamines, barbiturates and other sedatives. Only crack use did not change. Declines in the extent of drug use measured by mean number of days of use in the past month for heroin, other opiates, and cocaine were significant by 6 months, and remained significant at 12 months, although the further declines between 6 and 12 months were not significant.

Conclusions: Significant drops in HIV risk behaviours and use of heroin and other opiates seen in this cohort six months after enrolment in low threshold methadone have been sustained in those followed to 12 months. Low threshold methadone should be made more widely available to reduce harm from opiate use for drug users who are not ready to discontinue their use of illicit drugs.

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IHR-4

COMMUNITY-BASED RESEARCH: A SEAMLESS SOLUTION TO THE RESEARCH-TO-PRACTICE CHALLENGE

Lynne Leonard, University of Ottawa; Christine Navarro, Nicholas Birkett, University of Ottawa; Paul Lavigne, Geoffrey Dunkley, City of Ottawa Health Department; Connie Kristiansen, Carleton University; Robert Remis, University of Toronto.

Track/Theme: Sociobehavioural/Prevention and Education.

Plain Language Summary: Community-based research facilitates many opportunities for the transfer of knowledge. This paper describes the successful use of multiple knowledge transfer and exchange strategies to increase access for injection drug users to harm reduction, client-centered services in Ottawa and to promote the on-going collaboration between research and community partners.

Objectives: Community-based research, in which researchers, service users, service providers and policy makers are involved from a project's inception and throughout its data collection, analysis and dissemination phases, facilitates multiple opportunities for knowledge transfer and exchange (KTE). The objective of this paper is to describe the KTE strategies adopted to impact HIV prevention policy development and programming for injection drug users (IDUs) as a result of community-based research in the city of Ottawa.

Methods: Strategies for KTE included interactive presentations of research findings with service users, service providers and community-based agencies; formal presentations to Regional Councillors responsible for health and social service policies; and regional and provincial funders were invited to participate in discussions of study results. The network of dissemination of key messages went beyond agencies already involved in needle exchange. Addiction and treatment-based agencies, as well as other HIV/AIDS prevention, support and treatment agencies not previously engaged in HIV harm reduction among IDUs participated in discussions of the implications of the study results.

Results: Timely delivery of actionable, evidence-based messages resulted in the implementation of changes in needle exchange programme policy to increase needle distribution and injection equipment other than needles. The KTE strategies also facilitated a successful request for supplemental funding to increase services and the establishment of agreements with 12 community agencies willing to offer needle exchange.

Conclusions: Shared ownership in the project promoted collaboration between partners which was advanced through structured KTE activities. In order for front-line AIDS service organisations and other community agencies to provide evidence-based HIV prevention strategies, it is essential that methods that can facilitate the transfer of knowledge from the research domain to community providers are identified.

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Vaccine Development

VD-1

HIV VACCINE ACCEPTABILITY AMONG PERSONS AT RISK FOR HIV/AIDS

Peter Newman, University of Toronto; Naihua Duan, Seung-Jae Lee, William Cunningham, Ellen Rudy, UCLA.

Track/Theme: Sociobehavioural/Health Services and Access to CarePrevention and EducationLocal and Global Issues.

Plain Language Summary: HIV vaccines offer the best hope of controlling the spread of HIV/AIDS. Yet, consumer acceptability of future HIV vaccines is not guaranteed. We investigated preferences for eight different hypothetical HIV vaccines among 114 high risk consumers. Acceptability ratings ranged from 35 to 83 on a scale of 0 to 100, with the degree of vaccine efficacy having the greatest impact on intentions to be vaccinated. Educational interventions may help to ensure the success of future HIV vaccines in controlling the HIV/AIDS pandemic.

Objectives: HIV vaccines offer the best hope of controlling the AIDS pandemic. Yet, consumer adoption of future HIV vaccines is not guaranteed. Risk behavior increases subsequent to HIV vaccine availability could offset the benefits of partial efficacy vaccines. The purpose of this study is to assess HIV vaccine acceptability, and the impact of vaccine characteristics on acceptability, among consumers at elevated risk for HIV.

Methods: Participants (n=114) were recruited using purposive, venue-based sampling from needle exchange programs, gay/lesbian community centers, and Latino community agencies in Los Angeles, California. Consumer preferences were assessed in regard to eight different hypothetical HIV vaccines with seven dichotomous attributes. Vaccine characteristics included efficacy (95% vs. 50%), duration of protection (10 years vs. lifetime), side effects (none vs. minor), doses (2 vs. 5), cross-clade (vs. single-clade) protection, route of administration (oral vs. injection), and cost ($10 vs. $50). Data were analyzed using conjoint analysis and a fractional factorial design.

Results: On a 0-100 scale of likelihood of vaccine adoption (0 = highly unlikely, 25 = somewhat unlikely, 50 = neither likely nor unlikely, 75 = somewhat likely, 100 = highly likely), the highest ranked vaccine was rated 82.9 (SD=31.3) compared with a mean score of 59.4 across all eight hypothetical vaccines; the lowest ranked vaccine had a score of 32.5 (SD=34.9). Efficacy had the greatest impact on adoption intention, accounting for a difference of 21.7 points (e.g., from somewhat likely to highly likely), followed by side effects (13.5), cross-clade protection (12.9), and duration of protection (5.9 points).

Conclusions: The wide range of vaccine acceptability suggests HIV vaccine characteristics may strongly influence consumer adoption intentions. Given the likelihood that initial HIV vaccines will be only partially efficacious, educational and social marketing interventions tailored to different communities at risk may facilitate the success of HIV vaccines in controlling the HIV/AIDS pandemic.

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VD-2

CPG ADJUVANT PLUS HBV VACCINATION IN HIV INFECTION ACHIEVES SUSTAINED SEROPROTECTION AT 48 WEEKS

Curtis Cooper, Division of Infectious Diseases, University of Ottawa at The Ottawa Hospital; Canada; H.L. Davis, Wellesley MA, M.L. Morris, S.M. Elfer, Coley Pharmaceutical Group, Ottawa; D.W. Cameron, I. Seguin, J.B. Angel , Division of Infectious Diseases, University of Ottawa at The Ottawa Hospital;

Track/Theme: Clinical/Care and TreatmentImmunology and Virology.

Plain Language Summary: HIV infected patients are often not protected by HBV vaccination. By combining standard HBV vaccine with an immune stimulatory molecule called CpG 7909, HIV infected patients developed long lasting protection against infection with this virus.

Objectives: Persons with HIV frequently do not achieve protection after HBV vaccination. CpG oligodeoxynucleotide 7909 activates plasmacytoid dendritic cell function and promotes Th-1 biased immune responses.

Methods: In a phase Ib/IIa randomised, double-blind controlled clinical trial, CpG 7909 versus placebo adjuvant was compared in HBV vaccination with alum-adsorbed yeast-derived recombinant hepatitis B surface antigen(HBsAg) for safety, tolerance, and vaccine adjuvancy. Volunteers were HIV infected adults on HAART, with HIV RNA (50 copies/mL and CD4) 200 /mL. Susceptibles with anti-HBs (10 mIU/ml (19 HBV seronegative vaccine naive, 19 previous HBV vaccine failures) were vaccinated at 0, 1 and 2 months with divided IM injection of double-dose Engerix-B (GlaxoSmithKline, Rixensart BE) (total 40µg HbsAg), and were randomized to the addition of CpG 7909 1mg or saline. Immune subjects (n=20) with seropositive anti-HBs titers ()10 mIU/ml) received only CpG 7909 or placebo.

Results: CD4 counts and suppression of HIV RNA were maintained. Geometric mean anti-HBs titres were higher in the CpG than placebo control adjuvant group at all measured time points including wk 24 (p=0.016) and wk 48 (p=0.021). At 48 wks 19/19 (100%) of CpG recipients versus 12/19 (63%) (p=0.008) maintained SP titres (anti-HBs titre ≥10 mIU/mL). SP was greater in vaccinees with prior vaccine failure at 24 wks (9/9 CpG versus 6/10 control, p = 0.087) and at 48 wks (9/9 CpG versus 5/10 control, p=0.033). More CpG-Engerix subjects than controls had durable high-titre anti-HBs response (≥100 mIU/mL) at 24 (18/19 CpG versus 11/19 control, p=0.019) and 48 wks (14/19 CpG versus 7/19 control, p=0.049).

Conclusions: CpG 7909 adjuvancy represents an important strategy in achieving long-term hepatitis B seroprotection in HBV vaccine hyporesponsive populations.

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VD-3

IDENTIFICATION AND CHARACTERIZATION OF NOVEL HUMAN MHC CLASS I-RESTRICTED INFLUENZA A AHD HIV-1 T CELL EPITOPES USING HLA TRANSGENIC MICE DEFICIENT FOR H2 CLASS I EXPRESSION

Eve Cheuk, Hospital for Sick Children and Department of Immunology, University of Toronto; Celine D'Souza, Ningjie Hu, The Hospital for Sick Children; John Chamberlain, The Hospital for Sick Children and Department of Immunology, University of Toronto.

Track/Theme: Basic/Immunology and Virology.

Plain Language Summary: During an anti-viral immune response, our immune system gets rid of the virus by targeting a limited number of

Objectives: Our objective is to identify potential HIV-1 epitopes which may be used in the context of a vaccine to broaden initial immune anti-HIV-1 immune response after viral encounter.

Methods: In order to study human MHC function in mice without the influence of endogenous H2, our lab has generated a panel of Tg mice carrying the HLA-B27, HLA-B7, or HLA-A2 alleles (as HLA/H2-Kb hybrid molecules) expressed individually on the H2-Kb/H2-Db-double knockout background. Using influenza A as a validating tool, initial characterization studies have shown the recognition of the same human epitopes during the anti-viral response in these transgenic mice. Based on this finding and the unique binding motifs of HLA molecules, candidate CTL epitopes can be predicted from the amino acid sequences of all proteins for a given virus for a given HLA class I allele using two online prediction programs: the SYPFEITHI database and the BIMAS database. Peptide candidates were synthesized and then tested using ELISpot assay and chromium release assay. By employing similar strategies, studies involving the identification of novel HIV-1 epitopes are underway.

Results: Two new HLA-B27-restricted flu epitopes, M1.242-250 and PB1.571-579, have been identified using HLA-B27 transgenic mice. In addition, flu NP418-426 was identified as a major HLA-B7-restricted flu CTL epitope in both HLA-B7 transgenic mice and HLA-B7 humans.

Conclusions: The optimized HLA class I Tg/H2-K/H2-D DKO mouse model described here provides a sensitive and specific approach for identifying and characterizing new HLA-restricted CTL epitopes as vaccine candidates for a variety of human disease-associated antigens. By bypassing the limiting contraints in antigen processing and presentation and directly immunizing with a wide array of immunogenic peptides as should be identified by our studies, a more robust and efficient viral clearance may be launched after the initial encounter, thereby possibly preventing the emergence of CTL escape mutants.

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VD-4

LONG TERM DIVERSIFICATION OF CTL RESPONSES IN DNA/ MVA VACCINATED MACAQUES: DOES IT PREDICT PROTECTION FROM AIDS?

Jin Su, University of Toronto; Mark Luscher, Yelin Xiong, Bing Li, University of Toronto; Rama Rao Amara, Harriet Robinson, Emory University, USA; Kelly MacDonald, University of Toronto and Mount Sinai Hospital.

Track/Theme: Basic/Immunology and Virology

Plain Language Summary: The rapid spread of human immunodeficiency virus type 1 (HIV-1) worldwide underscore the urgent need for the development of a safe and effective AIDS vaccine. Cytotoxic T lymphocyte (CTL) responses have been shown crucial in controlling viral replication throughout the course of infection so one goal for AIDS vaccine is to elicit strong CTL responses against virus. However, virus with mutations in CTL epitope can escape from immune control. Hence, it is important to study the detail of various aspects of the vaccine elicited CTL responses and to determine the factors that involve in disease progression.

Objectives: To study the long term breadth and magnitude of CTL responses post vaccination/viral challenge and to determine if CTL diversification correlates with AIDS progression in macaques.

Methods: Vaccine regimen of DNA priming/Modified Vaccinia Ankara (MVA) boosting was used in a SHIV/rhesus macaque model. Four groups of a total 24 macaques were studied: Group1 received high dose of vaccine (2.5mg) intradermally (i.d.); group2 received high dose intramuscularly (i.m.); group3 received low dose (250mg) i.d. and group4 received low dose i.m. Blood samples were taken at multiple time points post challenge. PBMC were isolated and CTL responses were assessed with 395 SIV Gag overlapping peptides using ELISpot assay. MHC typing was performed by PCR-SSP and the MHC restriction analysis was done by flow cytometry. RT-PCR was performed on viral RNA from plasma followed by sequencing to detect mutant variants.

Results: MHC type of all the animals was determined with PCR-SSP. CTL responses towards Gag peptides were detected over time. Multiple new minimal CTL epitopes across Gag were identified. Trend towards both an increased breadth and magnitude of CTL responses was seen among the animals received higher dose of vaccine. By comparison of the CTL responses from different time points, shift and expansion in the specificity of CTL epitope responsiveness were observed with time and it was coincident with blips of viremia in some of the animals. Viral sequencing also revealed that mutations were commonly detected in those animals and the analysis is ongoing to determine if viral mutation is driving CTL diversification.

Conclusions: A broad array of anti-SIV CTL responses can be detected up to 82 weeks post challenge. They are associated with persistent low viral load and lack of clinical disease progression. Ongoing studies are being done to correlate the dynamics of CTL responses and the emergence of CTL escape mutants with long term viral containment.

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Tuesday, November 4, 2003 11:00 a.m.

Care & Treatment Issues

CT-1

PREVALENCE AND RISK FACTORS FOR HYPERLIPIDEMIA IN HEPATITIS C (HCV)/HUMAN IMMUNODEFICIENCY VIRUS (HIV) CO-INFECTED PATIENTS ON ANTIRETROVIRAL THERAPY (ART)

Elizabeth Phillips, Sunnybrook & Women's College Health Sciences Centre; Refik Saskin, Janet Raboud , Mount Sinai Hospital.

Track/Theme: Clinical/Immunology and Virology.

Plain Language Summary: High lipids (triglyceride and cholesterol) have been commonly associated with the treatment of HIV. Risk factors for high lipids in patients co-infected with viral hepatitis C have not been well worked out but this study sugggest that patients infected with both hepatitis C and HIV may in fact be at lower risk for the development of high lipids which may be related both to lower lifetime exposure to HIV drugs and their underlying disease.

Objectives: To determine the prevalence of hyperlipidemia in patients co-infected with HCV and HIV with respect to ART use, cumulative exposure and stage of liver disease.

Methods: All HIV Ontario Observational Database (HOOD) participants co-infected with HIV/HCV were identified. ART medication and laboratory adverse event data were obtained through bi-annual chart reviews. Multivariate proportional hazards models were used to determine risk factors for time to total cholesterol (Tchol)) 7 mmol/l and triglyceride (TG)) 3 mmol/l respectively.

Results: Of 515 patients HCV+ HIV patients fewer HCV+ HIV patients ever had Tchol) 7 mmol/l than HCV- HIV patients (14/515 (2.7%) vs 300/3087 (9.7%), p(.0001). Fewer HCV+ versus HCV- HIV patients had TG) 3 mmol/l(75/515 (15%) vs 695/3087 (22.5%), p=0.0001). HCV+ HIV patients were less likely to have taken lipid-lowering agents than HCV- HIV patients (2.3% vs 11%, p(0.0001). HCV+ HIV patients were as likely to have ever been on protease inhibitors (PIs) than HCV- HIV patients(265/317 (83.6%) vs 1492/1740 (86.8%), p=0.32), but the HCV+ PI-exposed group were much less likely to have experienced Tchol) 7 mmol/l versus HCV-HIV patients exposed to PIs (8/265 (3%) vs. 282/1492 (18.9%), p(0.0001). The HCV+ HIV patients had less cumulative exposure to ART as compared to the HCV- HIV group(4.75 yrs vs 5.29 yrs, p(0.0001). In multivariate models HCV+ status in the presence of Grade 3/4 AST/ALT was negatively associated and age, PI use and boosted PI use positively associated with Tchol) 7 mmol/l. HCV+ status was negatively associated and age, grade 3/4 AST/ALT, PI or boosted PI use, d4T use and the number of ARV positively associated with TG) 3 mmol/l.

Conclusions: HCV+ HIV patients are much less likely than HCV- HIV patients experience ART-associated dyslipidemias which may related in part to lower cumulative exposure or underlying disease.

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CT-2

MILK THISTLE AND INDINAVIR: A RANDOMIZED CONTROLLED PHARMACOKINETICS STUDY

Ed Mills, CCNM, Oxford, McMaster; Kumanan Wilson, Scott Walker, Wayne Gold , Elizabeth Phillips, University of Toronto; Brian Foster, University of Ottawa, Health Canada; Beth Rachlis, Nick DeGroot, CCNM; Stephen Myers, University of Queensland; Keith Gallicano, Watsom Laboratories; Mike Clarke, University of Oxford, UK Cochrane Centre.

Track/Theme: Clinical/Care and Treatment.

Plain Language Summary: We determined if taking the herbal medicine Milk Thistle would affect the metabolism of indinavir, a commonly used protease inhibitor. We used the best methods possible to test for this, a randomized controlled trial. Our findings suggest that the group receiving no Milk thistle had more of a reduction in blood levels that the group receiving the herb. This has important implications for interpreting previous studies of herbal medicine interactions with HIV medications, as no previous study used a control group.

Objectives: To determine if ingestion of Silybum marianum affects the metabolism of indinavir.

Methods: We conducted a Randomized controlled trial of 16 healthy participants. Baseline assessment of both groups determined metabolism of indinavir after 4 doses (Phase I). Blood sampling consisted of AUC 0-8, Cmax, C8, Tmax, and T1/2. The active group received Silybum marianum 456mg, tid, for 28 days, the control group received no herb. On day 29 & 30, dosing and sampling was repeated as before (Phase II). A wash-out period of 7 days followed. On days 35 & 36, dosing and sampling were repeated as before (Phase III).

Results: All participants completed the trial, but 2 were excluded from analysis due to protocol deviation. AUC0-8 indinavir reduced by a mean 4.4% (90% CI, -26 to 27.5%, P=0.6) from Phase I to Phase II in the active group, rebounding to a Phase III reduction of 17.3% (90% CI, -9 to 37.3%, P=0.6) of baseline. Control AUC0-8 reduced by 21.5% (90% CI, -8 to 43%, P=0.2) from Phase I to Phase II and rebounded to a further reduction at Phase III of 38.5% (90% CI, 15.3 to 55.3%, P=0.01) of baseline. C8 control reduced from baseline to Phase II by 53.1% (90% CI, 25.9 to 70.4%, P=(0.01) and rebounded in Phase III to 42.2% (90% CI, 8.7 to 63.5%, P=0.05). T1/2 increased from baseline to Phase II by 3.4% (90% CI, -8.4 to 16.7%, P=0.06) and further increased by 15.9% of baseline at Phase III (90% CI, 2.7 to 30.8%, P=0.04).

Conclusions: The significant decline of AUC0-8, and C8 in the control group indicates that factors other than the exposure of interest may affect drug metabolism. As this is the first RCT of herb-drug interactions, the findings of previous studies should be interpreted with caution.

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CT-3

THE STEADY-STATE PHARMACOKINETICS (PK) OF NELFINAVIR (NFV) AND M8 DURING PREGNANCY AND POSTPARTUM.

Rolf van Heeswijk Rolf, The Ottawa Health Research Institute, The Ottawa Hospital;Yasmin Khaliq, Kathy Fyke, Isabelle Seguin,The Ottawa Hospital; Keith Gallicano, Watson Pharmaceuticals, Corona, CA, USA; Marc Bourbeau, The Ottawa Health Research Institute; Elizabeth Phillips, Sunnybrook & Women's Health Sciences Center; Bill Cameron, The Ottawa Hospital, The Ottawa Health Research Institute.

Track/Theme: Clinical/Care and Treatment

Plain Language Summary: The blood levels of antiretroviral drugs may be altered during pregnancy, but data to support this are scarce. This study investigated the blood levels of the protease inhibitor nelfinavir and its metabolite M8 during pregnancy. In conclusion, pregnancy does not seem to have a significant effect on blood levels of nelfinavir (based on analysis of a small number of patients). However, concentrations of the M8 metabolite are about 50% lower during the third trimester of pregnancy compared to postpartum. The clinical implications of the decreased M8 concentrations need further investigation.

Objectives: The PK of antiretroviral drugs may be altered during pregnancy as a result of physiologic changes, but data to support this are scarce. This study investigated the PK of NFV and its equally potent metabolite M8 during pregnancy.

Methods: Pregnant, HIV+ women on NFV 1,250 mg bid were eligible for this longitudinal PK study. 12h PK of NFV and M8 were assessed during the third trimester (TT) and postpartum (PP). NFV and M8 were analysed by validated LC/MS/MS, and non-compartmental methods were used for PK analysis.

Results: Nine women completed the study thus far, PK data are available for four (mean age 29 yrs). PK was assessed during TT at a median (range) of 32 (31-33) weeks gestation (as determined by ultrasonography), and 7 (6-11) weeks PP. The geometric mean AUC12h, Cmax, and C12h for NFV during TT was, respectively, 35.3 h*mg/L, 5.6 mg/L, 0.9 mg/L, which is similar to population values. The geometric mean ratio (GMR; TT/PP) and 90% CI for the NFV AUC12h, Cmax, and C12h was 1.1 (0.8-1.4), 1.2 (0.8-1.7), 0.8 (0.4-1.4). The GMR and 90% CI for the M8 AUC12h, Cmax, and C12h was 0.5 (0.2-1.2), 0.5 (0.3-0.8), 0.4 (0.2-0.9). The median ratio of the AUC12h of M8 and NFV (M8/NFV) during TT and PP was 12% and 28%, respectively. NFV was generally well tolerated (n=9); adverse events were mild to moderate, and mainly gastrointestinal. The virological and immunological response was satisfactory during pregnancy and follow-up in all women.

Conclusions: Pregnancy does not seem to have a significant effect on NFV PK. However, concentrations of M8 are about 50% lower during the third trimester compared to postpartum, suggesting induction of hepatic CYP3A4 during pregnancy. However, inhibition of CYP2C19 cannot be excluded. The clinical implications of the decreased M8 concentrations need further investigation.

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CT-4

PROSPECTIVE STUDY OF TOXICITY IN INFANTS PERINATALLY EXPOSED TO ANTIRETROVIRALS (ART)

Adriana Costei, The Hospital for Sick Children; Susan King, Dale DeMatteo, Adriana Costei, The Hospital for Sick Children.

Track/Theme: Clinical/Care and Treatment.

Plain Language Summary: Perinatal ART has been shown to reduce mother-to-child transmission but the short and long-term toxicity for these exposed infants is unknown. Mitochondrial toxicity has been reported by one European group, but not by others.

Objectives: To assess the effects of ART agents and their combinations on both short term (morphology) and long-term (developmental) outcome for infants.

Methods: This is a prospective observational study. Pregnant women with HIV infection receiving ART are interviewed to obtain pregnancy, maternal and family information. Medical information is confirmed from medical records. Their infants are followed in pediatric HIV clinics. Infants are assessed at 0,1,2,6,and 18 months.

Results: Centres in eight Canadian cities participate. From data collected between January 1998 and June 2002 there were 117 evaluable pregnancies including 113 live births and one non drug-related stillbirth. Among women, 17% were on ART for all three trimesters; 56% were on ART in the 2nd and 3rd; and 23% were on ART in the 3rd trimester only. Three women received ART intrapartum only. Only 1 child is HIV-infected. Infant drug exposures include: AZT alone=23%; 2NRTI=16%; 1NRTI+PI=59%; 2NRTI+NNRTI=7%; other combinations=3%. There have been no deaths or major birth defects. The most common neonatal problem was rash (18). Eight children had a minor birth defect (6) or deformity (2). Three children were hospitalized prior to 3 months with apnea (2) or a febrile episode (1). Other neonatal problems include: hypoglycemia-hypocalcemia (1), and metabolic acidosis (1). Five children have shown global developmental delay (DD) without obvious cause. We identified that among infants whose blood work included lactate testing, 35% had a transient high level and one with DD has a persistently high level. Among those whose hemoglobin was reported, 45% had transient low levels (lowest 78) while on antiretroviral therapy.

Conclusions: Adverse outcomes are being identified in ART exposed infants but a larger sample size, longer follow-up and comparison with a control group are required before drawing conclusions on toxicity due to perinatal ART exposure.

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Trends & Risk Behaviours in HIV Infection

HIRB-1

ENHANCING HIV DIAGNOSTIC DATA FOR SURVEILLANCE OF HIV INFECTION: RESULTS FROM THE DETUNED ASSAY TO DECEMBER 2002

Robert Remis, Department of Public Health Sciences, University of Toronto, Robert Remis, Department of Public Health Sciences, University of Toronto;Carol Swantee, HIV Laboratory, Ontario Ministry of Health;Carol Major, Ontario HIV Treatment Network;Margaret Fearon, HIV Laboratory, Ontario Ministry of Health;Maraki Fikre, Department of Public Health Sciences, University of Toronto;Elaine Whittingham, Toronto Rehabilitation Institute;Robert Palmer, Department of Public Health Sciences, University of Toronto;Mark Fisher, HIV Laboratory, Ontario Ministry of Health;.

Track/Theme: Epidemiology/Prevention and Education

Plain Language Summary: HIV diagnostic data are useful in monitoring the HIV epidemic. The detuned assay on samples positive by the diagnostic test identifies persons who were recently infected and allows the calculation of HIV incidence. For two exposure categories, the proportions based on supplementary data were different than that based on the lab requisition: HIV-endemic countries 17% (versus 7%) and MSM 46% (versus 55%). The detuned assay revealed HIV incidence (per 100 person-years) as follows: MSM 2.2, MSM-IDU 2.4, IDU 0.23 and high risk heterosexuals 0.10. Though no clear increasing or decreasing trends were observed in any exposure category, HIV incidence was considerably higher among MSM in Toronto and among IDUs in Ottawa.

Objectives: HIV diagnostic test results provide important insights into trends in HIV infection. However, missing data on risk may limit interpretation. The detuned assay identifies persons who recently seroconverted and allows the estimation of HIV incidence.

Methods: For HIV-positive tests and a sample of negative tests, we included with the test result a questionnaire on HIV-related risk and previous HIV testing. We tested positive specimens by the detuned assay, using the Abbott 3A11 HIV-1 and Vironostika test kits rendered less sensitive by diluting the sample, shortening incubation time and increasing cut-off values. HIV incidence was calculated for each exposure category integrating data from the test requisition and the completed questionnaire

Results: From October 1999 to December 2002, 3,106 patients were diagnosed HIV-positive for the first time and sent questionnaires. By Kaplan-Meier analysis, 79% were returned by 10 months. Initially, information on risk was available for 46% of reports. The proportions of two exposure categories using enhanced data was different than that based on the lab requisition alone: HIV-endemic countries 17% (versus 7%) and MSM 46% (versus 55%). Based on the results of the detuned assay, HIV incidence (per 100 person-years) during the 3.25-year study period was: MSM 2.2, MSM-IDU 2.4, IDU 0.23 and persons with an HIV-infected or at-risk sexual partner of the opposite sex 0.10. There were no clear increasing or decreasing trends in any exposure category. However, HIV incidence was considerably higher among MSM in Toronto than elsewhere (2.9 versus 1.9) and among IDUs in Ottawa compared to elsewhere (0.71 versus 0.19).

Conclusions: The supplementary questionnaire provided important additional data on risk and HIV testing and helped to elucidate trends in HIV infection. The detuned assay coupled with enhanced data yields category-specific estimates of HIV incidence. The incidence observed is likely an overestimate of true incidence, especially for MSM. Nevertheless, the stable time trends in MSM and IDUs are reassuring.

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HIRB-2

PERCEPTIONS OF RISK BEHAVIOUR AMONG NEWLY INFECTED HETEROSEXUALS AND INJECTION DRUG USERS IN THE POLARIS COHORT

Wendy Medved, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto; Liviana Calzavara, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto and Department of Public Health Sciences; Ann Burchell, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto; Karen Ryder, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto and the Polaris Study Team.

Track/Theme: Sociobehavioural/Prevention and Education.

Objectives: To examine heterosexual and injection drug users' perceptions of how they became infected with HIV.

Methods: Data were drawn from Polaris, a longitudinal open-cohort of documented recent seroconverters and HIV-negative controls. Qualitative interviews were conducted with a subsample of 22 male and female seroconverters (11 heterosexuals, 8 IDU and 3 MSM-IDU). Participants were asked to describe how they believe they became infected with HIV, and about their sexual and/or injection drug use behaviour at time of infection.

Results: Most heterosexuals attributed their HIV infection to unprotected vaginal sex with a regular partner. They believed that being in a relationship with a regular partner ensured safety. It was assumed the relationship was monogamous and they could trust their partners. All were surprised to learn of their diagnosis, and expressed anger at learning of partner's affair, HIV-positive status, or prior high risk behaviour. Heterosexuals were self-critical and took responsibility for dissonance between knowing about and practicing safer sex. Reasons for not using condoms included: perception that partner was not at risk, being under the influence of drugs/alcohol, and compliance with partner's desire not to use condoms. Most IDUs ascribed infection to using shared needles or other injecting equipment, and a sub-sample to unprotected vaginal/anal sex or a combination of sex and IDU events. While all were aware of the risks associated with injecting with shared needles, many were unaware of the risks posed by sharing other injecting equipment. Reasons for unsafe injecting included: injecting in group setting, experiencing withdrawal, being too high to care, and feeling invincible.

Conclusions: These findings are consistent with those of other studies conducted in the early 1990s, indicating that to date prevention programs have had little or no impact on heterosexual and IDUs' perceptions of self-risk. Psychosocial and contextual issues specific to each group need to be addressed in refining HIV prevention strategies.

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HIRB-3

THE PERSONAL IMPACT OF REPEAT HIV-NEGATIVE TESTING AMONG MEN AND WOMEN IN THE POLARIS HIV SEROCONVERSION STUDY COHORT

Karen Ryder, University of Toronto, Karen Ryder, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto;Liviana Calzavara, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto and Department of Public Health Sciences, Faculty of Medicine, University of Toronto;Dennis J. Haubrich, School of Social Work, Faculty of Community Services, Ryerson University;Ann Burchell, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto;Ted Myers, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto and Department of Public Health Sciences, Faculty of Medicine, University of Toronto;Wendy Medved, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto;and the Polaris Study Team, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto;.

Track/Theme: Sociobehavioural/Prevention and Education

Plain Language Summary: Previous research from the Polaris HIV Seroconversion Study found that those who became infected with HIV were slightly more likely to have received risk-reduction counselling. This prompted us to try to understand how a negative test result is experienced by the tester. Sixty-four men and women participated in face-to-face interviews that addressed their experiences of repeat HIV-negative testing. It was found that the repeat HIV-negative test experience left some people confused about what represents HIV sexual risk behaviour. Results from this study point to the need to further examine counselling and educational messages regarding HIV risk behaviour and repeat negative HIV testing.

Objectives: Previous quantitative analysis on HIV seroconverters (n=102) and HIV-negative controls (n=184) found that those who became infected were marginally more likely to report having received risk reduction counselling at their last HIV negative test than those who remained negative. This finding prompted us to try to understand how a negative test result is perceived. The objective of this analysis is to describe the personal impact of repeat HIV-negative testing on subsequent risk behaviour.

Methods: A purposive sample of 64 participants (24 HIV-positive and 40 HIV-negative) from the Polaris HIV Seroconversion Study participated in qualitative interviews on their repeat HIV-negative testing experience. Transcribed texts of the interviews were analyzed for their thematic regularity. Case studies are presented as composite portraits of the participants' risk behaviour related to repeat HIV negative testing.

Results: Analysis of the interview texts indicate that a negative test result following risk behaviour leads to confusion as to what constitutes risk behaviour and, occasionally, to thoughts of immunity to HIV. As such, repeat negative-testing reinforces continuing behaviours that are discrepant from public health safer-sex discourse. Among the participants, women, in particular, reported that testing served as a confirmation of their partner's monogamy. Participants reported psychosocial factors such as depression, substance use, interpersonal context and risk locale influenced their return to risk behaviour more than their experiences of repeat HIV-negative testing.

Conclusions: The repeat HIV-negative test experience, as a stand-alone factor, does not clarify risk behaviour, nor does it reinforce or sustain risk reduction. The issues inherent in repeat HIV-negative testing require enhancements to HIV test counselling and education that address the complexities of individual circumstance such as a false sense of security or perceived sense of safety in assumed monogamy.

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HIRB-4

PREVALENCE AND CORRELATES OF HEPATITIS C (HCV) AMONG ONTARIO INMATES: PRELIMINARY RESULTS FROM THE ONTARIO REMAND STUDY

Nancy Ramuscak, HIV Social, Behavioural and Epidemiological Studies Unit, University of Toronto; Liviana Calzavara, Ted Myers, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto, Department of Public Health Sciences, Faculty of Medicine, University of Toronto; Ann Burchell, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto; Peter Ford, Department of Medicine, Queen's University; Margaret Fearon, HIV Laboratory, Laboratory Services Branch, Ontario Ministry of Health and Long Term Care; Carol Swantee, HIV Laboratory, Laboratory Services Branch, Ontario Ministry of Health and Long Term Care; Carol Major, Former Head of HIV Laboratory, HIV Laboratory, Laboratory Services Branch, Ontario Ministry of Health and Long Term Care; Andrea Anonychuk, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto.

Track/Theme: Epidemiology/Prevention and Education.

Plain Language Summary: Self-reported data from an on-going study of newly admitted inmates to provincial jails and detention centres across Ontario are analyzed to describe the presence of Hepatitis C and HIV and contributing factors. Rates of infection among inmates are much higher than in the general Ontario population. Of concern is the number of Hepatitis C positive participants who reported behaviours that may lead to infecting others.

Objectives: To describe the prevalence and correlates of self-reported HCV among inmates in selected Ontario remand facilities.

Methods: Newly admitted inmates to 7 remand facilities participated in an interviewer-administered survey and provided a saliva specimen for HIV/HCV screening. Participation was anonymous and voluntary. Preliminary survey results from the 587 inmates recruited as of September 2003 are presented.

Results: The majority were male (84.2%), adult offenders (92.9%), white (67.4%), and had been incarcerated previously (82.1%). The self-reported prevalence of HCV was 14.3% (83/582). Of those not diagnosed with HCV, 64.0% (301/469) reported being tested. The self-reported rate of HCV among injection drug users was much higher at 43.5% (76/174). The self-reported prevalence of HIV was 1.2% (7/584). Of those not diagnosed with HIV, 71.5% (398/556) reported being tested. The prevalence of HIV among injectors was 4.1% (7/174). Of those who are HCV-positive, 7.2% (6/83) were co-infected with HIV. After being diagnosed with HCV, 17.3% (13/75) reported passing used injection equipment to someone else, and 12.5% (10/80) reported passing a used toothbrush/razor. The independent correlates of self-reported HCV prevalence in multiple logistic regression were: ever injecting illicit drugs (ORadj = 17.8, 95% C.I. 7.09-44.65, p-value (0.0001), ever having a blood transfusion (ORadj = 3.5, 95% C.I. 1.34-9.02, p-value = 0.01), and having injected with a used needle (ORadj = 2.7, 95% C.I. 1.16-6.39, p-value = 0.02).

Conclusions: The self-reported rates of infection among inmates being admitted to provincial remand facilities are much higher than in the general Ontario population, and we anticipate that anonymous test results will indicate even higher rates. Of concern is the number of HCV-positives who reported behaviours that may lead to infecting others. Effective HCV and HIV education within the correctional system and access to voluntary, routine-screening, would reduce the risk of infections and ensure that those infected could obtain the necessary medical care.

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Reducing Risk Among Gay & Bisexual Men

IGBM-1

TALKING NEGATIVE: HIV-NEGATIVE GAY AND BISEXUAL MEN'S NARRATIVES OF HIV DISEASE

Domenico Calla, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto;

Karen Ryder, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto; Dennis J. Haubrich, School of Social Work, Faculty of Community Services, Ryerson University; Liviana Calzavara, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto and Department of Public Health Sciences, Faculty of Medicine, University of Toronto; Ted Myers, HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto and Department of Public Health Sciences, Faculty of Medicine, University of Toronto and the Polaris Study Team.

Track/Theme: Sociobehavioural/Prevention and Education.

Plain Language Summary: Fifty-eight HIV-negative gay and bisexual men participated in face-to-face interviews about the impact of HIV on their lives. The men were chosen from the Polaris HIV Seroconversion Study in Ontario. Analysis of the interviews suggests that an HIV-negative identity reflects stigma within the gay and bisexual men's community. This preliminary analysis ends with important questions for HIV risk and prevention.

Objectives: To explore the social construction of HIV-negative seroidentity among gay and bisexual men.

Methods: Semi-structured interviews were conducted with 58 HIV-negative gay and bisexual men from the Polaris HIV Seroconversion Study regarding the personal impact of HIV disease. Polaris is a longitudinal study of recent seroconverters and matched negative controls. The interviews were audio tape-recorded, transcribed verbatim, verified for accuracy and thematically analyzed. Preliminary analysis of the interview texts is informed by Michel Foucault's 'theory of dividing practices'. Further analysis of these data and in-depth follow-up interviews will expound the relationship between HIV-negative seroidentity and risk behaviour in this sample.

Results: The data indicate that the social construction of HIV-negative seroidentity among gay and bisexual men reflects intra-community stigma. Divisive practices are reflected in the participants' narratives about: personal responsibility for HIV negative status versus chance, the unintelligibility of an HIV negative identity, safety within monogamy, avoidance of serodiscordant relationships, HIV as a physical mark, HIV-positive men as untrustworthy, and risk associated with lifestyle.

Conclusions: The identification of divisive practices, associated with HIV-negative seroidentity among gay and bisexual men, leads to the following questions: In what ways does non-identification with HIV among this population relate to risk behaviour? What social and cognitive functions do stigmatizing divisions based on serostatus serve in the identity construction among HIV-negative men?

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IIGBM-2

INFLUENCE OF PENILE MODIFICATION, PENIS DIMENSIONS AND CONDOM USE SKILLS ON CONDOM BREAKAGE AND SLIPPAGE: RETHINKING THE DIMENSIONS OF PREVENTION.

Dan Allman, HIV Social Behavioural and Epidemiological Studies Unit, Dept. of Public Health Sciences; Liviana Calzavara, Ted Myers, HIV Social Behaviour and Epidemiological Studies Unit, Dept. of Public Health Sciences; Robert Remis, Robb Travers, HIV Social, Behavioural and Epidemiological Studies Unit; John Maxwell, AIDS Committee of Toronto.

Track/Theme: EpidemiologySociobehavioural/Prevention and Education.

Plain Language Summary: This analysis investigated the influence of penile modifications (circumcision and piercing), penile dimensions (length and circumference) and condom use skills on condom breakage and slippage among gay and bisexual men.Condom breakage and slippage should not be seen as solely related to condom use skills and techniques.

Objectives: To investigate the influence of penile modifications (circumcision and piercing), penile dimensions (length and circumference) and condom use skills on condom breakage and slippage among gay and bisexual men.

Methods: The Ontario Men's Survey was an anonymous, cross-sectional study conducted in 13 communities. Men were recruited within gay bars and bathhouses and through community events and organizations. A scale of condom use skills was developed based on 10 activities. Associations between variables were examined by Pearson Chi-Square tests; and multiple logistic regression was used to examine the independent correlates of condom breakage and slippage.

Results: 5,080 men were recruited. Mean age was 35. A subsample of n=2,963 men who had experienced anal intercourse with a condom in the previous 12 months and who had responded to questions on penis characteristics and condom use skills were the focus for this analysis. 13.2% and 13.9% respectively reported one or more episode of condom breakage and condom slippage during insertive anal intercourse with a man in the previous 12 months. 64.2% reported that they were circumcised. Condom use skills (OR=1.4, p(0.001), piercings (OR=2.4, p(0.001) and thickness (OR=1.3, p(0.05) were significant in condom breakage. With condom slippage, both condom use skill (OR=1.6, p(001) and a thin penis (OR=1.3, p(0.05) were significant.

Conclusions: This analysis furthers Richters et al's (1993, 1995) and Smith et al's (1998) assertions. While level of condom use skills is highly significant in explaining both condom breakage and slippage, after correction for skill level a pierced penis and/ or large penis circumference are associated with condom breakage and a below average penile circumference with slippage. Condom breakage and slippage should not be seen as solely related to condom use skills and techniques. This analysis supports the hypothesis that some gay and bisexual men in Ontario are physically more vulnerable than others.

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IGBM-3

IS THERE AN ASSOCIATION BETWEEN STRESSFUL RELATIONSHIP EVENTS AND HIV-RISK BEHAVIOUR AMONG MSM? RESULTS FROM THE POLARIS STUDY

Andrea Anonychuk, HIV Social, Behavioural and Epidemiological Studies Unit, University of Toronto; Liviana Calzavara, Ted Myers, Janet Raboud, Polaris Study Team HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto, Department of Public Health Sciences, Faculty of Medicine, University of Toronto.

Track/Theme: Epidemiology/ Prevention and Education

Plain Language Summary: The objectives of this presentation are to describe the number and types of stressful-relationship events that gay men report over a six-month period, and how these events are related to other life events and sexual risk-behaviour. Information from 254 HIV-positive and HIV-negative men participating in the Polaris Seroconversion Study was used. We found that stressful-relationship events are associated with the occurrence of other life events and more frequent episodes of unprotected anal sex with regular partner(s). These results contribute to our knowledge and understanding of psychosocial problems and HIV-risk behaviour among MSM.

Objectives: To describe the prevalence and context of stressful relationship events among men who have sex with men (MSM) enrolled in the Polaris Study.

Methods: Stressful life events, socio-demographic and behavioural information, and health status are obtained by interviewer and self-administered questionnaire from participants in a longitudinal open-cohort of recent HIV-positive and HIV-negative controls in Ontario. MSM who experienced a stressful relationship event during the 6-month period, following recruitment into the study, are compared to those who did not.

Results: Of the 254 MSM examined, 64% (163) were HIV-negative, the majority were highly educated (81% college/university), and had mid-to-high incomes (43% $30,000-$79,000, 32% over $80,000). 63%(155) reported experiencing a life event during the previous six-months. 34% (85/247) experienced a stressful-relationship event with a partner (SRE), and 53% (130/247) other life events. The most frequently experienced SRE events were "end of a romantic relationship" 20% (50/247), and "increased arguments with a partner" 20% (50/247). Those who experienced a SRE event were more likely to engage in unprotected anal sex with regular partner(s) (74% vs. 54% p=0.03). They were also more likely to have lower education (p=0.01) and to experience other life events including problems with drugs/alcohol (p=0.0008), financial crisis (p(0.0001), the ending of a close relationship (p(0.0001), diagnosis of a serious illness (p=0.005), being physically attacked/beaten (p=0.002), being sexually abused (p=0.01), and moving to a worse neighbourhood (p=0.01). There was no association with a SRE and income, HIV status, depression, poly-drug use, or heavy drinking.

Conclusions: Stressful-relationship events are associated with other life events and higher levels of unprotected anal sex with regular partner(s). Future longitudinal analysis will determine whether these are causes or consequences of stressful-relationship events. These results contribute to current knowledge and understanding of psychosocial problems and HIV-risk behaviour among MSM.

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IGBM-4

REFRAMING THE ROLE OF SUBSTANCE USE IN SEROCONVERSION AMONG GAY AND BISEXUAL MEN: "I THINK WE NEED TO LOOK AT A LOT OF THINGS"

Jeffrey P. Aguinaldo, Department of Public Health Sciences; Faculty of Medicine, University of Toronto; Ted Myers, Liviana Calzavara, Karen Ryder, HIV Social, Behavioural, and Epidemiological Studies Unit, University of Toronto;
Dennis J. Haubrich, School of Social Work, Faculty of Community Services, Ryerson University.

Track/Theme: Sociobehavioural/ Prevention and Education

Plain Language Summary: In-depth qualitative interviews with HIV positive gay and bisexual men who reported substance use around the time they became infected reveal a number of competing narratives to explain the men's seroconversion. These findings challenge the presupposition that (non-injection) substance use alone necessarily leads gay and bisexual men to engage in high risk sexual behaviours and seroconversion. Implications for research are discussed.

Objectives: Behavioural research that consistently links non-injection substance use with the incidence of seroconversion among gay and bisexual men has lead lay persons, educators, and researchers alike to believe gay and bisexual men who use recreational substances are at increased risk for seroconversion. What is often assumed from this research is that substance use in some way incapacitates gay and bisexual men from implementing safer sex practices and thus eventuates in seroconversion. As a result, many see abstinence as an effective form of HIV prevention among non-intravenous drug and alcohol users. This paper presents data collected as part of the Polaris HIV Seroconversion Study focussing on HIV positive gay and bisexual men who use substances and the explanations they give for their seroconversion.

Methods: In-depth audio-taped interviews were conducted with 30 HIV positive gay and bisexual men who reported substance use at the time of their seroconversion. Participants responded to questions relating to the ways in which they became HIV positive and the role of substance use in their seroconversion. A content analysis was conducted on these data.

Results: While some implicated substance use (and others clearly did not), participants put forth a number of competing narratives to explain their seroconversion: (i) "I didn't know what we did was unsafe"; (ii) "It was an accident"; and (iii) "It was because of my emotional state". These themes are discussed in relation to existing literature on seroconversion among substance using gay and bisexual men.

Conclusions: The research findings further our understanding of seroconversion among gay and bisexual men who use substances and more specifically, challenge the presupposition that simple exposure to substance use leads to risky sex and seroconversion. A more global understanding of the lives of gay and bisexual men who use substances is needed to effectively prevent the spread of HIV.

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Tuesday, November 4, 2003 3:00 pm

Immunology & Virology – HIV Transmission

HT-1

TRANSMISSION OF HIV IN HUMAN CERVIX

Erin MacDonald, McMaster; Ken Rosenthal, Charu Kaushic, Jennifer Newton, McMaster.

Track/Theme: Basic/Immunology and Virology.

Plain Language Summary: Currently it is not known how HIV initiates infection in women through heterosexual contact. We have developed a model to study HIV infection in the genital tract of women. This model has been used to determine where HIV infection initiates, and which strains of virus are thought to be responsible for the majority of infection in the genital tract of women.

Objectives: The factors affecting the susceptibility of female genital tract to HIV infection are not known. This has compromised efforts to develop preventative strategies against HIV infection. It is not clear if genital epithelial cells become infected with HIV or if they trancytose the virus, allowing other target cells to become infected. We have developed an in vitro system, using primary cell cultures from reproductive tract tissue of women to use as a tool to examine genital tract cell interaction with HIV.

Methods: Uterine and cervical tissues were obtained post-operatively. Epithelial cells from these tissues were purified and grown on matrigel–coated tissue culture inserts. Initial studies were conducted with HSV-2 to examine the usefulness of the system in examining epithelial-viral interactions. Epithelial monolayers, were inoculated with cell-associated macrophage-tropic (R5) and T-cell-tropic HIV. Target cells were cultured on the basolateral side. Apical and basolateral supernatants were collected over 24-120 hours post-infection and assayed for the quantity of HIV replication with a p24 ELISA.

Results: Purity of the epithelial cell cultures and formation of tight junctions was monitored by measuring transepithelial resistances across the confluent monolayers. The cultures were found to be relatively pure for epithelial markers. Following infection of monolayers, high titers of HSV-2 were detected 48hours after infection. Epithelial cells were found to preferentially transcytose cell-associated R5 strain of HIV. The transcytosed virus infected target cells cultured below the epithelial monolayers as seen by increasing amounts of p24 detected over 120 hours.

Conclusions: This system has shown that cervical and endometrial epithelial cells are capable of transcytosing R5 cell-associated strains of HIV. This confirms previous reports that this may be the primary form of virus transmitted heterosexually. This model will provide a useful tool in further examining the interactions of HIV with female genital tract tissues.

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HT-2

SAM68 ENHANCES HIV-1 UNSPLICED RNA 3' END PROCESSING

Meredith McLaren, Department of Molecular and Medical Genetics, University of Toronto; Kengo Asai, Alan Cochrane, Department of Molecular and Medical Genetics, University of Toronto.

Track/Theme: Basic/Immunology and Virology.

Plain Language Summary: The HIV-1 Rev protein plays an essential role in the viral lifecycle in that it is required for production of the viral structural and enzymatic proteins. The correct processing of viral RNA is also a requirement for successful viral replication. Altering the state of the infected cell to make it unable to support either Rev function or viral RNA processing would inhibit progression of the viral lifecycle. It has been shown that host cell factors can affect Rev activity and RNA metabolism in different ways. I working to determine the mechanism by which a human factor (Sam68) can regulate Rev activity and viral RNA processing.

Objectives: To determine the mechanism by which the host cell factor Sam68 enhances the activity of the essential viral protein Rev.

Methods: Various methods were used to determine the processing states of viral RNAs. To analyze the effect of Sam68 on splicing, RT-PCR reactions which amplify both the spliced and unspliced forms of viral RNA were carried out on. To visualize the position of viral unspliced RNAs, in situ hybridization was used. Finally, RNAse protection assays were employed to determine the distribution of cleaved and uncleaved viral RNAs.

Results: HIV-1 Rev functions to export unspliced viral transcripts from the nucleus, allowing expression of the structural and enzymatic proteins of the virus. Co-expression of the nuclear factor Sam68 (Src-associated during mitosis) results in potent stimulation of Rev activity. To define the mechanism by which Sam68 stimulates Rev function, its effects on unspliced viral RNA processing were tested. We have recently shown that RNAs lacking the exonic splicing enhancer (ESE) found within the terminal exon of HIV-1 transcripts are unavailable for Rev-mediated export. However, co-expression of Sam68 reverses this block to RNA export. To assess whether the above observations may reflect Sam68 alteration in viral RNA processing, the polyadenylation state of viral transcripts were explored. In the absence of the exonic splicing enhancer (ESE), much of the unspliced RNA is not polyadenylated. However, co-expression of Sam68 results in a shift of unspliced RNA to the polyadenylated state. Examination of the cleavage state of unspliced RNA revealed that Sam68 specifically increases the proportion of unspliced, cleaved viral RNA.

Conclusions: Given that previous studies have demonstrated a requirement for polyadenylation for Rev-mediated export, an increase in the proportion of unspliced viral RNA being properly processed via the actions of Sam68 would be expected to render more RNA available for transport.

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HT-3

DENDRITIC CELLS AND HIV TRANSMISSION IN THE FEMALE GENITAL TRACT

Charu Kaushic, McMaster University; Charu Kaushic, Tara Graham, Barbara Kuziora, Mary Louise Beecroft, Kenneth Rosenthal, McMaster University, Department of Pathology.

Track/Theme: Basic/Immunology and Virology.

Plain Language Summary: Heterosexual transmission of HIV accounts for 70-80% of HIV infection globally. Women have a much higher risk of contracting this infection compared to men. Yet, we do not understand the details of how the virus gets in and what cells it infects in the female reproductive tract. These studies were done to examine the cells in the genital tract of women that are believed to be harboring the virus to allow infection.

Objectives: In heterosexual transmission of HIV-1 from male to female the virus has to enter and infect cells of the female reproductive tract. The cells in the female reproductive tract that are potential targets for HIV remain poorly defined. There is substantial evidence that dendritic cells bearing C-type lectin, DC-SIGN, play a significant role in capturing HIV at mucosal sites and transmitting infection in trans to T cells. We localized DC-SIGN bearing dendritic cells in cervical and uterine tissue from women.

Methods: Human cervical and uterine tissue was obtained from patients undergoing surgery for unrelated reasons, with patient consent. Cells expressing MHC Class-II and DC-SIGN were localized in the cervical tissue by immunohistochemistry and correlated with the stage of the menstrual cycle.

Results: MHC Class-II positive cells were present abundantly in the human cervix and uterus and were localized individually throughout the stroma, as well as in groups mostly around glands and blood vessels. Majority of the Class II positive cells had dendritic cell morphology and a subset stained positive with DC-SIGN antibody. Two types of staining patterns were observed in the tissues: some samples had good correlation between Class-II and DC-SIGN bearing dendritic cells. Other samples had substantial Class-II positive cells with dendritic morphology but not many DC-SIGN positive DCs.

Conclusions: DC-SIGN positive dendritic cells may play an important role in transmission of HIV in the reproductive tract of women. We saw significant number of DC-SIGN positive DCs in both the uterine and cervical samples of women. The staining pattern with MHC Class-II and DC-SIGN revealed that there may be different subsets of DCs present in the female genital tract. Further studies are ongoing to characterize these subsets and examine their functions. These studies will lead to further understanding of the mechanism of heterosexual transmission of HIV.

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HT-4

SCREENING FOR CD8+ T CELL RESPONSES USING OVERLAPPING 15-MER POOLS MAY MISS LOW-FREQUENCY RESPONSES

Rupert Kaul, University of Toronto, Tara Beattie, Sarah Rowland-Jones, Oxford University; Rupert Kaul, University of Toronto.

Track/Theme: Basic/Immunology and Virology.

Plain Language Summary: When monitoring immune responses induced by HIV vaccines, pools of overlapping peptides spanning the whole HIV genome may be used. We show that this technique may miss the low-level immune responses often found in vaccinees and exposed, uninfected individuals. This should be considered when setting up vaccine trials.

Objectives: Overlapping peptide pools spanning entire HIV-1 genes have been used to examine epitope-specific CD8+ T cell responses in HIV-1-infected, vaccinated and exposed, seronegative (ES) cohorts. We have compared the utility of 15mer peptide pools with that of optimised CD8+ epitopes in detecting HIV-1-specific CD8+ responses.

Methods: CD8+ T-cell responses in 49 HIV-1-infected and 11 uninfected subjects were detected using pools of overlapping HIV-1 Gag 15-mers, and compared with responses detected using predefined HLA-matched HIV-1 Gag optimised epitopes.

Results: HIV-1 specific CD8+ responses were detected in 48/49 HIV-1 infected subjects (98.0%), and in 0/11 uninfected controls. Overlapping peptide pools detected responses to 12 novel epitopes in 15 individuals that were missed by the predefined epitopes. However, 17/87 (19.5%) responses to optimised epitopes were not detected by the pools of overlapping 15-mer peptides. This was more common for low-frequency responses to predefined epitopes: overlapping Gag peptides picked up 28/30 (93.3%) of strong responses, 30/36 (83.3%) of intermediate responses, and only 12/21 (57.1%) of weak responses to predefined epitopes.

Conclusions: Screening for HIV-1-specific CD8+ T cell responses using overlapping 15mer peptide pools detected several novel epitopes but missed many lower frequency responses. Therefore, the optimal screening technique will vary depending on the strength of the responses anticipated. This should be a consideration when screening CD8+ T cell responses in vaccinated or ES cohorts.

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ANTIRETROVIRAL PRESCRIBING PATTERNS IN ONTARIO: 1998 TO 2002

Christopher Jones, Ontario HIV Treatment Network; Anita Rachlis, University of Toronto, Sunnybrook and Women's College Health Sciences Centre, Ontario HIV Treatment Network; Carol Swantee, Keyi Wu , Ontario HIV Laboratory.

Track/Theme: Clinical/Health Services and Access to Care.

Plain Language Summary: An analysis of the specific combinations of antiretroviral drugs prescribed by Ontario clinicians from 1998 to 2002 when starting their patients on therapy demonstrates a high degree of conformity with clinical practice guidelines and emerging scientific evidence.

Objectives: In October, 2001, the formulary status of antiretrovirals (ARVs) for HIV available through the Ontario Drug Benefit (ODB) program was upgraded from Limited Use to General Benefit. In January, 2003, the OHTN undertook a study of prescribing patterns for HAART in Ontario to determine if this change remains appropriate in light of new evidence.

Methods: From January 1, 1998 through December 30, 2002, antiretroviral regimens reported on viral load test requisition forms administered by the Ontario HIV Laboratory were analyzed to determine the extent to which they conformed with recommendations for the initial treatment of established HIV infection developed by the US Department of Health and Human Services (DHHS). This matching analysis was adjusted in each year in relation to the version of the guidelines that were extant at the time.

Results: Overall alignment of initiating regimens with either “Strongly Recommended” or “Recommended as an Alternative” improved steadily from 65.7% in 1998 to 87% in 2001. However, for 2002, alignment declined to 76.7%. This 11.8% decline from 2001 to 2002 was driven by a corresponding 66.9% increase in the number of regimens that could not be matched with any DHHS category. Subsequent analysis of the 121 “outlier” regimens in 2002 demonstrated that 81% were consistent either with recommendations for initial HAART developed by the International AIDS Society (USA Panel), or emerging clinical evidence

Conclusions: This study confirms that overall prescribing of HAART in Ontario remains aligned with DHHS guidelines, despite the 2001 formulary change. Moreover, in an analytical context that includes other leading guidelines, as well as emerging clinical evidence, the modest decline in alignment with DHHS guidelines from 2001 to 2002 does not necessarily reflect a trend away from evidence-based prescribing. However, significant year-over-year shifts in the number of “outlier” regimens suggest further monitoring of Ontario prescribing patterns is warranted.

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TAR-2

TWENTY YEARS OF AIDS IN ONTARIO. HAS ART PLAYED A ROLE IN THE EVOLUTION OF HIV?

Richard Pilon, National HIV & Retrovirology Laboratories, Health Canada; Ann Burchell, Liviana Calzavara, University of Toronto; Stan Read, Hospital for Sick Children; Paul Sandstrom, National HIV & Retrovirology Laboratories, Health Canada and the Polaris Study Team.

Track/Theme: BasicClinical/Care and TreatmentImmunology and Virology.

Plain Language Summary: When HIV develops the ability to replicate in the presence of antiretroviral therapy (ART), its ability to replicate in the absence of ART can be greatly reduced. Still, a number of mutations relating to drug resistance have become more prevalent in treated populations. In order to evaluate the role ART may have played in the molecular evolution of HIV since the first Ontario AIDS case was diagnosed 20 years ago, we compared viral sequences from the current Ontario HIV epidemic to those from the early 1980's. Our findings indicate that the HIV protease and reverse transcriptase genes, as a whole, are under the influence of purifying selection although the increased prevalence of certain mutated sites would indicate positive selection for the mutant. Analysis suggests that some of those sites were also under the influence of positive selection in the early 1980s, prior to the introduction of ART.

Objectives: Evaluate the molecular evolution of HIV in Ontario over the past 20 years, from the time of the first AIDS cases to the era of highly active antiretroviral therapy (HAART).

Methods: Comparative phylogenetic analyses were performed on HIV sequences from 60 HIV-1-infected individuals from specimens collected between 1982 and 1985 in Ontario and from 78 individuals enrolled in the Polaris HIV Seroconversion Study between1998 and 2002.

Results: An increased in the prevalence of a number of resistance-associated secondary mutations and polymorphisms was found between 1982-1985 and 1998-2002. Most notable were increases at protease sites M36I (2-fold), D60E (increase from 0% to 12%), L63P (2-fold), V71T (3-fold) and V77I (0% to 40%). Regression of phylogenetic distances indicated a linear rate of evolution which varied the virus genome has evolved at a linear rate, which varied between HIV genes. We detected a non-synonymous/synonymous mutation ratio indicative of purifying selection on the pol gene, although a number of sites were found to be under positive selection.

Conclusions: (1) Divergence of HIV-1 pol sequences is largely confined to synonymous sites, suggesting that fitness of the pol gene products in this population has been maintained at a relatively stable peak over the past 20 years by purifying selection. Evaluation of env indicates evolution nearing neutrality, implying no selection, which could make it difficult to identify conserved targets for vaccine development. (2) Although protease and RT have been subjected to strong purifying selection, the individual sites within those genes under positive selection may be the result of evolutionary pressures other than ART, such as host immune response.

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TAR-3

FORGETTING TO TAKE HAART DOSES: NEUROCOGNITIVE IMPAIRMENT OR THOUGHT AVOIDANCE?

Sarah Rubenstein, St. Michael's Hospital, Sarah Rubenstein, St. Michael's Hospital; William Lancee, University of Toronto, Mt. Sinai Hospital;Douglas Saunders, University of Toronto; Sean Rourke, University of Toronto, St. Michael's Hospital.

Track/Theme: Sociobehavioural/Care and Treatment

Plain Language Summary: One of the most commonly reported reasons for missing doses of HAART is forgetting. This problem of forgetting could be related to the memory difficulties that we see in 30%-55% of people with HIV-infection, or it could be related to avoidance of thoughts associated with having HIV/AIDS. Of the 82 participants who participated in at least 6 months of the HAART Adherence Project follow-up period, 17 of them had real memory problems but they were not more likely to report forgetting to take their medications. However, the people who reported frequent thought avoidance were more likely to report forgetting HAART doses; that is, unless the impact of living with HIV/AIDS was extreme and they were not able to successfully avoid thoughts about HIV.

Objectives: Adherence to HAART requires ensuring supply, organizing of doses, remembering to carry meds, remembering scheduled times, accuracy of dosing, and finding water and privacy to take the pills. The most common reported reasons for missed doses are related to remembering to carry meds and taking them at scheduled times. Neurocognitive impairment occurs in 30%-55% of adults living with HIV/AIDS. These impairments, and specifically memory deficits, have been cited as a potential cause of missed doses. Another cognitive process, unrelated to neurocognitive impairment, is thought avoidance. In the present investigation it was hypothesized that neurocognitive impairment would be related to reported forgetting of missed doses, and that the type of thought avoidance that is common among individuals acutely affected by being HIV positive would also contribute to forgetting in HAART adherence.

Methods: 82 participants completed at least 6 months of the HAART Adherence Project follow-up period. The present analysis uses data from the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), the Impact of Events Scale (IES; a measure of traumatic stress), and the Reasons for Missed Doses Questionnaire (REASONS).

Results: There were 17 participants out of 82 (21%) who had evidence of immediate or delayed memory impairment (at least one standard deviation below the mean on the RBANS subscales) and they were not more likely to report forgetting HAART doses (F[1,80]=0.71, N.S.). In contrast, individuals who reported frequent thought avoidance were more likely to report forgetting HAART doses; however this was only true in the low to moderate range of IES scores (F[1,58]=5.93, p(0.02). When the impact of the HIV experience was more extreme, attempts at thought avoidance failed and reported forgetting decreased (F[1,43]=4.12, p(0.05).

Conclusions: These results will be discussed within the theoretical framework of schema theory.

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TAR-4

WHAT ARE THE PREDICTORS OF HIV DRUG RESISTANCE IN DRUG NAIVE INDIVIDUALS STARTING TRIPLE THERAPY?

Richard Harrigan, BC Centre for Excellence in HIV/AIDS; Winnie Dong, Melanie Rusch, Chris Alexander, Benita Yip, Lillian Ting, Brian Wynhoven, Justin Woodward, Theresa Mo, Julio Montaner, Robert Hogg, BC Centre for Excellence in HIV/AIDS.

Track/Theme: Clinical/Care and TreatmentImmunology and Virology.

Plain Language Summary: Predictors of development of resistance are presented, based on studies conducted on a large cohort of HIV positive individuals on treatment in British Columbia.

Objectives: To determine the predictors of drug resistance in a large population of drug naïve individuals starting initial triple therapy in BC.

Methods: A total of 1219 individuals starting triple drug antiretroviral therapy in British Columbia between 08/1996 and 09/1999 were eligible. All samples with a pVL)1000 copies/mL within 30 months after initiation were genotyped for HIV RT or PI resistance mutations, with resistance assignments based upon the IAS-USA table. Adherence was estimated by prescription refills within the first year of therapy and also by measurement of plasma drug levels for PIs and NNRTIs in the post-therapy samples. Isolates with pVL (1000 copies/mL were assumed not resistant.

Results: A median of 2 genotypes were analysed per patient. In multivariate analyses, the main determinants of the development of any key mutation were high baseline pVL (risk ratio = 1.6 per log increase; p=0.0001) and intermediate levels of adherence. There was a bell-shaped relationship between adherence and resistance - multivariate risk ratios were highest at intermediate levels of adherence ((20 % adherence RR= 1.0, 20-(40% RR=0.83; 40-(60% RR=2.4; 60-(80% RR=3.2; 80-(90% RR=3.9; 90-(95% RR=2.8;)95% RR=1.6). Breaking down the group with)95% prescription refill adherence by the detection of adequate antiretroviral levels on the first two visits defined additional categories for risk of resistance. Initial use of NNRTIs, history of injection drug use and baseline SI status were NOT predictive of resistance development. Census tract linkage indicated that resistance was more likely to be observed in rural areas, regions with higher unemployment, lower median income and lower education levels.

Conclusions: The highest risks for developing resistance in drug naïve individuals starting triple therapy were associated with high baseline viral loads, prescription refills nearing 60-90% and/or low plasma drug levels. Development of HIV resistance appeared most rapidly in regions with lower socio-economic status.

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Mother to Child Transmission

MTCT-1

UPTAKE OF HIV TESTING AMONG PREGNANT WOMEN IN ONTARIO: RESULTS TO JUNE 2003

Robert Remis, Department of Public Health Sciences, University of Toronto; Carol Swantee, Keyi Wu, Mark Fisher, HIV Laboratory, Ontario Ministry of Health; Carol Major, Ontario HIV Treatment Network; Robert Palmer, Department of Public Health Sciences, University of Toronto; Susan King, Hospital for Sick Children; Peggy Millson, Liviana Calzavara, Department of Public Health Sciences, University of Toronto; Elaine Whittingham, Toronto Rehabilitation Institute; Maraki Fikre, Department of Public Health Sciences, University of Toronto.

Track/Theme: Epidemiology/Prevention and Education.

Plain Language Summary: Following the implementation of a universal HIV screening policy among pregnant women in Ontario, we evaluated HIV test uptake. The proportion of pregnancies tested for HIV increased from 40% in January 1999 to 82% in the second quarter of 2003. In 2002, of women who were not tested, 21 were found to HIV-infected in the anonymous serologic component of the study. Though uptake of HIV testing improved dramatically with the implementation of the screening program, HIV prevalence among the untested in 2002 was double that among pregnancies tested in the same year (0.62 versus 0.31/1,000).

Objectives: Few pregnant women in Ontario were tested for HIV in the four years following release of the ACTG 076 trial results in early 1994. Following the implementation by the Ministry of Health of a program to offer HIV screening to pregnant women in January 1999, we examined the patterns of HIV testing among pregnant women.

Methods: In Ontario, all prenatal screening for HIV and for most other infectious markers is carried out at the Public Health Laboratory. We determined the number of pregnancies for which any test was prescribed and the proportion with an HIV test carried out through the prenatal program or the HIV diagnostic program. In a second stage of the study, in 2002, we tested anonymously specimens from women who were not tested through either program.

Results: From January 1999 to June 2003, 640,646 pregnancies tested for at least one marker were included in the study (2,740/week). The proportion of pregnancies tested for HIV increased from 40% in January 1999 to 82% in the second quarter of 2003. 148 pregnancies tested HIV positive, for a rate of 0.36 per 1,000; 110 of the positive tests were carried out for the

Conclusions: Uptake of HIV testing improved dramatically with the implementation of the screening program. The increase was partly related to a reminder memo sent to physicians in 2001-02. It is noteworthy that HIV prevalence among the untested in 2002 was double that among pregnancies tested in the same year (0.62 versus 0.31/1,000).

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MTCT-2

ARE MEDICAL RECORDS AND WOMEN'S SELF REPORT RELIABLE SOURCES FOR DETERMINING WHETHER PRENATAL HIV TESTING WAS DONE?

Dale Guenter, McMaster University; Susan King, Randi Zlotnik Shaul, Angela Barbara, University of Toronto; Dale Guenter, McMaster University.

Track/Theme: Clinical/Prevention and Education.

Plain Language Summary: In preparation for a study that will offer rapid HIV testing during labour, we set out to determine whether the medical record and the self-report of a post-partum patient provide reliable information about whether or not prenatal testing has been done. In this group of women, health records and patient reports were both unreliable for determining who has had HIV testing and who has not had testing.

Objectives: In preparation for a study that will offer rapid HIV testing during labour, we set out to determine whether the medical record and the self-report of a post-partum patient provide reliable information about whether or not prenatal testing has been done.

Methods: Post-partum women were recruited for participation on the maternity ward of a Toronto teaching hospital from November 2002 to February 2003. Following informed consent, the presence or absence of prenatal HIV testing was assessed by three approaches: (1) interviews with women 4 to 152 hours post-partum; (2) review of the labour and delivery charts; and (3) Provincial Laboratory HIV Testing Database and Prenatal Testing Database.

Results: There were 135 women invited to participate, and 99 agreed (73%). All women had at least 4 prenatal care visits, and 90% had prenatal records on their labour and delivery charts; 40% had documentation of HIV status on their charts; 31% had documentation that HIV testing was performed; and, 33% had documentation of HIV test counselling. In interviews, 71% recalled their provider talking to them about HIV testing (48% of those who had an OB/GYN for prenatal care, and 94% of those who had a family doctor for prenatal care); 73% reported having an HIV test during this pregnancy; and, 3% refused the test. Laboratory test results in the 2 laboratory databases could be found for 71% of these women within 1 year of their delivery date. Medical records tended to underestimate the women who had been tested (sensitivity 45%, specificity 84%). Self-report tended to over-estimate the women who had been tested (sensitivity 90%, specificity 44%).

Conclusions: In this group of women, health records and patient reports are both unreliable for determining who has had HIV testing and who has not had testing. This raises a challenge for offering rapid testing during labour and delivery.

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MTCT-3

RAPID HIV TESTING IN THE DELIVERY ROOM: WHAT IS IT LIKE TO BE OFFERED AN HIV TEST DURING PREGNANCY?

Angela Barbara, Hospital for Sick Children; Susan King, Hospital for Sick Children; Angela Barbara, Hospital for Sick Children; Dale Guenter, McMaster University; Randi Zlotnick Shaul, Hospital for Sick Children;

Track/Theme: Clinical/ Prevention and Education

Plain Language Summary: Women who had just given birth were interviewed in the maternity wards of 2 Toronto teaching hospitals. Participants were asked about their HIV testing experiences during the pregnancy. Approximately 73% of the women had been offered an HIV test. Although the findings fell short of Ontario's goals of offering all pregnant women HIV testing by informed consent, most women felt that they received adequate information and were satisfied with their testing experience.

Objectives: To ascertain women's HIV testing experiences during pregnancy and to gather information on possible reasons for unknown HIV status.

Methods: Post-partum women were recruited for participation at 2 Toronto teaching hospitals from November 2002 to August 2003. Women were approached 4 to 152 hours post-partum in hospital and interviewed about their HIV testing experiences during their recent pregnancy.

Results: A total of 199 women were interviewed (70% of those approached). 99.5% of participants reported having had any prenatal care. While 73% of the women interviewed claimed that a health care provider talked to them about having an HIV test during pregnancy, fewer women (61%) indicated that a health provider discussed the topic of HIV in general. Of the 146 women with whom HIV testing was discussed, 76% felt it was a routine test, the same as all other prenatal blood tests; 72% felt they had the option to refuse the HIV test if they wanted to; 15% wished they had more information before making a decision about the test; 85% stated that they were satisfied with how the HIV test was explained to them; and 89% agreed to test. Of the 12 women who declined the test, the most common reasons given were: not at risk for HIV (50%), and tested before this pregnancy (42%). Of those women (n=9) who claimed to be unsatisfied with the HIV test explanation, all believed that they had been tested for HIV during their pregnancy.

Conclusions: This data suggests that Ontario's goal of offering all women HIV testing by informed consent has not been reached, with shortfalls in offering testing, and in giving women the option to decline. In spite of this shortfall in 'best practice', most women feel they are receiving adequate information and are satisfied with their testing experience.

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MTCT-4

RAPID HIV TESTING IN THE DELIVERY ROOM: IS A VALID INFORMED CONSENT POSSIBLE?

Randi Zlotnik-Shaul, Bioethics Department, The Hospital for Sick Children; Susan King, Infectious Diseases, The Hospital for Sick Children; Dale Guenter, Dept of Family Medicine, McMaster University; Angela Barbara, Centre for Addiction and Mental Health.

Track/Theme: Clinical/Prevention and Education

Plain Language Summary: In preparation for a study of rapid HIV testing in labour and delivery, we sought to explore whether women who had recently been in labour felt they could have provided informed consent for testing during labour.

Objectives: Despite highly effective interventions for decreasing perinatal HIV transmission, and a policy of universal offering of HIV testing in pregnancy, babies continue to be born with HIV infection in Ontario. In preparation for a study of rapid HIV testing in labour and delivery, we sought to explore whether women who had recently been in labour felt that they could have provided informed consent for testing during labour.

Methods: Women who had given birth within the past 5 years in Canada were approached at 4 Ontario health care institutions. They were invited to participate in a study to review drafts of consent forms for a rapid testing study. They were asked to review 2 consent forms: one for participation in a rapid testing study during labour; and one for intrapartum treatment for those testing positive for HIV. The interview included both open-ended and closed-ended questions about HIV perceptions, feedback on the proposed plan and consent process, emotional responses to the study, decision-making processes and comprehension of the information in the consent forms.

Results: A total of 16 women participated. The recurring themes in the women's responses where (1) women with HIV feel strongly that this test should be available at delivery (2) it is unwise not to test during pregnancy (3) women in labour could understand what a Rapid HIV test is and appreciated the implications of having this test (4) information read and discussed during the consent process was generally recalled well.

Conclusions: While the researchers remain uncertain about how the events and emotions of labour will affect a woman's ability to give informed consent, based on the study data, it is reasonable to presume that many women in labour would be able to provide valid informed consent to a rapid HIV test.

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