

Vulnerable Populations

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LONGTERM TRENDS IN HIV PREVALENCE AND RISK BEHAVIOURS AMONG INJECTION DRUG USERS IN TORONTO AND SUDBURY

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Plain Language Summary: This analysis examines trends in HIV infections and associated risk behaviours among injection drug users in Toronto and Sudbury using results from three survey studies in Toronto between 1992-2003 and two in Sudbury between 1997-2003. Factors associated with being HIV positive are also compared. Results show that HIV prevalence has not changed significantly in Toronto or Sudbury over the periods studied. Needle sharing and sharing of other injection equipment have declined significantly in Toronto over the decade studied, while condom use has not increased. Injection of cocaine, sharing of equipment, and more years of drug injection are all associated with being HIV positive. In the earliest study in Toronto, being a man who had sex with other men as well as an IDU was also a significant risk factor.

Objectives: 1. To examine trends in prevalence of HIV and associated risk behaviours in Toronto and Sudbury injection drug users (IDUs) across research surveys conducted since 1992. 2. To compare correlates of HIV positivity across these studies.

Methods: This analysis compiled results of three studies conducted in Toronto between 1992-2003 and two in Sudbury (1998 & 2002-3). HIV prevalences and with 95% confidence intervals were compared for Toronto from the WHO study (1992-4, N=1309), the NEP study (1997-8, N=171), and the I-Track study (2002-3, N=221). For Sudbury, HIV prevalence and confidence intervals were compared from the NEP study (N=76) and I-Track (N=169). Prevalence of needle sharing, equipment sharing, and condom use with 95% confidence intervals were also compared. Univariate analyses of correlates of HIV positivity were also examined.

Results: HIV prevalence has not changed significantly in Toronto since 1992-4, with rates of 5.5, 8.6 and 5.1 measured in the three studies. Sudbury's prevalence was 12.2 in 1997 and 10.1 in 2002; this difference is not statistically significant. Needle sharing and equipment sharing declined significantly in Toronto over the decade studied ($p < 0.05$), while condom use has not increased. Injection of cocaine, sharing of injection paraphernalia, and longer duration of injection are associated with being HIV positive. Males in the WHO study had significantly higher rates of HIV, associated with being MSM, but this was not seen in later studies. Numbers of MSM in the later studies were small and may have resulted in inadequate sample size to detect this factor, however overall gender differences seen in the WHO study were also not seen in later studies.

Conclusions: These findings support the importance of the harm reduction work which has gone on over the past number of years in avoiding HIV outbreaks seen elsewhere. However, stable prevalence is maintained by new incident cases as others die or move away. This underlines the continuing need for prevention efforts, and the merits of looking for additional harm reduction strategies in an effort to reduce incidence further. Repeated cross-sectional surveys are valuable monitoring tools at relatively low cost, and could be valuable for other Ontario cities beyond Toronto, Sudbury and Ottawa where they are already well established.

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AIDS, REPRESENTATION AND HIV RISK IN YOUTH

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Plain Language Summary: While most HIV education programs aim to change individual behaviour, it is a general finding that knowledge about HIV/AIDS does not typically transfer to safer sex practices. Part of this disjuncture may have to do with the "anybody else but me" attitudes to HIV infection supported by narratives of AIDS as a disease of "foreign" places and sexually deviant bodies (Patton, 2002, 1999; Treichler, 1988). In this paper we discuss the ways youth invoke such narratives as a strategy to distance themselves from the disease.

Objectives: The objectives of this project were: to identify risk factors for HIV infection in youth; to explore how youth understand concepts of risk; to develop HIV prevention programming that goes beyond a focus on individual sexual practices.

Methods: We conducted 17 focus groups with a total of 138 youth from diverse populations including urban and rural settings in south-western Ontario. The focus groups included an agree/disagree activity designed to determine youth's knowledge of HIV/AIDS and a series of eight questions that explored how youth defined terms such as 'sex', 'risk', and 'negotiation' and how they assessed the quality of their HIV education.

Results: A major risk factor that emerged was the tendency for youth to distance themselves from the possibility of HIV infection by drawing on narratives of AIDS as a disease of "foreign" places and sexually deviant bodies (Patton, 2002, 1999; Treichler, 1988). Such narratives were invoked through the use of representations of AIDS that draw on racist, classist, and sexist stereotypes associated with the disease. A critique of dominant representations of AIDS is a necessary component of HIV prevention programs targeted at youth.

Conclusions: To be effective, HIV prevention programming for youth must go beyond a focus on individual sexual practices to include a critique of dominant representations of AIDS.

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DETERMINING THE MOST APPROPRIATE METHODS OF HIV/AIDS PREVENTION AND ACCESSING SERVICES AMONG AFRICANS LIVING IN TORONTO - A NEEDS ASSESSMENT

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Plain Language Summary: HIV/AIDS in Ontario is highest among immigrants from HIV endemic countries. It is therefore a major community concern and efforts to identify ways of reducing the spread need to be stepped up. One of the leading causes of the spread of HIV/AIDS among Africans is misinformation and poor implementation of HIV/AIDS programs in the community. A needs assessment was therefore conducted with representatives from the community as a first step to identifying areas of priority in fighting HIV/AIDS in these communities and the wider population. Members identified misinformation and lack of education as major causes of the spread of HIV/AIDS.

Objectives: 1. To assess the level of understanding of HIV/AIDS issues among African immigrants living in Toronto; 2. To identify the best methods of presenting information and education on HIV/AIDS to African immigrants living in Toronto.

Methods: Focus group interviews were conducted with representatives from Eastern, Southern, Central and Western African regions. The interview tool was piloted with 2 women and 1 man but the 2 interview groups were homogenous. All interviews were based on the same interview guide and lasted approximately 2 hours. Participants were given an Information Form and asked to sign a Consent Form. No personal identifiers were used in this report. Interviews were taped, transcribed verbatim and reviewed for recurrent themes. The draft analysis was presented to interviewees for member checking.

Results: Participants expressed issues about HIV/AIDS in their communities. The hard to reach communities still do not accept that AIDS exists. Some participants confessed that it was the first time they have been involved in discussions on HIV/AIDS. However, they all acknowledged the importance of community awareness and will contribute to spreading awareness in their communities. They all agreed that there is lack of knowledge on HIV/AIDS among African communities in Toronto. They identified stigma, fear and discrimination, lack of community mobilization, and poor or lack of implementation of HIV/AIDS programs as some of the barriers to fighting HIV/AIDS.

Conclusions: There is therefore an urgent need to improve methods of information education and communication (IEC) currently being used in the control of HIV/AIDS. The following recommendations were made: More resource mobilization for African communities; Policies of confidentiality assurance, self-testing kits need to be made available to encourage Voluntary Counseling and Testing (VCT); African professionals have to be identified in the community and given the much needed support to help fight HIV/AIDS

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ADDRESSING HOMOPHOBIA IN RELATION TO HIV/AIDS IN ABORIGINAL COMMUNITIES

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Plain Language Summary: Results of a national survey about the experiences of homophobia in relation to HIV/AIDS amongst Aboriginal people who identify as two spirit, gay, lesbian, bisexual or transgender will be presented in order for service providers and organizations to have greater understanding to create supportive and non-judgmental environments for this population. A partnership between the Canadian Aboriginal AIDS Network and the University of Manitoba, Women Studies Program, data was collected on 86 individuals in summer 2004 through six HIV/AIDS organizations that serve Aboriginals. This presentation will focus on descriptive statistics to provide demographic background and ways in which homophobia has been experienced and dealt with.

Objectives: The objective of this study is to understand the nature of homophobic experiences of Aboriginal two spirit/GLBT individuals in order to create supportive and nonjudgmental environments for two spirit people (gay, lesbian, bisexual and transgender) particularly for HIV/AIDS service organizations who work within Aboriginal populations.

Methods: This is a community based research project that is driven by a National Steering Committee representative of the two spirit population in Canada. Six off reserve organizations which work in HIV/AIDS with Aboriginal communities acted as recruitment sites. Through convenience sampling, 86 individuals over the age of 18 and self identifying as two spirit/GLBT filled out a questionnaire. SPSS 11.5 is being used to analyze data frequencies and cross-tabulations.

Results: With the data collection just completed in August 2004, this study is a work in progress. However, quantitative data is available to provide preliminary results, which provide a descriptive understanding of homophobic experiences of the Aboriginal two spirit population in Canada. Variables of interest include type of reported homophobic experiences, degree of comfort coming out with service organizations, if homophobia has caused them to discontinue using services and if corrective action was sought when homophobia was experienced at a service organization. Further analysis of these variables will be by Aboriginal status, mobility, current living conditions, education level, age, gender identification, history of HIV testing and HIV status.

Conclusions: Homophobia is a common experience for Aboriginals who self identify as two spirit/GLBT. By surveying Aboriginal two spirit/GLBT, a record of homophobic discrimination and the result of such practices provide a way of highlighting and legitimizing their experiences. This in turn will hopefully encourage service providers and organizations to be more sensitive to their needs and to have a better understanding of how to reduce homophobia.

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THE EFFECT OF HIV-RELATED STIGMA ON ACCESS TO HEALTH SERVICES: VOICES OF ABORIGINAL PEOPLE LIVING WITH HIV

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Plain Language Summary: For many Aboriginal and non-aboriginal people living with HIV/AIDS (A/PHA), HIV illness continues to elicit profound feelings of stigma. We will report preliminary findings from the study “The influence of stigma on access to health services by persons with HIV illness”. The purpose of the study is to develop an intervention for the provision of health services to persons living with HIV that mitigates the impact of stigma on access to appropriate health services. In this presentation we focus attention on Aboriginal representation of stigma in the context of HIV illness. A two-fold rationale guides a focus on Aboriginal people. First, HIV infection continues to be a serious health concern, where Aboriginal people are over represented relative to their non-aboriginal counterparts (Health Canada, 2004). Second, cultural values, beliefs and practices in the context of well-being and health may promote varying experiences and understanding (Tafoya, 1996)

Objectives: The purpose of the study is to develop an intervention for the provision of health services to persons living with HIV that mitigates the impact of stigma on access to appropriate health services. In this presentation we focus attention on Aboriginal representation of stigma in the context of HIV illness. A two-fold rationale guides a focus on Aboriginal people. First, HIV infection continues to be a serious health concern, where Aboriginal people are over represented relative to their non-aboriginal counterparts (Health Canada, 2004). Second, cultural values, beliefs and practices in the context of well-being and health may promote varying experiences and understanding (Tafoya, 1996)

Methods: The project received assistance from eight (8) individual organizations located in Edmonton and Ottawa to recruit study participants. A participatory action research (PAR) protocol was achieved by involving members of the community on the research team and through participation of two research advisory committees. A qualitative methodology was adopted and this part of the larger study involved in-depth interviews with 33 study participants, of which 16 were Aboriginal people. Interviews were transcribed and later coded and analysed using a qualitative software package (N6) to assist in identification of major themes.

Results: Preliminary analyses of data identified several themes specific to the Aboriginal community of persons living with HIV/AIDS. (1) Some APHAs have experienced stigma related to HIV/AIDS within their own families, communities, and when accessing health services. (2) Innovative health delivery programs specific to marginalized populations (e.g., inner-city) were well-received by those APHAs who accessed these services. Specifically, those APHAs valued the existence of such services as well as the support and opportunity to interact with a peer-group. (3) Health care providers may not have been aware of the specific import of APHA health-related decisions (e.g., the decision not to have more children) (4) Some APHAs included cultural practices, beliefs, and values in their care. (5) Some APHAs felt strongly about the need to educate young people about HIV/AIDS. Some were actively involved in awareness and prevention activities.

Conclusions: The impact of stigma on the experience of HIV illness for APHA study participants is associated with cultural understanding and historical circumstance. Findings suggest that any interventions that focus on mitigating stigma and that promote optimal access to health care must attend to these features.

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“OPERATION HAIRSPRAY”

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Plain Language Summary: Operation Hairspray is an innovative peer-led health promotion initiative, which seeks to engage African and Caribbean hairdressers and barbers as a channel to reach people from countries where HIV is endemic. In 2001, HIV infections among people from African and Caribbean countries where HIV is endemic represented a quarter of all reported HIV cases in Ottawa. This trend is not limited to Ottawa, epidemiological data show a similar pattern of increase occurring provincially and nationally. Ottawa Public Health wishes to address these issues by implementing a peer-led health promotion strategy to ensure better access to knowledge and support for members of the African and Caribbean communities.

Objectives: Objectives of this unique initiative include: Increasing community capacity; increasing access/reducing barriers to health information on STI's and HIV/AIDS prevention and evaluating the effectiveness of a peer-led model as a channel to increase knowledge about HIV/AIDS prevention within the African and Caribbean communities in Ottawa. Several studies and research projects have demonstrated that the peer-led model is an effective health promotion strategy. With adults, interventions with popular opinion leaders have been proven very effective in motivating behavioural change around HIV.

Methods: Recruitment of a Project Advisory Group (PAG), consisting of at least one community member and at least one hairdresser/barber from the African or Caribbean communities, public health representatives, and an academic researcher in the field of HIV/AIDS, will monitor the development, implementation and evaluation of the initiative. Recruitment of Hairdressers and Barbers, who provide services to the African and Caribbean communities, in Ottawa. These volunteers will participate in a training to become peer educators. Through this training, participants acquire 1) the knowledge and the skills needed to integrate STI and HIV/AIDS prevention education within their practice and 2) the ability to recognise opportune moments to share this information within client conversations. Hairdressers and barbers are specifically targeted for recruitment due to the nature of their work, the quality of their client interactions and their strong communication skills. Recent research findings, from consultations with the African and Caribbean communities, highlight the importance of involving people from within their communities as volunteers, role models or workers for effective HIV/AIDS education, prevention and dissemination strategies. Data collection tools include: Pre and post training questionnaires for Peer Educators, Log Sheets to track type and number of community contacts, Reaction sheets. These are some examples of tools that will be used to gather both qualitative and quantitative data for analysis.

Results: Project in progress, however in the evaluation component of this project, some critical questions to be answered will be around the following areas: Education and Skills Development, Training and Collaboration and Partnerships.

Conclusions: Project in progress, conclusions to follow.

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FROM RESEARCH TO ACTION AND BACK AGAIN: DEVELOPING BEST PRACTICES IN HIV PREVENTION EDUCATION FOR GAY/BISEXUAL MEN

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Plain Language Summary: This research project proposes to design and implement new HIV prevention programming for gay and bisexual men, then examine their uptake of safer sex messages, as well as new trends facilitating or inhibiting safe sex. Building on past research this project develops evidence-based prevention programming and employs multiple methodologies to understand what works, and what does not work, in communicating with diverse sectors of men who have sex with men.

Objectives: To design and implement new evidence-based HIV prevention programming in the Toronto area grounded in findings from our own recently completed research (Adam, et al. 2003), the Ontario Men's Survey (OMS), and the scholarly research literature. To discover the degree to which messages contained in this new HIV prevention programming are recognized and assessed by gay and bisexual men, and even more importantly how they enter into the reasoning processes of gay and bisexual men in their everyday sexual practices; and to identify what other sources of information are informing men's reasoning processes in relation to their sexual activities. To delineate 'microcultures' of shared understandings and assumptions underlying sexual interaction. To provide a well-informed foundation for targeted HIV prevention program development based on specific and multi-faceted needs of a vulnerable population.

Methods: Findings from previous research with gay/bi men in Toronto indicated four main areas to be addressed in education initiatives: the rise of a so-called 'bareback culture', the salience of condoms and erectile issues; relationship-building issues; and momentary safer sex 'lapses' and 'trade-offs', personal turmoil and depression. This project implements three HIV prevention initiatives targeting gay and bisexual men: 1) the 'Assumptions' campaign (June 2004), 2) a campaign addressing issues related to condom use (Fall 2004), and 3) a campaign that addresses relationship building (Fall 2004). A rapid assessment of the impact of the interventions among 500 men, will be held at Toronto Pride (June 2005), and 100 men will be recruited at Toronto Pride 2005 for a Q-sort. This analysis will allow us to see how these various messages, conventional wisdoms, and pieces of moral reasoning "hang together" as 'microcultures' of shared understandings, by sorting respondents into affinity groups according to similarity of response pattern.

Results: The Assumptions campaign (part of a national social marketing initiative for gay and bisexual men) had high visibility in Toronto's gay community during the summer of 2004. Since then, work has begun on the development of the condom-use and relationship initiatives with the input of an Advisory committee. Key messaging for both initiatives have been developed utilizing the results of past research with gay and bisexual men, the input of advisory committee members (who represent a broad cross-section of gay men's HIV prevention educators and others concerned about the health of gay and bisexual men) and input from gay men who have volunteered as models for the campaigns. The condom use/relationship-building initiatives are being developed for launch during mid-November. These two campaigns will be bolstered by community programming held during the last week of November as part of ACT's gay men's "Sexploration" week, a series of workshops, discussions and gatherings.

Conclusions: These new campaigns reflects a commitment to new approaches to HIV prevention for gay and bisexual men in an era when some communities of men already know the basic facts of HIV infection. Building on past research results, these new campaigns represent a need to further "target" HIV prevention messages to subcultures of gay and bisexual men. To be effective, new prevention messages should be responsive to the shifting and complex understandings and meanings about safety among gay and bisexual men.

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RISK BEHAVIOURS AMONG HIV-NEGATIVE MSM WHO SEROCONVERTED DURING FOLLOW-UP IN THE POLARIS COHORT

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Plain Language Summary: Our goal was to report the rate of new HIV infections among men who have sex with men, and to describe who is most likely to become infected. 196 initially HIV-negative men in Polaris were followed between June 1998 and January 2004. Eight men became infected, for a rate of 1.78 new infections among 100 men over one year. Compared to men who remained HIV-negative, men who became infected were younger and had engaged in unprotected receptive anal sex with casual partners. They had more sexual partners and experienced more stressful life events prior to becoming infected.

Objectives: To report HIV incidence and describe characteristics of initially HIV-negative participants in Polaris who became infected during follow-up.

Methods: Participants are recruited through the Ontario HIV diagnostic laboratory, physician referrals, community organizations, and media. HIV-negative participants are interviewed at baseline and every six months thereafter. A sub-sample of 173 MSM enrolled and followed between June 1998 and January 2004 was analyzed (448 person-years of observation). Data sources included baseline and follow-up quantitative interviews. In addition, men who seroconverted were asked to describe how they believe they became infected with HIV. Incidence density was calculated with 95% confidence intervals. Associations between baseline and time-varying covariates and HIV infection were examined using the Cox proportional hazards model. Results are reported as hazard rate ratios (RR).

Results: As of January 2004, 8 initially HIV-negative participants had seroconverted. The HIV incidence among MSM is 1.78 per 100 person years (95% CI 0.89-3.57). Cox regression indicated higher rates of infection among those who engaged in unprotected receptive anal sex with casual partners than those who did not (RR=2.66, 95% CI 1.69-4.17). There was also a marginally significant decreasing risk with age at time of induction (RR=0.90, 95% CI 0.80-1.01), such that younger men were more likely to seroconvert than those who were older upon enrollment. Plots, of time-varying covariates for men who became infected, showed increases in the number of sexual partners and stressful life events prior to seroconversion. Qualitative interviews with those who seroconverted during follow-up indicate that men who self-identified as "barebackers" attributed their infection to unprotected receptive anal sex with a casual or regular partner. Although men were aware of the high-risk associated with their sexual behaviour, they did not perceive themselves to be at-risk because of feelings of immunity and perceived safety of their partner. Others attributed their infection to a single event (e.g. receptive oral sex, oral-anal sex, and unprotected receptive or insertive anal sex) and their lack of condom use to sexual coercion, their emotional state, and/or being under the influence of drugs/alcohol.

Conclusions: Rates of new infections among MSM remain unacceptably high. The rate of infection in the Polaris cohort is similar to 2002 estimates based on MSM in Ontario undergoing repeat diagnostic testing (1.50 per 100 person-years (95% CI 1.13-1.94)) and on the STARHS (detuned assay) with first-time HIV-positive tests (2.10 per 100 person-years). Longitudinal information provides insights into why they are occurring, and how prevention efforts need to change over time.

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PARTY DRUGS IN THE HOUSE: ISSUES FOR HIV PREVENTION FOR GAY CLUBBERS IN TORONTO

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Plain Language Summary: Five AIDS Service Organizations in Toronto interviewed 74 gay and bisexual men who used drugs and participated in Toronto's gay dance club scene. Participants provided insight into aspects of the scene that were of importance, including a sense of community, personal safety, music and dancing, drugs, and a sexualized environment. A minority of participants (13%) described unprotected anal sex associated with their participation in scene. Asian and Caribbean participants noted a privileging of 'whiteness' in the scene, which they felt diminished their presence and created a sense of alienation. Most participants reported not engaging in unprotected anal sex as part of their experience of this scene, despite poly-drug use.

Objectives: This qualitative study in Toronto was designed to: (1) determine the significance of gay dance clubs for gay and bisexual men; (2) understand how gay and bisexual men interpret their drug use in the gay dance club scene; (3) understand how drugs may or may not be associated with unsafe sex; and (4) identify the role for harm reduction and prevention education.

Methods: Participants were recruited through gay dance clubs and events, advertisements in the gay press, and Internet-based posters. After screening, 74 men participated in 90-minute semi-structured interviews. The audio-taped interviews were transcribed verbatim and coded for analysis.

Results: Participants are mainly young (average age of 32 years) and represent a high degree of ethno-racial diversity (East and Southeast Asian, Latino, Black/Caribbean, White, First Nations and South Asian). Participants narrated different aspects of attraction to the gay dance club scene: music and dancing; socializing with other gay men; a sense of community; drugs; safety (i.e. personal safety, safe spaces to be gay and to use drugs); and the sensuous and sexualized atmosphere. A variety of different recreational drugs are used in this drug-positive environment. But, participants vary the types, quantities, timing and sequence of consumption to enhance different experiences or attributes of the scene, within self-imposed safety rules. Participants did not attribute much significance to sex (i.e. finding a sex partner or getting laid) within their expectations or experiences of the scene. Ten participants (13%) described occasions of high risk anal sex associated with or attributed to their most recent dance club experience.

Conclusions: In most cases, men who get high and have unsafe sex may have a low threshold for safer sex for other reasons. HIV prevention education in the gay dance club environment is warranted, but should not focus exclusively on the relation between 'drugs' and risky sex.

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THE ACCEPTABILITY, EFFECTIVENESS AND EFFICIENCY OF A BATHHOUSE OUTREACH PROGRAMME CALLED SXPERT FOR ASIAN MEN WHO HAVE SEX WITH MEN (AMSM)

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Plain Language Summary: To study the acceptability of a bathhouse outreach program offered to Asian men using bathhouses in Toronto. This is a tailored program designed to break the culture of silence, a barrier to negotiating safer sex and promote more awareness of HIV/AIDS education and prevention resulting in risk reduction behaviors.

Objectives: The rationale for this undertaking has been identified by ACAS who have been developing programs and providing HIV/AIDS education prevention to Asian men having sex with men in Toronto. Increasing numbers of MSM infected with HIV and STIs in the gay community has resulted in bathhouse outreach programs being developed to target and increase awareness of HIV/AIDS education and sexual risk behaviors promoting safer sex with their sexual partners and their willingness to change. A staff member will work with participants to promote safer sex and drug related behaviors and provide education and training to participants.

Methods: Willing participants are recruited via an outreach worker in the bathhouse to participate in a 1 hour interview to measure their sexual/other risk behaviors. Stigma, depression, attitudes and belonging measures are also included. Participants are asked if they are interested in becoming a Sexpert which involves meetings with a staff member to educate/promote safer risk behaviors. Those who consent to become Sexperts are randomized to either Sexpert training group versus waiting list group. Both groups will be interviewed again at 3 months.

Results: Preliminary results available in 2005. Implementing this study in the bathhouses and challenges will be discussed.

Conclusions: The expected important findings are that Sexpert will have a significant impact on the prevalence of STDs and reduction in risk behavior.

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REINFECTION DISCOURSES AMONG HIV-POSITIVE MEN

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Plain Language Summary: Interviews with high risk gay and bisexual men in Toronto, and with recent sero-converts, show a widespread attentiveness to the question of HIV reinfection as a concern of HIV-positive men in safer sex decision-making. Examination of HIV reinfection discourse shows how medical evidence enters into the construction of risk for sero-positive men. While not an issue that overrides all others, reinfection concerns play a salient role among the reasons mentioned by those practising safe sex, and are often weighed against competing incentives and discourses by those who do not.

Objectives: Discover the role of risk of HIV reinfection to HIV-positive men in safer sex decision-making.

Methods: Interviews with 51 MSM having had unprotected sex within the last 6 months, and 51 who had sero-converted within the last 5 years.

Results: The transmission of resistant strains or more virulent strains, and the possibility of accelerating the progression of HIV disease figure prominently in the narratives of HIV-positive men in Toronto when considering the choice between protected and unprotected sex. In our interviews, these considerations did not prove to be definitive in determining that choice, but the salience of these narratives suggests that better scientific knowledge could have an impact in tipping the balance in safer sex decision-making for many men who do not practise safe sex consistently or who have abandoned it altogether.

Conclusions: Reinfection risk tends to be weighed against countervailing and confirming discourses in arriving at personal policies concerning un/safe sex. Reinfection risk is an important consideration for those also concerned with protecting a weakened immune system against any risk of infection, but tends to be discounted among those whose sexual function is diminished by condom use and who experience sero-positivity as a "relief" from having to worry about infection in general.

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INTERVIEW ACCOUNTS OF HIV RISK EVENTS AMONG GAY AND BISEXUAL MEN ENROLLED IN THE POLARIS HIV SEROCONVERSION STUDY

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Plain Language Summary: This study identifies and describes HIV risk events among gay and bisexual men. Sixty gay and bisexual men (25 HIV-positive and 35 HIV-negative) were interviewed about an HIV risk event. HIV-positive men were asked about the risk event that led to their seroconversion, while HIV-negative men were asked about the risk event that led to their most recent HIV test. Several psychological and social factors play a combined role in HIV risk-taking. While HIV risk is reported to be unavoidable, risk-taking is seen as irresponsible. 'Knowing your partner' and monogamy provide a false sense of personal safety from HIV infection.

Objectives: To identify and describe self-reported HIV risk events among gay and bisexual men in the Polaris cohort.

Methods: Polaris is a longitudinal, open-cohort study of recent seroconverters and HIV-negative controls in Ontario. Participants are recruited through Ontario's HIV diagnostic testing database, physicians, community organizations and media. Data are drawn from face-to-face, semi-structured interviews with 60 gay and bisexual men (25 HIV-positive and 35 HIV-negative) who enrolled in the study between January 2003 and March 2004. HIV-positive men were asked about the risk event that led to their seroconversion, while HIV-negative men were asked about the risk event that led to their most recent HIV test. Interviews were audio-taped and transcribed verbatim. Interview texts were analyzed to identify salient themes.

Results: The men's accounts of their HIV risk event identify a confluence of factors that are common to both HIV-positive and HIV-negative men, such as: depression, low self-valuation, substance use, relational difficulties, occupational stress, loss, bereavement and condom fatigue. The men also account for their risk event in self-negating characterizations of personal irresponsibility, as well as attributions of chance that portray HIV risk as unavoidable, and an inherent part of gay culture. Narratives of 'heat of the moment' risks highlight the ways in which the men speak about loss of control during sex and the pleasure of risk-taking. Sexual positioning is an important factor in the men's constructions of insertive anal intercourse as less dangerous. Sexual coercion and assault constituted some men's risk events. Although both HIV-positive and HIV-negative men address trust in relation to their risk event, HIV-positive men construct risk as a violation of trust, whereas HIV-negative men construct risk as not knowing or trusting their sexual partner.

Conclusions: The psychosocial influences on HIV risk behaviour continue to pose multiple challenges to HIV education and prevention programs. In particular, our findings point to trust as a critical factor in HIV risk. Notions of trust, such as 'knowing your partner' and assumed monogamy, provide a false sense of safety from perceived HIV risk. Future research should examine trust as a risk factor in seroconversion.

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APPROPRIATENESS OF ANTIRETROVIRAL THERAPY AT INITIATION OF TREATMENT FOR HIV IN ONTARIO: 2003

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Plain Language Summary: This study demonstrated that the specific combinations of antiretrovirals prescribed by Ontario physicians in 2003 when first starting to treat PHAs for HIV were, in a significant majority of cases, aligned with leading clinical practice guidelines.

Objectives: This study was conducted to measure the extent to which the particular antiretroviral medications prescribed by Ontario physicians in 2003 when initiating patients on treatment for established HIV infection were aligned with practice guidelines.

Methods: The drug or drugs specified in the first report of antiretroviral therapy noted in the viral load testing histories of all individuals who received a viral load test administered by the Ontario HIV Laboratory in 2003 were analyzed to determine their consistency with one of the four categories of drug combinations recommended by the February 4, 2002, version of the US Department of Health and Human Services' Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. Any drug or drug combination that could not be matched with any DHHS category was deemed an outlier.

Results: Of 538 initiations in 2003, 51.5% (277) were Strongly Recommended and an additional 20.4% (110) were Recommended as an Alternative. Combinations that are Not Recommended represented 1.5% (8) of all initiations. Outlier regimens that could not be matched with any DHHS category represented 27.0% (145) of all initiations. Of these 145 outlier regimens, 56.6% (82) fell outside DHHS guidelines because of their use of abacavir (51.7%) or tenofovir (4.8%) in the 2-nucleoside analog backbones of three-drug combinations completed by either a non-nucleoside analog or a protease inhibitor. Quad therapy regimens comprised of 3 nucleoside analogs in combination with either a non-nucleoside or a protease inhibitor represented an additional 17.9% (26) of outlier regimens.

Conclusions: For 2003, a large majority (71.9%) of initiating antiretroviral regimens were either Strongly Recommended or Recommended as an Alternative by DHHS guidelines. Also, a majority of outlier regimens appear to be consistent either with emerging evidence or current debate.

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FINDING THE ART TO STARTING HAART: INFORMING, EMPOWERING, AND PSYCHOLOGICALLY PREPARING PATIENTS FOR HAART AND TREATMENT ADHERENCE (2004)

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Plain Language Summary: Patients benefit from feeling involved in their treatment care decision process. The goal of this study was to examine how to help better prepare HIV patients, so that they feel more informed and ready to begin HIV medications. The goal of this study is also to help patients develop effective adherence strategies so that they can benefit the most from their HIV treatments when they start taking HIV medications.

Objectives: HAART has significantly slowed HIV disease progression, decreased the incidence of opportunistic infections, significantly reduced hospitalizations, and generally improved patients' overall quality of life. Although near perfect adherence (>95%) is required for optimal viral suppression (Paterson et al., 2000) and to prevent the development and transmission of multi-drug resistant strains of the HIV virus (Bangsberg et al., 2000; Boden et al., 1999), poly-drug regimens remain complex and demanding. This study is one of the first randomized control trials of a novel, standardized psycho-educational intervention aimed at increasing patients readiness for HIV medications before initiating HAART. The intervention is designed to specifically improve patients' adherence to HAART regimens.

Methods: Participants are HIV+ men and women not currently on HAART. They are recruited on an ongoing basis from the HIV outpatient clinic at the Ottawa Hospital, General Campus. Subjects are randomly assigned to either the STAART adherence enhancement intervention group or the control-group (standard HIV care). The STAART intervention consists of four psycho-educational one hour sessions conducted over 4 weeks that are designed to enhance medication adherence by addressing issues related to HIV, antiretroviral medications and side-effects, barriers to adherence, and coping with stress and depression. Participants complete a battery of psychological measures pre- and post- the STAART interventions (Phase I) as well as once they have initiated HAART (Phase II).

Results: To date, 81 HIV+ patients have been recruited into the STAART study. Preliminary findings indicate that, overall, depressed patients have lower adherence than non-depressed patients. Depressed patients receiving the STAART intervention also have greater medication adherence than depressed patients in the control condition. More specifically, depressed patient receiving the intervention show an increase in treatment adherence over time, whereas, on a temporal basis, depressed patients in the control condition show a decrease in their treatment adherence.

Conclusions: Although preliminary, results suggest that the STAART intervention is most beneficial for depressed HIV+ patients. Findings also indicate that psycho-educational interventions can effectively enhance HIV treatment by better preparing patients for HAART before they actually initiate antiretroviral medication regimens. Based on these findings, a follow-up, randomized control trial targeting depressed HIV+ patients is being conducted.

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GENOTYPIC RESISTANCE ASSAY FOR ENTIRE gp-41 SEQUENCE WITH IDENTIFICATION OF gp-41 POLYMORPHISMS IN ENFUVIRTIDE-NAÏVE PATIENTS AND NEW gp-41 MUTATIONS IN PATIENTS FAILING ENFUVIRTIDE

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Plain Language Summary: A new resistance assay has been successfully developed to assess gp-41 which is the target for the new fusion inhibitor, FUZEON. Further detail of the gene sequence of gp-41 across subtypes of HIV was determined. New gp-41 mutations which are likely clinically relevant were identified.

Objectives: Enfuvirtide is a recently released fusion inhibitor. Resistance testing has generally been limited to 10 gp-41 amino acid (AA) positions. Our objectives were to: 1) Develop a new genotypic resistance assay that assesses the entire gp-41 sequence; 2) Determine polymorphisms in a large untreated cohort and 3) Determine new gp-41 mutations in patients failing enfuvirtide.

Methods: Following standard viral RNA extraction from plasma, a 1200 bp nested RT-PCR product encompassing almost the entire gp-41 region was generated. The assay was tested on 400 naïve individuals (62 non-B clade) to determine polymorphisms. 44 individuals were assessed before and after enfuvirtide failure to determine novel gp-41 mutations.

Results: Conserved and polymorphic regions of gp-41 were identified in Clade B isolates with 141 of 328 (43.3%) being highly conserved (<1.0% variation) and 75 of 328 codons (22.9%) being partially conserved (1.0%-5.0%), with insertions being common at positions 3 and 215. Natural polymorphisms were observed throughout gp-41 in non-B clade viruses ranging from a low of 10 (clade D) to a high of 39 (CRF AE). The assay detected mutations associated with clinically significant enfuvirtide resistance (IAS USA Drug Resistance Group) in 31 of the 44 patients at positions 36D, 38A, 38M, 42T and 43D. Other mutations within the key 10 AA region of unknown significance were selected at 36A, 36V, 38E, 38V, 40H, 40P, 40T, 42D, 43H, 43K, 43S, 44M and 45M in 13 patients. Of 5 patients with no other known mutations, 3 developed a 40H and 45M together. Reversion to wild-type gp-41 was observed as early as 30 days after discontinuing enfuvirtide.

Conclusions: A new gp-41 genotypic resistance assay assessing the entire AA sequence has been successfully developed. Conserved and polymorphic regions of gp-41 across clades were determined. New gp-41 mutations which are likely clinically relevant were identified.

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ANTI-RETROVIRAL EXPOSURE AND CAROTID INTIMAL MEDIAL THICKNESS IN A MULTI-CENTRE CANADIAN HIV COHORT

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Plain Language Summary: There is concern that HIV treatment may lead to heart attacks and strokes. Using high-resolution ultrasound of the carotid arteries in the neck, we measured thickening of the arteries as a non-invasive measure of "hardening of the arteries" and future cardiovascular risk. Among 162 subjects studied to date, thicker arteries were found with older age, male gender, smoking, higher cholesterol, blood sugar, or blood pressure. HIV medications were not independently associated with artery thickness, after adjusting for standard risk factors. However, we need longer-term observation to verify whether medications cause vascular disease.

Objectives: Treatment of HIV is associated with a pro-atherogenic lipid and glucose profile, but whether treatment accelerates atherosclerosis remains unclear. We are investigating the determinants of atherosclerosis, using a well-validated and reproducible measure of carotid artery thickening.

Methods: HIV subjects aged 35 years or older, attending university-affiliated clinics in five Canadian centers, are being recruited into a prospective study of cardiovascular risk. Clinical risk factors, fasting lipids and glucose, immunologic parameters, and medication exposure are recorded. Subjects undergo yearly high-resolution carotid artery ultrasound, according to a standardized and quality-controlled protocol. Videotaped images are read by computer-assisted algorithms to determine 12-segment mean maximal intimal medial thickness (IMT). We sought an association between carotid IMT and clinical and metabolic variables, and with a history of exposure to zidovudine, stavudine, efavirenz, or to protease inhibitors, by simple and multiple linear regression. Of 162 subjects studied at baseline, 59 have undergone one-year follow-up.

Results: Mean (SD) age of patients was 45.8 (8.0) years; 93.2% were men; and 41.4% were current smokers. Mean CD4-lymphocyte count was 479, mean log viral load of 2.26. A history of exposure to zidovudine, stavudine, efavirenz, or protease inhibitors was present in 79.6%, 60.5%, 60.5% and 70.4%, respectively, for a mean of 41.9, 37.7, 25.9, and 46.1 months, respectively. Carotid IMT was 0.82 (0.25) mm at baseline and increased by 0.04 (0.09) mm/year. Carotid IMT was associated with multiple clinical (age, smoking, history of hypertension or diabetes, systolic and diastolic blood pressure), and metabolic variables (total cholesterol, LDL-cholesterol, triglycerides, glucose). Exposure to zidovudine (P=0.03), stavudine (0.01), or protease inhibitors (0.02), but not to efavirenz (0.17), was associated with greater carotid IMT. In multi-variable linear regression, only age, current smoking, systolic blood pressure, total cholesterol and glucose remained significant predictors, whereas anti-retrovirals and triglycerides were not associated. One-year carotid IMT was not associated with anti-retroviral exposure.

Conclusions: Age, gender, smoking, cholesterol, glucose and systolic blood pressure, but not antiretroviral exposure, were the main determinants of atherosclerosis in HIV subjects. Longer-term follow-up is needed to determine more precisely whether anti-retrovirals accelerate atherosclerosis.

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HIV-1 ENTRY TO LYMPHOID CELL LINES IS BLOCKED BY DOWNREGULATION OF CCR5 EXPRESSION USING MULTIMERIC HAMMERHEAD RIBOZYMES

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Plain Language Summary: HIV virus needs a co-receptor to enter to the target cells. In the first cells that the HIV infects, monocytes and macrophages, the co-receptor is called CCR5. This CCR5 is a protein, which is produced in the cell and represented on the cell surfaces. We hypothesized that by stopping CCR5 production, the virus will lose its pathway to enter the cell. Using the multimeric hammerhead ribozymes, the RNA molecules that can cleave other RNAs, we targeted the CCR5 mRNA, which is an intermediate molecule in CCR5 production process. By introducing these ribozymes to monocytes, we showed that production of CCR5 was downregulated and HIV could not infect those cells.

Objectives: CCR5 chemokine receptor is the co-receptor that R5 (M-tropic) HIV-1 uses to enter its first targets, macrophages and monocytes. It is hypothesized that gene therapy strategies, which downregulate CCR5 expression, should be effective in preventing viral entry and disease progression. The objective is to develop and test retroviral vectors expressing a multimeric hammerhead ribozyme (mHHR) against CCR5 mRNA, which upon transduction into human peripheral blood mononuclear cells or hematopoietic stem/progenitor cells, will inhibit CCR5 expression in these and their progeny cells.

Methods: An anti-CCR5 mHHR consisting of seven monomeric ribozymes targeted against seven unique sites within the CCR5 mRNA has been designed and shown that each individual ribozyme is catalytically active in vitro. The mHHR was cloned into MGIN (a mouse stem cell virus-based) and HEG1 (an HIV-1-based) vectors. A human CD4+ CCR5+ T lymphoid cell line, PM1, was transduced with the retroviral vector particles expressing the mHHR. The stable transductants were isolated by FACS. The R5 M-tropic HIV-1 (Ba-L) and X4 T-tropic HIV-1 (NL4-3) with M.O.I of 0.3 are used in infection assays to determine resistance of the transduced cells to HIV-1 entry/infection.

Results: By RT-PCR we showed that the stable transduced cells expressed ribozymes gene. Decrease in CCR5 protein level in mHHR-expressing cells was shown by flow cytometry using anti-CCR5 monoclonal antibodies. By ELISA, we could show that in the cells, which were expressing mHHR from MGIN vector, the infection was inhibited for 90 days (till the experiments lasted). We also recently obtained the results from the cells expressing the mHHR from HEG1 vectors, showing that the infection is lowered for 30 days, so far. HIV-1 infection also causes a cytopathic effect called syncytia (fusion) formation causing cell death. In our experiments, the cells expressing the ribozyme did not form any syncytia in the culture.

Conclusions: We conclude that the function of mHHR was enough to inhibit HIV-1 infection and syncytia formation in the ribozyme-expressing cells at the cell line level. Soon, it will be tested in animal models.

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A NOVEL STRATEGY TO INHIBIT HIV-1 REPLICATION

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Plain Language Summary: The continuing appearance of HIV-1 variants resistant to the current drug cocktails indicates that greater emphasis must be placed on the development of new strategies to inhibit virus replication. We are investigating whether methods to disrupt HIV-1 RNA processing can be employed to prevent virus gene expression. In this study, we demonstrate that one such strategy results in a significant suppression of HIV-1 replication. Current and future efforts will examine whether the technique used provides a durable and broad spectrum suppression of viral gene expression.

Objectives: To test whether modified U1 snRNAs could be used to inhibit HIV-1 gene expression.

Methods: Modified variants of U1 snRNA were constructed by substituting the first 10 nts with sequences complementary to conserved regions within the terminal exon of HIV-1. Constructs expressing the modified U1 snRNAs were subsequently cotransfected with replication-deficient HIV-1 proviruses and the level of p24, gp120 and viral RNA monitored by Western blot or RNase protection assays.

Results: Of the five U1 snRNA constructs able to hybridize to conserved regions within the terminal exon of HIV-1, two yielded a significant reduction (>90%) in the level of p24 or gp120 produced. Furthermore, co-expression of these inhibitory U1 snRNA variant resulted in even further reduction in viral gene expression, suggesting that they can act in a synergistic fashion. U1 snRNA constructs that lacked complementary sequences had no effect on HIV-1 protein synthesis. Changes in viral protein synthesis were accompanied by similar reductions in the level of HIV-1 RNA abundance. All constructs had little to no effect on expression of other co-transfected genes, indicating that the suppression observed is specific to HIV-1.

Conclusions: We have successfully demonstrated that modified U1 snRNAs can be used to disrupt HIV-1 RNA processing and protein expression. Current and future efforts will examine whether this approach yields a durable suppression of viral gene expression for a broad range of HIV-1 strains. The conserved nature of the viral sequences targeted and the ability to use a combination of modified U1 snRNAs suggests that a significant barrier to HIV-1 replication can be achieved that would prove difficult for the virus to evolve resistance to.

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ALLO-IMMUNIZATION WITH Mamu-A*01 AND DRw201 VACCINE FAILED TO PROTECT RHESUS MACAQUE FROM INFECTION OF SIVmac239 DERIVED FROM Mamu-A*01 AND DRw201 POSITIVE PBMC

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Plain Language Summary: When HIV or SIV bud from a cell they take host molecules called MHC into their own membrane. MHC are immunogenic and allow recognition of nonself. We have previously shown that in humans antibodies (Ab) against these molecules can neutralize HIV. We wanted to see if high levels of Anti-MHC antibodies can protect from SIV challenge in monkeys. High levels of Ab could not neutralize the virus. This may be the result of insufficient MHC in the viral membrane.

Objectives: We have shown that human alloantibodies against MHC can neutralize HIV. Since MHC molecules are variable yet are not subject to rapid mutation unlike viral proteins. MHC allo-immunization has been proposed as a preventative AIDS vaccine strategy. We used the SIV/macaca model to test a vaccine designed to induce allo-immune responses against MHC.

Methods: Mamu-A*01 and DRw201 negative Rhesus macaques were randomized to receive vaccine or placebo. Immunogens were derived from a macaque that was mA*01 and DRw201 positive (index monkey). A prime-boost immunization schedule including two DNA, one NYVAC, and three protein immunogens were given either mucosally or systematically, to induce anti-mA*01 and DRw201Ab. Animals were challenged with SIVmac239 derived from the index monkey's PBMC.

Results: Strong anti-mA*01 and DRw201 humoral and cellular allo-immune responses were successfully achieved with the prime boost strategy. However, it failed to protect vaccinees from intrarectal or intravenous challenge with SIVmac239 stock. Challenge SIV virus could not be neutralized in vitro by the strong anti-mA*01 and DRw201 alloantibodies unlike previous studies with human anti-MHC antibodies. High concentrations of monoclonal antibodies W6/32 (anti-MHC class I) and HB180 (anti-MHC class II) were only partially neutralizing. No cross reactivity to other MHC alleles or loss of self tolerance was detected.

Conclusions: High titre anti-MHC allo-immune responses can be achieved and even aggressive MHC allo-immunization is tolerated but sterilizing immunity against infection by SIVmac 239 was not achieved. This may be due to insufficient incorporation of the mA*01 and DRw201 molecules into SIV virions of the challenge stock. The results emphasize the difficulty of studying such vaccine strategies with SIVmac239 which is difficult to neutralize and highlight the need to better understand the trafficking and incorporation of host molecules in the viral envelope.

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PROTECTION AND GENERATION OF MUCOSAL MEMORY T-CELLS IN THE GENITAL TRACT FOLLOWING MUCOSAL IMMUNIZATION WITH VESICULAR STOMATITIS VIRUS VECTOR EXPRESSING HIV-1 gag

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Plain Language Summary: In current study we examined that intranasal (i.n.) immunization with recombinant vesicular stomatitis virus (VSV) and mutant VSVAV3 expressing HIV-1 clade A gag to generate mucosal immunity and protection in a mouse model. Prime and boost of both VSV-gag and VSVAV3-gag induced protection in mouse ovaries after IVAG challenge. This is associated with high level of IFN-g production and CD107a/b expression on CD8+ T cells. Finally, mice immunized with VSV-gag robust memory T cell level in both iliac lymph node and genital tract. These findings indicate that mucosal immunization with VSV-gag induces potent immune responses in the genital mucosal site capable of protection against local IVAG challenge.

Objectives: To evaluate whether intranasal immunization with recombinant VSV and mutant VSVAV3 expressing HIV-1 gag could generate mucosal immunity and protection against intravaginal challenge in a mouse model.

Methods: Recombinant VSV viruses and mutant AV3 capable of expressing either myristoylated or non-myristoylated HIV-1 clade A gag were constructed. Mice were immunized intranasally with VSV-gag alone or with CpG-ODN. The lymphocytes isolated from genital tract and iliac lymph node were phenotyped and ICCS for IFN-gamma by FACS. Protection of immunized mice challenged intravaginally with recombinant vaccinia viruses encoding HIV-1 gag was assessed.

Results: 1. Mucosal prime and boost with viral vector VSV expressing HIV-1 gag induces protection against virus challenge in mouse ovary after mucosal challenge with rVV-gag, however, single immunization doesn't generate protection in this model. 2. High level of IFN-gamma in immunized mouse vaginal washes might contribute to local mucosal anti-viral immune responses. 3. VSV-gag immunization induced robust CD8 antigen-specific anti-viral functions, including cytokine (IFN-gamma) production and perforin release (CD107a/b). 4. Mucosal vaccination with VSV-gag induces great amount of memory T cell in both iliac lymph node and genital tract.

Conclusions: mucosal immunization with VSV-gag induces potent immune responses in the genital mucosal site capable of protection against local IVAG challenge.

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IMMUNOGENICITY OF SINGLE AND COMBINED HIV-1/HCV CANDIDATE VACCINES IN A HLA-A2.1 MURINE MODEL

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Plain Language Summary: Dual infections with HIV and hepatitis C virus (HCV) may act in concert to cause severe disease. Patients with these infections have more severe liver disease and progress faster to AIDS than those that are infected with a single virus. Unfortunately, these infections coexist frequently. We developed a candidate combined HIV/HCV vaccine with the viral structural proteins. Humanized mice were immunized with HIV and HCV antigens alone or in combination and immune responses were analyzed. We observed humoral responses in the group of mice that received HIV and HCV alone or in combination. However, the group that received the combined vaccine had better cell-mediated immune responses than the groups that received HIV or HCV alone.

Objectives: Humoral and cellular immune responses play crucial roles in the control of HIV/HCV infections. Thus, a candidate vaccine needs to elicit a strong humoral as well as CD8/CD4 T cell response. In this study, we assessed and compared the immunogenicity of HIV/HCV antigens alone or in combination in HLA-A2.1 mice.

Methods: Multiple DNA constructs containing HIV-1 structural genes (gp120, gag and pol) and HCV structural genes (Core, E1 and E2) were designed. The recombinant proteins were expressed, purified and characterized in a mammalian cell line (CHO cells). Five groups of HLA-A2.1 mice were immunized with DNA constructs, recombinant proteins and the adjuvants Montanide/CpG at 0, 2, 4 and 8 weeks. Humoral responses were measured by titrating HIV-1 and HCV-specific antibodies. Cell-mediated immune responses were identified by assessing lymphocyte proliferation as well as HIV/HCV-specific CD8+ T-cells using Intracellular IFN- γ staining and ELISPOT.

Results: Mice immunized with the combination of HIV/HCV DNA constructs, recombinant proteins and adjuvants showed similar HIV/HCV antibody titers and lymphocyte proliferative responses to the groups receiving HIV or HCV immunogens alone. However, the combined vaccine elicited higher Viral-specific-CD8+ T cell responses in comparison to groups immunized with HIV or HCV alone.

Conclusions: Based on this study, the manipulation and enhancement of effector responses against HIV/HCV are possible using combined vaccination strategies involving multiple expression vectors, recombinant structural proteins and adjuvants CPG/Montanide. We show that a combined vaccine could be used to boost the immune response against HIV-1 or HCV. These results suggest that the use of two different DNA/proteins for priming and boosting has a synergistic effect on the immune response and can induce a multispecific CD8+ T cell response against both HIV-1 and HCV.

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DISTINCT COSTIMULATORY REQUIREMENTS OF HIV-SPECIFIC CD8 T CELLS IN RECENTLY VS. CHRONICALLY INFECTED HIV+ INDIVIDUALS

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Plain Language Summary: In this work, HIV-specific killer T cells are shown to require different activation signals depending on the duration of infection.

Objectives: Analyze the response of HIV-specific T cells in HIV patients to costimulatory ligands 4-1BBL and B7.1, separately or in combination.

Methods: Adenovirus-transduced, HIV antigen-pulsed monocytes were used as antigen presenting cells. T cells were stimulated for 8 days and analyzed for expansion and effector function, including cytokine production and cytotoxicity.

Results: Donors at the early stages of infection (<14 months) show no benefit of dual costimulation (4-1BBL and B7.1), similar to healthy donors. This is due to excessive activation and accumulation of inhibitory cytokines such as IFN gamma, IL-10, and TNF alpha. Donors infected for more than 4 years, however, show a benefit of dual costimulation, with little cytokine accumulation. Neutralization of cytokines in healthy donors restores the benefit of dual costimulation.

Conclusions: These results suggest that in the later stages of HIV infection, cytotoxic T cell responsiveness is decreased to a degree where multiple costimulatory signals are required for optimal activation. Thus, distinct treatment regimens will be required depending on the duration of HIV infection.

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INDUCTION OF T CELL DEVELOPMENT FROM HUMAN CORD BLOOD HEMATOPOIETIC STEM CELLS BY DELTA-LIKE 1 IN VITRO

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Plain Language Summary: Individuals infected with HIV undergo a severe depletion of their T cell compartment, resulting in a state of immune deficiency. To restore T cell numbers and immune competency, we are developing a novel system for the generation of T cells from defined sources of stem cells in vitro, with the hope that in the future these stem cells can be engineered to be resistant to HIV infection.

Objectives: The Notch signaling pathway plays a key role at several stages of T lymphocyte differentiation. However, it remained unclear whether signals induced by the Notch ligand Delta-like 1 could support full T cell differentiation from a defined source of human hematopoietic stem cells (HSCs) in vitro.

Methods: Our studies employ an in vitro differentiation system whereby umbilical cord blood-derived HSCs (CD34+ CD38- cells) are cocultured on the OP9 bone marrow stromal line that have been retrovirally transduced to express the Notch receptor ligand Delta-like-1 (OP9-DL1).

Results: Here, we show that human cord blood-derived HSCs cultured on OP9-DL1 cells undergo efficient T cell lineage commitment and sustained T cell differentiation. A normal stage-specific program of T cell development was observed, including the generation of CD4 and CD8 alpha/beta-TCR-bearing cells. Induction of T cell differentiation was dependent on the expression of Delta-like 1 by the OP9 cells. Stimulation of the in vitro-differentiated T cells by TCR engagement induced the expression of T cell activation markers and costimulatory receptors.

Conclusions: These results establish an efficient in vitro coculture system for the generation of T cells from human HSCs, providing a new avenue for the study of early T cell differentiation and function.

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INTERLEUKIN-7 RECEPTOR (CD127) EXPRESSION ON THYMOCYTES AT DIFFERENT STAGES OF MATURATION AND THE EFFECT OF IL-7, TNF- α AND HIV INFECTION

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Plain Language Summary: Impairment of host immune function is a contributing factor to the persistence of HIV infection. Thymocytes are a subset of cells that play a major role in host immunity. Thymocytes mature in the thymus before they are released to the circulating blood system. The cytokine interleukin-7 (IL-7) and its receptor CD127 are essential for the normal generation of thymocytes. HIV infection has been demonstrated to alter normal thymocyte function. The exact cause of thymic dysfunction due to HIV remains unclear. We hypothesize that HIV induced downregulation of CD127 plays a role in impaired thymic function observed in HIV infection

Objectives: HIV infection is associated with impaired thymic function, which, based on in vitro studies appears to occur at an early stage of thymocyte development. IL-7, through interactions with the IL-7 receptor complex (CD127), plays a significant role in the intrathymic maturation of immunocompetent T-cells. Since CD127 expression is decreased on circulating CD8 cells in HIV infection we hypothesize that impaired thymic function is due to a decrease in CD127 expression on developing thymocytes. Based on preliminary data that IL-7 and TNF- α decrease CD127 expression on circulating CD8+ T-cells, we further hypothesize that the same mechanism holds true for developing thymocytes.

Methods: Thymocytes were isolated from thymus obtain from children undergoing elective cardiac surgery and co-cultured with thymic epithelial cells. The expression of CD127 was determined by flow cytometry on the various developmental stages of T-cell maturation: triple negative CD3-CD4-CD8-(TN), double positives CD3-CD4+CD8+(CD3-DP), CD3+CD4+CD8+(CD3+DP) and single positive cells CD3+CD4+CD8-(SP4) and CD3+CD4-CD8+(SP8). Thymocytes were cultured for up to 96 hours with increasing concentrations of TNF- α (0-1000 ng/ml) and IL-7 (0-5000 pg/ml) and CD127 expression was determined at different stages of development. Thymocytes were also cultured with X4 tropic (HIVIII_B), at a M.O.I of 0.01 for up to 9 days. CD127 expression of the different subsets was determined.

Results: The most prominent thymocyte subset was the CD3-DP. CD127 was expressed on all thymocyte subsets. SP8 cells had the highest level of expression (up to 70%). TNF- α resulted in decreased CD127 expression on CD3+DP and SP8 but not on SP4 or TN. IL-7 (up to 1000 pg/ml) caused a transient decrease in CD127 expression on all subsets. At higher concentrations (5000 pg/ml) the reduction in CD127 expression was sustained. In vitro HIV infection results in a decrease in CD127 on the CD3+DP subset and SP8 subset.

Conclusions: CD127 expression on thymocytes varies with the different stages of development and is downregulated in vitro by X4 tropic HIV as well as IL-7 and TNF- α , two cytokines implicated in HIV pathogenesis. The fact that the various thymocyte subsets are differentially affected by these cytokines supports a complex mechanism of CD127 regulation on thymocyte during development.

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PHA Issues

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CHARACTERISTICS OF PHAS WHO USE CBAOS' SUPPORTIVE CARE SERVICES IN ONTARIO: LESSONS FROM FOUR STUDIES

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Plain Language Summary: In four studies, Ambulatory PHAs who used CBAOs most intensely had significantly poorer physical and mental health, more depression, were the most poor and generated greater total per person per annum expenditures for the use of direct health services. PHAs in hospice or on home care for greater than one year are, compared to those on home care less than one year, poorer in physical and mental health function yet consume 33% less in expenditures for health and social services.

Objectives: One of the first steps in evaluating supportive care services is to identify who with what characteristics are CBAOs reaching and do CBAOs in rural/urban areas serve the same types of people. The purpose of this paper summarizes lessons learned from four evaluations.

Methods: All four studies were historic cohort analytic studies of the characteristics, health, depression and expenditures for use of all other health and social services by PHAs who never or rarely used CBAOs' services compared to PHAs who more intensely used the CBAO service. In all four studies, information was gathered on their current (after using CBAO services) sociodemographic, economic, CD4% count, Centre for Epidemiological Studies of Depression (CES-D) score, MOS-HIV measures of physical and mental functioning and the Browne expenditures for Health and Social Service Utilization.

Results: In all four studies, the trend was similar. Ambulatory PHAs who used CBAOs most intensely had significantly poorer physical and mental health, more depression, were the most poor and generated greater total per person per annum expenditures for the use of direct health services. PHAs in hospice or on home care for greater than one year are, compared to those on home care less than one year, poorer in physical and mental health function yet consume 33% less in expenditures for health and social services.

Conclusions: CBAOs have access to the most ill, poor and expensive of PHAs. For ambulatory PHAs, interventions through local service strategic alliances, especially with mental health and social assistance, would enhance CBAO capacity to serve the social and emotional needs of a growing population of surviving PHAs without increases in their own budget. More enduring hospice and home care for this population, associated with lower expenditures for use of other services, could pay for itself within one to two years.

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A WHOLE GREATER THAN ITS PARTS: A COMMUNITY-BASED MODEL FOR HIV/AIDS TREATMENT INFORMATION EXCHANGE

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Plain Language Summary: This presentation summarizes the results of a series of evaluations of a community-based organization that provides information about HIV/AIDS treatment, the Canadian AIDS Treatment Information Exchange (CATIE). Using the results of the evaluations, we suggest some ways of providing community-based treatment information that support empowerment of people and communities.

Objectives: HIV/AIDS treatment information provision involves working with large amounts of changing information from a range of sources. Developing accessible and meaningful information resources that speak to the diverse health communication needs of people living with HIV/AIDS (PHAs) and their caregivers is complex and challenging. This paper discusses evaluation research that assesses the context, effectiveness and impact of a community-based model developed by the Canadian AIDS Treatment Information Exchange (CATIE). CATIE is a bilingual, non-profit organization committed to improving the health and quality of life of PHAs in Canada through treatment information.

Methods: This study analyzes data from six studies undertaken from 2002-2003: * Key informant interviews (program outcomes; needs and issues) (n=106) (2003) * User surveys (Web site; workshops; treatment publications; membership) (n=1168) (2002-2003)

Results: Aggregate results demonstrate that CATIE has achieved several key outcomes related to individual and community empowerment. Furthermore, they illustrate the following elements of success: * community-based action (PHA involvement, peer-based programs, community capacity development); * high quality information (unbiased information from trustworthy sources); * accessibility (multiple formats, targeting diverse audiences, providing context through personal stories); * adult education/empowerment approach (skills development, plain language information, respecting choice); and * "determinants of health" approach ("treatment" includes medical treatments, quality of life, complementary therapies, etc.).

Conclusions: A community-based, empowerment model is a successful approach to providing treatment information to PHAs and their caregivers. This model may help inform development of best practices in HIV/AIDS information exchange and community-based HIV practice.

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HEALTH-RELATED QUALITY OF LIFE DIMENSIONS AND EMPLOYMENT STATUS IN HIV/AIDS.

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Plain Language Summary: Employment status is associated with a variety of health-related quality of life dimensions. This cross-sectional study suggests that there may be a therapeutic benefit associated with finding and keeping a job. Alternatively, it may be that higher quality of life is a necessary condition to maintain employment.

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

Methods: A total of 321 adult participants (74% unemployed) completed a HRQOL questionnaire (MOS-HIV). A structured interview was used to determine employment status, HIV disease markers (CD4 counts and CDC stages), and number of medical symptoms. Neurocognitive tests included: Digit Span (attention), CVLT (learning efficiency) and Symbol Digit Modalities (processing speed). Linear regression analyses were performed to evaluate the contribution of employment status to 6 dimensions of HRQOL (Depression, Health Distress, Functional Limitations, Overall Health, Cognitive Function, and Physical Function). These dimensions were derived through Principal Components Analysis and the resulting 6-factor solution explained approximately 70 % of the variance.

Results: Employment status was significantly associated with depression, health distress, functional limitations, and overall health. These relationships were all in the expected direction (i.e., better health is associated with employment) with the exception of depression. This counterintuitive finding suggests that not working may have a protective effect against depression although the cross-sectional nature of the data does not allow to rule out alternative explanations. In addition, number of medical symptoms was associated with all 6 dimensions of HRQOL suggesting that the participants' subjective report of symptoms is more important in predicting quality of life than biological or clinical HIV disease markers, such as CD4 counts and CDC stages.

Conclusions: Employment status is associated with a variety of HRQOL dimensions, including health distress, functional limitations, and overall health. This cross-sectional study suggests that there may be a therapeutic benefit associated with the transition from unemployment to employment. Alternatively, it may be that higher HRQOL is a necessary condition to maintain employment, or that both selection and causation mechanisms operate at the same time. Prospective studies are needed to determine the direction of causality in the relationship between employment status and HRQOL.

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HUNGER PAINS: STRATEGIES FOR MEETING THE NEEDS OF PHAS LIVING IN POVERTY

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Plain Language Summary: People living with HIV/AIDS (PHAs) receiving Ontario Disability Support Program (ODSP) or Ontario Works (OW) benefits are eligible for a monthly special diet benefit of up to \$250.00. This cash supplement can make a difference in the lives of PHAs living in poverty by meeting their nutritional needs more effectively. We summarize the Immunodeficiency Clinic's activities assisting PHAs to receive this benefit as well as its impact on overall monthly and food budget.

Objectives: Previous literature has established a relationship between adequate nutrition and HIV-related survival and quality of life. Local estimates suggest that following expenditures for merely two essential needs (i.e., accommodation and clothing) OW and ODSP food budgets, respectively, amount to approximately -\$230.00 and -\$4.00 per month. We examine the impact of special diet benefits provided by OW or ODSP on PHAs living in poverty.

Methods: Data related to the initiation, success, and renewal of applications for the diet benefit on behalf of 126 clinic patients to date were collected over four consecutive intervals from 1998 to October 2004.

Results: The special diet recipients have cumulatively obtained a total of \$714,000.00 over the four uptake periods. However, the \$250.00 supplement is offset by the absence of an 18% cumulative cost of living increase over the past 11 years that might have occurred if benefits had not been frozen over that time. It is evident that without the special diet benefit, PHAs receiving social assistance in Ontario would be living in even worse dire straits situations, jeopardizing their access to basic resources as well as their ability to receive optimum care.

Conclusions: It is imperative for HIV-related treatment providers to facilitate special diet benefits applications for guaranteeing PHAs in need up to \$3,000.00 extra per year for their nutritional needs. Both OW and the ODSP need to recognize the effects of freezing benefits rates in the context of cost of living increases endured by chronically ill recipients. This will help ensure that PHAs potentially receive the basic respect and human dignity required for living above the designated poverty line.

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HEPATITIS C PREVALENCE AMONG NEWLY ADMITTED MALE AND FEMALE INMATES IN ONTARIO JAILS AND DETENTION CENTRES

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Plain Language Summary: Prevalence studies are useful in estimating the actual number of people who are infected. This information is essential in allocating resources for care, treatment, services and education. This study provides the first such estimate for Hepatitis C among inmates in Ontario jails and detention centres. 1,644 male and female adult inmates were interviewed and tested for Hepatitis C using anonymous saliva samples. The results suggest that between 17.0% and 21.0% of newly-admitted inmates have Hepatitis C. Rates were higher for those with a history of injecting drugs and for females. An estimated 5,048 of newly-admitted inmates in Ontario are unaware that they have Hepatitis C.

Objectives: To estimate the prevalence of Hepatitis C (HCV) infection in adults admitted to Ontario jails and detention centres.

Methods: Between February 2003 and June 2004, data were collected on 1,644 adult inmates admitted to 11 remand facilities located across Ontario. All newly admitted inmates were eligible. Participation was anonymous and voluntary. The response rate was 90%. Participants underwent a brief, interviewer-administered survey, then were asked to provide an anonymous saliva specimen for HIV and HCV screening (96% provided one). HCV screening was done with the Ortho Diagnostic HCV 3.0 SAvE ELISA test kit. A total of 1,503 had valid saliva screen results. HCV prevalence rates were calculated with 95% confidence intervals (CI) and compared using chi-squared tests.

Results: 19% of participants were female and 81% were male. The mean age was 32.4 years. 83% had a history of previous incarceration, of whom 13% reported previous incarceration in a federal facility. The overall prevalence of HCV was 19.0% (95% CI 17.0-21.0). Prevalence rates ranged from 14.9% (95% CI 11.3-18.5) in the Northern region to 24.5% (95% CI 19.9-29.2) in the Eastern region. Females had a higher rate compared to males (29.6% vs. 16.5% p<0.0001). HCV rates were highest among those with a self-reported history of injection drug use (IDU). Among male IDU the prevalence was 53.6% (n=308; 95% CI 48.0-59.1), and among female IDU the prevalence was 56.1% (n=132; 95% CI 47.6-64.5). 63.6% (182/286) of those who tested positive for HCV had been previously diagnosed; the remaining 36.4% were unaware of their infection. Among inmates who were aware they had HCV (n=159), risk behaviours since diagnosis that could result in further transmission were passing on piercing equipment (2.5%), tattooing equipment (4.4%), a toothbrush/razor (14.7%), or injecting equipment (23.9%). Given the 73,000 adult admissions annually in Ontario, an estimated 13,870 are infected with HCV, of whom 5,048 are undiagnosed.

Conclusions: HCV prevalence among newly-admitted adult inmates is 24 times greater than in the general population (the latter is estimated at 0.8% [Patrick et al. CJPB 2000; 91(suppl. 1):S18-21]). A large number of inmates are infected, and an unacceptably high number remain undiagnosed. HCV testing, treatment and education would reduce both the burden of illness and further transmission.

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HAART DISCONTINUATION FOR LIVER TOXICITY IS RARE IN HIV-HCV CO-INFECTION

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Plain Language Summary: Both patients living with HIV-HCV co-infection and health care providers are concerned about liver toxicity with the use of HIV medications. We assessed all HIV-HCV co-infected patients receiving care at our Immunodeficiency Clinic at the Ottawa Hospital since 1996. Our findings suggest that liver side effects are rarely serious enough to require interruption in HIV medications. We found that substance abuse negatively affects patients ability to remain on treatment and should be addressed by HIV care givers.

Objectives: Treatment strategies resulting in longterm adherence to HAART are required in HIV-HCV co-infection. Understanding why co-infected patients interrupt HAART may facilitate this.

Methods: Clinical, laboratory, and virologic results pertaining to the all HAART regimens initiated in HIV-HCV co-infected subjects at The Ottawa Hospital Immunodeficiency Clinic between January 1994 and December 2003 were assessed by computerized SPSS 11.0 database analysis.

Results: 548 rounds of HAART were initiated in 216 of 287 (75%) subjects. Median duration of therapy was 7 months. 84% of regimens were discontinued or altered for: inadequate adherence (19%), gastrointestinal intolerance (17%), loss to follow-up (14%), neurologic and psychiatric complications (6%), substance abuse relapse (5%), and improved antiretroviral treatment options (5%). Twelve regimens in 12 subjects (2.9% of all regimens) were interrupted for clinically apparent liver toxicity (11 of 322 PI-treated, 1 of 105 non-PI-treated; 3 of 132 NNRTI-treated, 2 of 106 <400mg bid ritonavir regimens). By univariate Cox regression, injection drug history, CD4 <200 cells/ μ L and baseline HIV RNA >50,000 copies/mL predicted earlier discontinuation of HAART. Subjects with a history of daily alcohol use >50g were more likely to have never initiated HAART (21% versus 10%; p<0.001, Chi Square) and to remain off HAART after discontinuing a regimen (22% versus 16%; p=0.06).

Conclusions: Contrary to common perception, HAART is rarely interrupted for clinically apparent liver toxicity in HIV-HCV co-infection. Strategies which target substance abuse and address common antiretroviral side effects are predicted to diminish treatment interruption.

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HCV PREVALENCE AND HIV/HCV CO-INFECTION IN A DIVERSE PROVINCIAL SAMPLE OF GAY AND BISEXUAL MEN

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Plain Language Summary: Our goal was to describe the prevalence of HCV, and HCV/HIV co-infection in a diverse sample of gay and bisexual men in Ontario. Conclusive laboratory results for HIV and HCV were available for 3,304 saliva samples. Highest rates of infection were found among men with a history of drug injection. The findings reflect the results of other studies of gay and bisexual men, which show higher rates among HIV positive men. Further investigation of correlates is necessary.

Objectives: To describe the prevalence of HCV and HCV/HIV co-infection in a diverse sample of gay and bisexual men in Ontario.

Methods: An anonymous, self-completed survey with optional collection of a saliva sample for laboratory HIV and HCV testing was conducted in 13 Ontario communities. The test procedure for HIV is described elsewhere (Myers et al, 2004). The Hepatitis C Screen test was performed using the OrthoDiagnostic HCV3.0 SAve ELIZA test kit. Variables describing HIV and HCV prevalence and co-infection were cross-tabulated with geographic and personal characteristics of the study sample.

Results: Of 5,080 men who participated in the survey, 3,635 (71.6%) agreed to provide saliva. After testing for HIV there was only adequate saliva to test for HCV among 3,312 saliva samples. Of the 3,304 samples with conclusive results for both HCV and HIV, the HIV prevalence was 9.0% (95%CI 8.1-10.1), and HCV prevalence was 1.9% (95%CI 1.5-2.5). This varied across the 13 regions from 0.0% to 3.6%. Prevalence was highest in Toronto (2.2%; 95%CI 1.5-3.0) and Southern Ontario (2.2%; 95%CI 1.4-3.2), compared to Ottawa (1.0%; 95%CI 0.3-2.6) and the North (0.81%; 95%CI 0.1-2.9). HCV was strongly associated with a history of drug injection; the rate of HCV infection among those who reported ever injecting was 19.5% (95%CI 14.0-26.0) versus 0.76% (95%CI 0.5-1.1) for those who had not (relative risk 25.8). Significantly higher HCV infection rates were found with age with the highest (3.4%) in the 45–54 age group; lower education (6.7%), and income <\$30,000 (2.8%) and French language (3.8%). Highly significant differences in HCV were found between those men who tested HIV-positive (7.7%; 95%CI 4.9-11.4) and those who testing HIV negative (1.4%; 95%CI 1.0-1.8).

Conclusions: Rates of HCV infection in this population were higher than those generally reported in the population at large. The higher rates of HCV among HIV positive men concur with other studies. This in part may be reflected by the higher proportion of participants who have ever injected and who may have shared needles. The HCV prevalence rate of 1.9% was somewhat higher than the estimated male population rate of 1.2%, likely due to the higher reported lifetime history of drug injection (6.1% among participants versus 2% in the adult male general population). While sexual practices may play some role in HCV transmission for this population, it is difficult to determine in this analysis. Further investigation of risk factors and correlates is necessary.

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THE NEED TO SCALE-UP ACCESS TO HEPATITIS C VIRUS TESTING AMONG INJECTION DRUG USERS

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Plain Language Summary: Early diagnosis of hepatitis C virus (HCV) infection is important as it enables access to early treatment and the adoption of practices to prevent further transmission. We tested 485 injection drug users (IDUs) in Ottawa for HCV infection. We obtained positive HCV results for the majority, including 31 IDUs who reported negative HCV status and for 20 IDUs who had not previously been tested. IDUs did not access HCV testing if they thought they were at low risk of acquiring HCV. Conversely, IDUs who accessed drug treatment and needle exchange services were less likely to be non HCV-testers. We conclude that needle exchange programmes and drug treatment services need to develop and promote their HCV testing service.

Objectives: Co-infection with HIV and hepatitis C virus (HCV) is problematic due to potential complications in the clinical course and treatment of both infections. In the context of some of the highest levels of HIV among injection drug users (IDUs) in Canada, we undertook a study of HCV incidence and prevalence among Ottawa IDUs. This report examines HCV testing behaviour among Ottawa IDUs and identifies strategies for increased access to HCV testing.

Methods: From October 2002 to January 2003, 506 street-recruited IDUs completed baseline interviews; 485 consented to anonymous HCV saliva testing. Using multivariate logistic regression, we determined factors related to no previous history of HCV testing.

Results: At baseline, 278/485 IDUs tested HCV-positive (57.3%, 95% CI: 52.8, 61.8). HCV tests were positive in 31 IDUs who self-reported negative HCV status and in 20 IDUs who had not been previously tested for HCV. Overall, IDUs who had not tested previously (95/506) were significantly more likely to: inject less than daily (AOR=2.8, 95% CI: 1.4, 5.9), to have injected in crack houses in the past six months (AOR=3.4, 95% CI: 1.9, 6.0), and to have a low or no self-perceived chance of acquiring HCV infection (AOR=4.0, 95% CI: 2.4, 6.8). Conversely, IDUs with a history of accessing drug treatment (AOR=0.2, 95% CI: 0.1, 0.4) or who had accessed the services of the Ottawa needle exchange programme for a year or more (AOR=0.3, 95% CI: 0.2, 0.6) were significantly less likely to be HCV non-testers.

Conclusions: Not all IDUs have been tested for HCV, mostly related to lower perceived HCV risk and lack of use of facilities where testing is offered. For IDUs to initiate HCV and HIV preventive behaviours and practices and to benefit from access to early HCV treatment there is value in all IDUs being afforded the opportunity to know their HCV status. NEPs and drug treatment agencies appear to be well-positioned to scale up their HCV testing activities.

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Global Impact of HIV

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CRITICAL PUBLIC HEALTH ETHICS AND HIV/AIDS: ONTARIO, CANADA AND THE WORLD

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Plain Language Summary: This presentation introduces a way of thinking about HIV/AIDS issues called “critical public health ethics”. It is important to have a range of ways to think about HIV/AIDS since each perspective offers something different and, hopefully, valuable. This perspective sheds light on the social, political and economic forces that shape decisions. The presentation illustrates this kind of perspective by looking specifically at the ways in the Government of Canada has responded to the HIV pandemic outside of its borders. The presentation also looks at lessons for Ontario.

Objectives: The field of ethics, and critical public health ethics in particular, has much to contribute to policy, programming and advocacy inquiries about HIV/AIDS. The purpose of this paper is to introduce the emerging field of critical public health ethics using the case study of Canada’s international response to the global HIV pandemic.

Methods: Stage 1 of the study involved the development of a descriptive inventory of Canada’s international responses to the global HIV pandemic over time, including contributions from Ontario. Stage 2 involved interviews with 23 experts at the provincial, national and international levels within and outside of government regarding the political, economic and social forces that have shaped Canada’s international responses, and the ethical principles that underpin them. These methods draw on critical discourse analysis, which involves close reading of the texts (e.g., policy documents, G-8 speeches, interviews) for ideas, contradictions and discursive patterns that inform the research questions.

Results: In terms of Canada’s international response to the global HIV pandemic, there is a disconnect between policy and action that reflects conflicting ideological goals of Canadian foreign policy. Critical public health ethics offers a useful lens for revealing social, political and economic forces shaping international health issues.

Conclusions: This study draws on the emerging field of critical public health ethics to inform analysis of the ideologies and ethical principles underlying Canada’s international response to the HIV pandemic and the political, economic and social forces that have shaped it over time. Canada’s international actions are understood to be intimately connected to Canadian foreign policy which, like public health ethics, is shaped by the pervasive forces of economic globalization.

The purpose of conducting such an inquiry is twofold: (1) to offer a normative analysis of Canada’s international responses to the global HIV pandemic, and (2) to articulate lessons for advancing the field of critical public health ethics, with particular emphasis on the forces of economic globalization.

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STUDENT INTERNSHIPS IN CAMBODIA (II): SEXUAL TOURISTS, YOUNG SOUVENIR VENDORS AND HIV/AIDS PREVENTION EDUCATION AT ANGKOR WAT, CAMBODIA.

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Plain Language Summary: Thesis and intern students, (Alison McNeil, Meghan McCourt in 2002) helped build local research/intervention capacity in Cambodia, with HIV/AIDS peer-educator prevention programs. Now “street-proofing” and AIDS awareness programs are designed for young persons selling souvenirs at Angkor Wat, frequently propositioned by sexual tourists. No epidemiological data for Cambodian children’s HIV/AIDS rates are available; a pediatric hospital reported children 23% seropositive (VCCT voluntary testing). Students show young vendors “polite” ways of engaging tourists and avoiding risks of exploitation; they develop “street-proofing” programs with local NGO SiRCHESI. Guelph students assess risks of sexual exploitation through filmed interviews, to prepare further prevention/education programs.

Objectives: Student internships and thesis projects build local capacity for monitoring risk, creating and strengthening prevention and research programs concerning the HIV/AIDS pandemic in Siem Reap, Cambodia. Specific attention is paid young persons, not usually part of government HIV/AIDS Sentinel Surveillance programs.

Methods: Since 2002, students, in a series of field visits, have helped local staff conduct baseline survey research, qualitative interviews, SPSS statistical analyses, and develop other research/data-gathering skills. 68 young souvenir vendors were interviewed (aged 9-22); with help from peer representatives, workshops were designed to sensitize young persons about sexual tourism, pedophiles, trafficking, sexually transmitted infections, HIV/AIDS, and polite ways to earn money from tourists while avoiding risks.

Results: Two training sessions were held for 53(Aug. 2003) and 82 (August, 2004) young vendors. An Angkor Wat Young Vendors Association was created to attempt negotiating better working conditions with local police authorities. Sex education and AIDS/STI prevention information were presented, and 6 peer-educators maintain continuous contact. Student interns interviewed tourists to informally assess the effects of politeness training. At University of Guelph, one project asks students to assess risky behaviours discussed in interviews by young vendors. We hope to also develop “best practices” for local “street-proofing”.

Conclusions: Child HIV/AIDS seropositivity has not been systematically studied, in terms of the role played by sexual tourists approaching young persons. A study of young persons living with HIV/AIDS in orphanages is lacking. Data exist at one hospital concerning a mother-child transmission trial, and some children have been put on ARVT at another children's hospital. "AIDS orphans" have been increasingly seen in the downtown streets. Work with the Young Vendors Association and the NGO SirCHESI is designed to provoke further interest in prevention and treatment for younger persons

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CHARACTERIZATION OF AN EMERGING HETEROSEXUAL HIV EPIDEMIC IN RUSSIA USING A CASE-CONTROL APPROACH

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Plain Language Summary: Russia is currently experiencing one of the fastest growing HIV epidemics worldwide. The majority of cases have been diagnosed among injection drug users (IDU), but there is concern that HIV transmission could expand to the non-IDU population. This study identified the key factors that lead to heterosexually-acquired HIV infection in four regions of Russia. Characteristics of recently-infected persons were compared to those who remained HIV-negative. The main sources of infection were regular sex partners for women, multiple partners for men, and regular sex partners who were IDU for both men and women. Having another sexually transmitted infection also substantially increased the likelihood of HIV infection.

Objectives: To identify sexual risk factors for recent HIV infection among Russians who do not report recent injection drug use; to determine the relative importance of identified risk factors; and to describe knowledge and attitudes that may inform prevention policies.

Methods: A case-control study was conducted in the regions of Altay, Krasnoyarsk, Saratov and Tver in Russia. Participants were recruited through regional AIDS centres based on results of HIV-antibody tests. Cases had medical evidence of HIV infection within 12 months of the first HIV-positive test. HIV-negative controls were frequency-matched by gender, region, and exposure category (IDU, heterosexual non-IDU). All completed a face-to-face interview and self-completed survey which collected information on HIV knowledge, attitudes, and risk factors. The analysis was restricted to those who reported heterosexual activity but no recent injection drug use within the 12 months prior to the HIV antibody test. Data from men and women recruited as of September 2004 were analysed. Risks factors were identified using chi-squared tests, Mantel-Haenszel stratified analysis, and multiple logistic regression. Results are reported as adjusted odds ratios (AOR) with 95% confidence intervals (CI).

Results: A total of 166 participants met the inclusion criteria for analysis (19 HIV+ and 22 HIV- men, 67 HIV+ and 58 HIV- women). Risk factors for recent infection were: unprotected sex with an HIV+/status unknown regular partner (among women only: AOR=5.35, 95% CI 2.13-13.4); having a regular sexual partner who was an IDU (AOR=3.58, 95% CI 1.51-8.49); having 5 or more sexual partners (among men only: AOR=2.73, 95% CI 0.66-11.4); unprotected sex with a partner who had a diagnosed sexually transmitted infection (STI) or signs/symptoms of an STI (AOR=6.39, 95% CI 1.07-38.1); and undiagnosed signs/symptoms of an STI (AOR=3.36, 95% CI 1.50-7.55). The proportion of ongoing HIV infections that can be attributed to these risk factors were 69%, 31%, 33%, 12%, and 37%, respectively. Among controls, predominant reasons for unprotected sex were being with one's regular partner, thinking self or partner did not have HIV/STI, not liking/wanting to use a condom, arousal, (male) partners not wanting to use condoms, and not having a condom at the time.

Conclusions: These data provide evidence of bridging between the IDU and non-IDU populations. Concomitant STI appear to have a major role in fueling the Russian HIV epidemic. Recommendations for HIV prevention include expansion of STI screening and treatment, and increasing the acceptability of condoms, particularly among men and among couples in regular sexual partnerships.

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"CONCEPTUAL EVENTS": ADVANCING A CULTURALLY COMPELLING METHOD FOR HIV INTERVENTIONS

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Plain Language Summary: HIV interventions are often predicated on scientific evidence. Assuming that persons who hear the evidence of risk do not necessarily act accordingly, this research tests a novel intervention process. "Conceptual events" – an innovative methodology based on principles of participatory action – brings stakeholders together to reflect and act differently when fully appreciating risk stories. Best practices from Malawi and Zimbabwe are pertinent to HIV interventions in Ontario. In both instances, where there are discrepancies between the public health system approach and the experienced reality of vulnerable peoples, an intervention method that transcends divergent realities is required.

Objectives: This paper defines and evaluates the impact of an HIV intervention methodology called "conceptual events" – a process based on participatory principles. Best practices, from Malawi and Zimbabwe, which implements this methodology are discussed, as well as the implications for programs in Ontario.

Methods: "Conceptual events" are trans-disciplinary, -contextual, and -experiential colloquia that intentionally nudge persons coming from different truth perspectives, paradigms, or experiences, to construct a shared, ethically compelling framework for understanding the HIV/AIDS problematic. In the process, these stakeholders negotiate behavioural and social solutions. "Conceptual events" are usually one- to four-day meetings of persons who come together for an intense period of facilitated discussion. In a safe environment, they reflect on their particular understandings of HIV/AIDS. The premise is that differences in opinion and understanding divide, and are a deterrent to problem solving. Utilizing participatory action research (PAR) methods, "conceptual events" enable the synthesizing of HIV/AIDS narratives (scientific, social-cultural, faith-based, and other evidences of ethical reasoning), thereby achieving solidarity of opinion, as well as an agreement for follow-up action.

Results: “Conceptual events” were successfully introduced in two Sub-Saharan African countries. In Malawi, faith community leaders – representing divergent faith perspectives (Muslim, Christian, Independent) – met over a period of 4 days. After an intense period of debate and deliberation, they produced a Declaration called “Our Faiths and HIV: Expressions of Hope and Compassion for the People of Malawi”. This prompted a series of subsequent “conceptual events” that are currently addressing issues of condom use, access to ARVs, home-based care, and a theology of HIV/AIDS. In Zimbabwe, men and women from a high density suburb of Harare came together to reflect on and examine why there are such differences in sexual experience and expression between men and women. During the “conceptual event”, the experiential differences between men and women were alarming, and yet together, they ultimately co-produced a statement of how men and women (as sexual partners) should live so as to preserve the health of families and minimize their risk for HIV transmission.

Conclusions: “Conceptual events” have been evaluated to be effective in Malawi and Zimbabwe. Ongoing work in Uganda also underscores the fact that interventions need to appropriate the problem-solving capacities, resources, and skills of persons vulnerable or at-risk for HIV. This method can be used in Ontario as well, especially in instances where the social-cultural divide compels public health researchers and planners to graft their message of HIV risk (scientific reality) to the lived experiences of vulnerable persons and groups (social-cultural reality).

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WOMEN'S EXPERIENCES OF HIV TESTING DURING PREGNANCY

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Plain Language Summary: This study examines women's HIV testing experiences during pregnancy. Women were interviewed in the maternity wards at 3 Toronto hospitals. 220 of the women interviewed said that a health care provider talked to them about having an HIV test during pregnancy: 80% felt it was a routine prenatal blood test; 71% felt testing was their choice; 88% were happy with the explanation; and 90% agreed to test. The main reasons that 18 women refused testing were: tested before this pregnancy and not at risk for HIV.

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 3 Toronto teaching hospitals from November 2002 to February 2004. Women were approached 4 to 162 hours post-partum in hospital and interviewed about their HIV testing experiences during their recent pregnancy.

Results: A total of 299 women were interviewed (67% of those approached). 99.7% of participants reported having had any prenatal care. While 74% of the women interviewed claimed that a health care provider talked to them about having an HIV test during pregnancy, fewer women (56%) indicated that a health provider discussed the topic of HIV in general. Of the 220 women with whom HIV testing was discussed, 80% felt it was a routine test, the same as all other prenatal blood tests; 71% felt they had the option to refuse the HIV test if they wanted to; 14% wished they had more information before making a decision about the test; 88% stated that they were satisfied with how the HIV test was explained to them; and 90% agreed to test. Of the 18 women who declined the HIV test offer, the main reasons given were for not testing were: tested before this pregnancy (50%), not at risk for HIV (39%), no need for HIV testing (5.5%), and intended to test but did not (5.5%).

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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VITAMIN SUPPLEMENTATION FOR PREVENTION OF MOTHER-TO-CHILD TRANSMISSION OF HIV AND PRE-TERM DELIVERY: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RCTS INCLUDING MORE THAN 2800 WOMEN

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Plain Language Summary: Several cohort studies have indicated that the use of vitamins may have a protective effect in preventing mother to child transmission (MTCT) of HIV and pre-term delivery. We examined all randomized controlled studies and pooled the results. We identified that Vitamin A is not protective for MTCT and may be harmful. We found that multivitamins had no impact on MTCT or preterm delivery.

Objectives: MTCT is responsible for 5-10% of the total of new HIV infections each year in many developing countries, with more than 500,000 children being infected each year. We aimed to determine the efficacy of vitamins on the prevention of MTCT and preterm delivery by meta-analysing the available randomized controlled trials (RCTs).

Methods: We conducted systematic searches of 7 electronic databases. We extracted data from the RCTs independently, in duplicate. We assessed the primary outcomes of MTCT and preterm delivery. Where appropriate, we pooled the results using a random effects model and determined the appropriate relative risks (RR).

Results: We included 7 trials in our analysis. The combined RR of vitamin A for prevention of MTCT yielded a moderately significant RR of 1.12 (95% CI, 0.9-1.4, p=0.056, I²=54%, heterogeneity P=0.1), indicating possible harm. The single trial examining a multivitamin for prevention of MTCT yielded a non-significant RR of 1.12 (95% CI, 0.9-1.4). Two trials examined the protection of vitamin A for pre-term delivery and yielded a significant pooled RR of 0.78 (95% CI, 0.60-1.01, P=0.02, I²=0%, heterogeneity P=0.2). Two trials examined the role of multivitamins for prevention of pre-term delivery. The combined RR yielded a non-significant RR of 1.01 (95% CI, 0.82-1.25, P=0.8, I²=0%, heterogeneity P=0.5).

Conclusions: The use of vitamins to prevent MTCT and preterm delivery is not supported by the available evidence and may be associated with increased harm. Physicians should discuss vitamin use with pregnant patients and discourage use of vitamin A supplementation.

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INTERACTION OF PRIMARY GENITAL EPITHELIAL CELLS WITH SEXUALLY TRANSMITTED VIRAL AGENTS AND EFFECT OF SEX HORMONES ON SUSCEPTIBILITY: IMPLICATIONS IN HETEROSEXUAL TRANSMISSION OF HIV IN WOMEN

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Plain Language Summary: Globally, women are much more easily infected by sexually transmitted infections such as HIV, than men. Transmission of this virus is spreading so fast that women now makeup, for the first time, half of all people infected by HIV. The reason why the virus is spread so easily into women is not clear. Since HIV does not infect small animals like mice, this problem is not easy to study. We have developed a cell culture system, where we take genital tract tissues from women who are undergoing surgery and grow them in culture. This culture system has allowed us to examine which cells get infected by viruses such as HIV and how we can best prevent this infection.

Objectives: Objective: According to latest UNAIDS report, women now account for 50% of HIV-infected people. Clinical studies show that transmissibility rates from men to women are much higher than women to men. Efforts to understand the factors that regulate susceptibility suffer from lack of appropriate models where viral interactions in the genital tract of women can be examined directly. We have developed and standardized an ex-vivo primary culture model from human endometrium and cervical tissues and used this to examine the interactions of sexually transmitted viral agents, HSV-2 and HIV-1 with female genital mucosa.

Methods: Epithelial and stromal cells were isolated from endometrial and cervical tissue samples, obtained from women undergoing hysterectomies at McMaster University Health Sciences Center. Epithelial cells were isolated from the tissue samples and grown on tissue culture inserts. Fully differentiated, polarized monolayers of epithelial cells were infected with HSV-2. Infection kinetics were examined. The influence of factors such as anti-virals and sex hormones, estradiol and progesterone, on susceptibility was examined. Similar experiments have been initiated with HIV-1.

Results: Uterine and cervical epithelial cells formed confluent, polarized monolayers after 5-7 days in culture. The monolayers were free from any significant contamination of other cell types. They also expressed receptors for estradiol and progesterone. Both endometrial and cervical epithelial cells were highly susceptible to infection with HSV-2. The kinetic of infection was similar to the in vivo infection and viral shedding was seen predominantly from the apical side of cells. Treatment of the cultures with anti-virals such as acyclovir and Poly I:C showed significant drop in HSV-2 infection. Estradiol treatment increased infection in endometrial epithelial cells, while susceptibility decreased following treatment with progesterone. Similar studies are underway to examine the interaction of HIV-1 with endometrial and cervical epithelial cells. Epithelial cell monolayers exposed to cell-associated HIVADA, an R5 tropic strain showed significant infection of target cells on the basolateral side. Infection with X4 HIV-1 strains led to high p24 levels in both apical and basolateral compartments.

Conclusions: The results from the studies done so far show that the primary culture system from reproductive tract tissue of women, holds great promise in helping us understand the interactions between sexually transmitted viral pathogens and genital epithelium. It was also clear that estradiol and progesterone may directly regulate susceptibility to sexually transmitted viruses. Ongoing studies are examining the effect of sex hormones on HIV-1 infection. These studies have direct implications in developing better preventative and vaccine strategies for HIV-1 infection in women.

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ROLE OF DENDRITIC CELL SUBSETS IN THE HUMAN CERVIX AND ENDOMETRIUM IN HETEROSEXUAL TRANSMISSION OF HIV IN WOMEN

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Plain Language Summary: Women are more susceptible to HIV infection than men. The reason for this is not clear. Also how HIV infects and spreads in women's reproductive tract after sexual transmission is not understood. Although we know the type of cells that get infected by HIV, where these cells are located in the genital tract has not been shown. We took endometrial and cervical samples from women undergoing surgery and looked at the different types of cells that HIV can infect. It was clear from these studies that cervix has many more cells that could be infected by HIV than uterus. These cells were also located close to the cervix where the virus can reach easily. These studies will help us understand how best we can prevent transmission of HIV.

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 different subsets of dendritic cells may play a key role in transmission of HIV. The objective of this study was to identify different subsets of DCs in the genital tract.

Methods: Human cervical (35 patients) and endometrial (25 patients) tissue was obtained from women undergoing surgery for unrelated reasons, with patient consent. Cells expressing HLA Class-II, DC-SIGN, CD4, CD1a, and CD11c were localized in the cervical and endometrial tissue by immunohistochemistry.

Results: Consistent staining patterns were observed in the patient population group examined. MHC Class-II positive cells were present abundantly in the human cervix and endometrium and were localized individually throughout the stroma, as well as in groups around glands and blood vessels in both cervix and endometrium. CD1a, DC-SIGN, CD4 and CD11c positive cells were all consistently present in the cervix and most of the DC subsets were localized in either basal layers of cervical epithelium or the subepithelial stroma. In the endometrium, CD1a, DC-SIGN, CD4 and CD11c positive cells were present in fewer numbers and mostly around endometrial glands. Lymphoid aggregates containing CD4+ and CD11C+ cells were also found in both endometrium and transitional zone of cervix.

Conclusions: A large number of cells carrying DC markers were found to be consistently present in the human cervix. These cells were less abundant in the endometrium. In the cervix, different subsets of DCs were localized close to the squamous epithelium suggesting that they may be easily targeted by HIV for infection. The transitional zone in the cervix, may provide a particularly target-rich zone for HIV. The endometrium on the other hand may not provide a big reservoir of DCs for HIV targeting. Defining these populations is necessary to determine the natural susceptibility to heterosexual HIV transmission as well as developing preventative/therapeutic strategies.

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