Vaccines And Immunology

200

IMMUNOGENICITY OF A POLYVALENT HIV-1 CANDIDATE VACCINE BASED ON GP120 PROTEINS

Ali Azizi [1,2]; Rita Frost [1]; Masoud Ghorbani [1]; David Montefiori [3]; David Anderson [4]; Francisco Diaz-Mitoma [1,2];
1-Infectious Disease and Vaccine Research Centre, Research Institute Children's Hospital of Eastern Ontario, 401 Smyth Road, Ottawa, ON, K1H 8L1, Canada; 2-Department of Biochemistry, Microbiology and Immunology, Faculty of Medicine, University of Ottawa, Ottawa, ON, K1H 8M2, Canada; 3-Human Vaccine Institute, Duke University, Durham, NC, 27710, USA; 4-Harvard Medical School, 77 Avenue Louis Pasteur, Boston, MA, 02115, USA;

Plain Language Summary: One of the major obstacles in the design of an effective vaccine is the hypervariability of HIV-1 envelope glycoprotein. Most HIV-1 vaccine candidates have utilized envelope glycoprotein from a single virus isolate, but to date, none of them have elicited a cross reactivity response against primary isolates. Here, golden hamsters were immunized with a single gp120, a combination of four gp120s, or a combination of fourteen gp120s and immune responses were analyzed.

Objectives: A polyvalent HIV-1 gp120 protein from different strains could increase the breadth and potency of anti-HIV-1 immune response.

Methods: Fourteen gp120s from primary HIV-1 isolates strain B were amplified and cloned into DNA expression vectors. To express the recombinant gp120 proteins, mammalian cells (CHO cells) were transfected and the recombinant proteins were purified using immobilized metal affinity chromatography. The recombinant gp120 proteins were characterized by western blotting and IFA staining. Golden hamsters were immunized with a single gp120, a combination of four gp120, or a combination of fourteen gp120s. Two weeks after the last immunization, specific antibody titer, neutralization and lymphocyte proliferation were assessed against subtypes A/E, B and C.

Results: The group that received a cocktail of fourteen gp120 proteins subtype B (polyvalent) had a higher proliferative response to different HIV-1 gp120 subtypes (A/E, B and C). In addition, higher levels of antibody titers to gp120 subtypes were detected in the group of hamsters that received a cocktail of wild type gp120 proteins. Furthermore, the breadth of neutralizing antibody response was evaluated against HIV-1 strains MN and SF162. The group that received a cocktail of gp120 proteins induced higher neutralizing antibody response to MN than gp120 immunogen alone. However, the breadth and potency of neutralization properties to SF162 was unimpressive.

Conclusions: These results suggest that the use of a polyvalent HIV-1 gp120 candidate vaccine might be a good strategy for induction of a multispecific immune response against various HIV-1 subtypes. However, understanding the ability of each immunogen to elicit a broadly cross-reactive response is critical for development of an effective polyvalent vaccine.

Contact Information: Ali Azizi, Tel: 613-737-7600 x3911, Email: aliazizi555@yahoo.ca

201

INTERLEUKIN-7 RECEPTOR EXPRESSION ON CD8 T-CELLS IS DOWN REGULATED BY THE HIV TAT PROTEIN

Elliott Faller [1,3]; Mark McVey [1]; Paul MacPherson [1,2,3];
1-Ottawa Health Research Institute; 2-Division of Infectious Diseases, Ottawa Hospital General Campus, Ottawa, ON; 3-Departments of Medicine, and Biochemistry, Microbiology and Immunology, Ottawa, ON;

Plain Language Summary: We have previously shown decreased expression of the IL-7 receptor □-chain (CD127) on CD8 T-cells in HIV infected patients, and an apparent recovery of this receptor in those receiving antiretroviral therapy with sustained viral suppression. Here we demonstrate that the HIV Tat protein specifically down regulates cell surface expression of CD127 on human CD8 T-cells in a dose- and time-dependent manner. The effects of Tat on CD127 expression could be blocked with anti-Tat monoclonal antibodies or by pre-incubating Tat with heparin. Tat had no effect on the expression of other cell surface proteins examined including CD132, or on cell viability over 72 hours. Further, CD127 expression was not altered by other HIV proteins including gp160 or Nef. Pre-incubation of purified CD8 T-cells with Tat protein inhibited CD8 T-cell proliferation and perforin synthesis following stimulation with IL-7. Since IL-7 signalling is essential for optimal CD8 T-cell proliferation and function, the down regulation of CD127 and apparent inhibition of cytotoxic activity by Tat may play an important role in HIV induced immune dysregulation and impaired cell mediated immunity.

Objectives: To determine the effect of HIV-1 Tat protein on the CD127 surface receptor and the functional deficits that result from decreased CD127 surface expression on CD8 T cells.

Methods: Isolated CD8 T cells were cultured from healthy donors and flow cytometry was used to monitor various surface and intracellular antigens in response to incubation with the HIV Tat protein. Proliferation Assays were used to determine the ability of CD8T cells to proliferate after exposure to HIV Tat protein.

Results: HIV Tat protein down regulates surface expression of CD127 in a time and dose dependant manner on CD8 T cells. This down regulation results in a reduced ability of CD8 cells to proliferate and produce perforin when stimulated with CD3, CD28 and Il-7.

Conclusions: Since IL-7 signaling is essential for optimal CD8 T-cell proliferation and function, the down regulation of CD127 and apparent inhibition of cytotoxic activity by Tat may play an important role in HIV induced immune dysregulation and impaired cell mediated immunity.

Contact Information: Elliott Faller, Tel: 613-688-3412, Email: efaller@ohri.ca

202

EVALUATION OF VACCINE VECTORS IMPLEMENTED WITH IMMUNO-MODULATORY MECHANISMS AS HIV VACCINE CANDIDATES

Jin Su [1,2]; Philippe-Alexandre Gilber [1]; Greg Dekaban [1,2]; Grant McFadden [1,2];
1-Department of Microbiology and Immunology, University of Western Ontario, London, Canada; 2-Department of Biotherapeutics, The John P. Robarts Research Institute, London, Canada;

Plain Language Summary: HIV-specific cytotoxic T lymphocyte (CTL) responses play an important role in controlling viral replication and disease progression therefore the ability to elicit potent CTL has become a priority for AIDS vaccine candidates. However, induction of effective and durable CTL memory responses remains a hurdle for CTL-based vaccine. Recently, the virus-encoded immuno-modulatory proteins have drawn attention to their therapeutic potentials because these proteins act on the host defense system that assists the virus in evading immune clearance. This provides the possibility of incorporating such immune-modulators into HIV vaccine to facilitate the persistence of the immunogen expression and to achieve better immunogenicity. we construct a number of DNA cassettes expressing the HIV genes in addition to the gene coding for an immune-modulator, M11L. The efficacy of such vaccine candidates to stimulate anti-HIV responses will be evaluated in BALB/C mice.

Objectives: We constructed HIV vaccines implemented with an immuno-modulatory protein M11L, an apoptosis inhibitor encoded by myxoma virus (rabbit poxvirus), to investigate the ability of M11L-containing DNA vaccine vectors to resist apoptosis in vitro and in vivo and to evaluate the immunogenicity of an HIV DNA vaccine that co-expresses M11L in vivo.

Methods: Multiple DNA cassettes containing M11L were constructed in a novel DNA vaccine vector pHERO that is stably maintained even in dividing cells, together with the Rev independent, codon optimized HIV clade B envelope sequence and a CpG motif in some constructs. Mouse fibroblast cells were transfected with the DNA plasmids and the expression of HIV Env and M11L were confirmed. The anti-apoptotic activity of M11L in vitro was examined. Immunogenicity of these constructs in vivo will be evaluated in BALB/C mice. Spleens and lymph nodes from the vaccinated mice will be collected and HIV-specific CTL responses will be analyzed by ELISPOT using pools of 15mer overlapping peptides corresponding to HIV Env. Vaccine-elicited antibody will be examined as well using western blot.

Results: Gene expression of myxoma M11L and HIV Env was confirmed in mouse fibroblasts. Cells transfected with the plasmids containing M11L became apoptosis-resistant and expressed higher level of HIV Env. Evaluation of the CTL responses elicited by these DNA plasmids in vivo will be conducted in BALB/c mice. Cells isolated from spleens and lymph nodes of the vaccinated animals will be stimulated with HIV Env peptides and ELISPOT and CTL cytotoxic killing assays will be carried out to detect HIV-specific T cell responses.

Conclusions: Our study is aiming to address whether a vaccine can provide long-term protection against HIV. Positive results from this investigation will help overcome a major hurdle that limits the efficacy of current vaccine strategies and provide valuable insight into the correlates of protection against HIV infection.

Contact Information: Jin Su, Tel: 519-663-4527, Email: jsu@robarts.ca

203

HIV-1 TAT PROTEIN INDUCES DOWNREGULATION OF CD127 TRANSCRIPTS IN CD8 T-CELLS

Juzer Kakal [1]; Elliott Faller [1,2]; Paul MacPherson [1,2,3];
1-Ottawa Health Research Institute; 2-University of Ottawa; 3-Department of Infectious Diseases, The Ottawa, Hospital, Ottawa, Canada;

Plain Language Summary: It has been recently established in this laboratory that HIV-1 Tat protein (Tat) causes a specific and rapid downregulation of Interleukin-7 receptor-alpha (CD127) surface protein on CD8+ T-cells in a time and dose dependent manner. We hypothesize that this down regulation by Tat occurs at the level of transcription initiation within the CD127 gene promoter.

Objectives: To determine if Tat induces a decrease in the level of CD127 transcripts in CD8 T-cells and if this decrease reflects a reduction in the rate of gene transcription.

Methods: Blood Samples were collected from healthy HIV seronegative volunteers (n=6) and CD8+ T-cells were isolated using the AutoMACS Microbead CD8+ Isolation System. The cells were incubated either in medium alone or in the presence of purified Tat protein (10 □g/ml) for 12 or 24 hours. The cells were then sorted by FACS into CD127hi and CD127lo populations. Total RNA was harvested and CD127 mRNA transcripts were quantified using Real Time PCR and normalized to S18 expression.

Results: Addition of purified Tat protein to CD8+ T-cells induced a significant decrease in the level of CD127 mRNA. The majority of CD8+ T-cells cultured in media alone remained CD127hi over 24 hours and contained high levels of CD127 transcripts. In contrast, the bulk of the CD8+ T-cells cultured in the presence of Tat shifted to CD127lo and demonstrated a 6-fold decrease in CD127 mRNA ($p < 0.05$). To determine if Tat affected CD127 transcript stability, mRNA levels were measured in the presence and absence of Tat in cells transcriptionally arrested with Actinomycin D. In CD8+ T-cells treated with Actinomycin D (5ug/ml) or Actinomycin D plus Tat (10ug/ml) for 12 and 24 hours, equivalent levels of CD127 mRNA were found indicating Tat does not enhance CD127 mRNA degradation but rather down regulates CD127 expression at the level of transcription initiation.

Conclusions: Tat induces a decrease in the rate of CD127 gene transcription in CD8+ T-cells resulting in a shift from CD127hi surface expression to CD127lo. Tat has previously been shown to down regulate IL-2 gene expression in Jurkat cells through alterations in the AP1 complex. We have now cloned the putative human CD127 promoter and five deletion mutants upstream of the luciferase gene. By creating deletion mutations, we plan to identify those sequences within the promoter responsive to Tat-induced down regulation

Contact Information: Juzer Kakal, Tel: (613) 737 8160, Email: jkakal@ohri.ca

204

HUMAN T-LYMPHOPOIESIS IN-VITRO: FROM HEMATOPOIETIC STEM CELLS TO T CELLS UTILIZING THE OP9-DL1 CO-CULTURE SYSTEM

Génève Awong [1,2]; Ross La Motte-Mohs [1,2]; Juan Carlos Zúñiga-Pflücker [1,2];
1-Molecular & Cellular Biology Division, Sunnybrook and Women's Health Sciences Centre; 2-Department of Immunology, University of Toronto, Toronto, Ontario, Canada;

Plain Language Summary: T cells undergo differentiation in the specialized microenvironment of the thymus. Unlike their murine counterparts whose development has been well characterized, the study of human T cell progenitors has been hindered by the lack of cell surface antigens and assays to define these cells. Our lab has generated OP9 bone-marrow stromal cells engineered to express the Notch ligand Delta-like 1 (OP9-DL1) that upon co-culture with umbilical cord-blood hematopoietic stem cells robustly and efficiently supports human T cell differentiation. Here, we characterize the expression of various cell surface antigens and specific genes associated with T cell development.

Objectives: This investigation uses the OP9-DL1 co-culture system to assess the phenotypic and molecular changes that occur during human T-lymphopoiesis when initiated from a defined source of hematopoietic stem cells (HSCs).

Methods: Human cord-blood samples were obtained from consenting mothers following delivery at Women's College. Cord-blood was separated by ficoll-hypaque density centrifugation into a mononuclear cell fraction, washed three times, and then enriched for CD34+ stem cells using an AutoMACS. Human CD34+ cells were then sorted for CD34+CD38- primitive stem cells and added to individual wells of a 6-well plate confluent with either OP9-control or OP9-DL1 cells in medium supplemented with recombinant human Flt-3L (5ng/mL), interleukin-7 (5ng/mL) and stem cell factor (30ng/mL). Co-cultures were disaggregated by vigorous pipetting and passaged through a nylon filter at the various time-points. Cells were either stained with a combination of antibodies for flow cytometry or RNA was isolated and reverse-transcribed into cDNA for PCR.

Results: Hematopoietic stem cell differentiation toward the T cell lineage was characterized by the acquisition of cell-surface markers CD7, CD1a, CD5, CD4 and CD8. CD7hi progenitor T cells appear by day 6 of co-culture and CD1a, a marker strongly associated with T cell commitment appears by day 10. At the molecular level, T cell associated genes were induced in OP9-DL1 co-cultures. These genes include GATA-3, Deltex-1 and HES-1.

Conclusions: The OP9-DL1 co-culture system efficiently initiates and supports T cell differentiation from human cord-blood progenitors. We show that T cell specification and commitment events were induced at both the phenotypic and molecular level. This system has important potential as it provides the foundation for a large supply of human T lymphocyte progenitors which could be used in the clinical setting for immune-reconstitution of HIV-infected individuals.

Contact Information: Génève Awong, Tel: 416-480-6100 x7340, Email: g.awong@utoronto.ca

205

DIFFERENTIAL EFFECTS OF HNRNP E1 AND HNRNP E2 PROTEINS ON HIV-1 RNA METABOLISM

Kengo Asai [1]; **Kathryn Woolaway** [1]; Andrew Emili [2]; Alan Cochrane [1];
1-Department of Molecular and Medical Genetics, University of Toronto, Toronto, Ontario; 2-Best Institute, University of Toronto, Toronto, Ontario;

Plain Language Summary: Current treatments for HIV target only reverse transcription and virus maturation. The effectiveness of these treatments is continually being reduced by the appearance of resistant viral strains. We are attempting to develop new therapeutic targets at the stage of viral RNA metabolism (RNA processing, transport and translation). Many cellular as well as viral proteins have an effect on viral RNA metabolism. Our aim is to identify these cellular factors and determine how they exert their effect to gain a greater understanding of HIV-1 RNA metabolism and ways in which it can be regulated therapeutically.

Objectives: Previous work has identified trans-acting factor hnRNP A1 as one component of a complex that modulates activity of the exon splicing silencer (ESS) in tat/rev exon 3. However, mutagenesis studies suggest hnRNP A1 binding alone is not sufficient for full activity. We attempted to identify additional factors that associate with ESS3 and affect virus expression.

Methods: RNA affinity columns programmed with tandem RNA affinity purification (TRAP) tagged RNA transcripts of ESS3a were used to isolate proteins that associate with ESS3. One protein was isolated and sequenced by mass spectrometry and its identity confirmed by Western blot to be hnRNP E2. Proteins hnRNP E1 and hnRNP E2 are 89% homologous at the amino acid level therefore, we looked at the effect of both hnRNP E1 and hnRNP E2 on HIV-1 gene expression. HIV-1 provirus or a HIV-1 expression construct were cotransfected into cells alongside hnRNP E1/ hnRNP E2 and the effect on viral protein expression determined by Western blot. Deletion mutants of hnRNP E1/ hnRNP E2 were constructed and their ability to effect virus protein expression and their cellular location examined by Western blot and immunofluorescence.

Results: Overexpression of hnRNP E1 resulted in the specific inhibition of the virus proteins p24, gp120 and Rev, while overexpression of hnRNP E2 had no effect on HIV-1 protein expression. Deletion mutagenesis showed the N-terminus of hnRNP E1 had minimal effect on E1 function, while deletion of the C-terminus resulted in redistribution of the protein from the nucleus to the cytoplasm and complete abrogation of the protein's ability to inhibit HIV-1 gene expression.

Conclusions: We show that hnRNP E1 is able to interact with element ESS3a of the bipartite ESS in tat/rev exon 3 of HIV-1 and that overexpression of hnRNP E1 inhibits production of Rev, in part through a decrease in rev mRNA levels.

Contact Information: Kathryn Woolaway, Tel: 416-978-2500, Email: kew@hotmail.co.uk

206

INFECTION OF CD8+ T CELL SUBSETS BY HIV-1

Naveed Gulzar [1]; Sowmya Balasubramanian [1]; Greg Beaudoin [1]; **Karen Copeland** [1];
1-Centre for Molecular Medicine, Ottawa Health Research Institute, Ottawa, Ontario, Canada;

Plain Language Summary: CD8+ T cells are important in the control of HIV-1 replication. We have examined the ability of HIV-1 to infect CD8+ T cells and found that the virus was able to infect certain subsets of these cells more easily than others. In addition, infection resulted in greater antiviral activity.

Objectives: CD8+ T cells play a key role in controlling HIV-1 infection by eliminating infected cells and secreting soluble factors that inhibit viral replication. To investigate the mechanism and significance of infection of primary CD8+ T cells by HIV-1 in vitro, we examined the susceptibility of these cells to infection.

Methods: Peripheral blood mononuclear cells of uninfected volunteers were isolated by Ficoll gradient and CD8+ T cell subsets were positively selected with Miltenyi Multisort antibodies conjugated to magnetic beads. Infections were performed with the T cell tropic laboratory strain HIVIIIB (300 TCID50 per ml). Cell surface expression of receptors was examined by flow cytometry. IFNgamma production was measured by ELISA and cytotoxicity by mixed lymphocyte reaction.

Results: CD8+ T cells supported greater levels of replication with T cell tropic strains of HIV-1, although viral production was lower than that observed in CD4+ T cells. We demonstrated an up-regulation of the CD4 receptor on CD8+ T cells during the course of in vitro infection which accounted for less than 1% of the HIV infected population. The CD8+CD45RO+ memory T cell subset supported higher levels of HIV-1 replication than CD8+CD45RA+ naïve T cells. The CD8+CD28+, CD8+CD38+ and CD8+HLA-DR+ subsets all supported very low levels of HIV-1 replication. In contrast, 2.5 - 4 fold higher levels of replication were supported in the CD8+CD28-, CD8+CD38- and CD8+HLA-DR- subsets. Both PHA and IL-15 induced strong production of IFNgamma by infected cells. Initiation of a Tc2 to Tc1 shift resulted in a 6-fold increase in HIV-1 replication and 2-3 fold higher levels of IFNgamma.

Conclusions: These results suggest that HIV-1 replication may be more strongly supported by different subsets of CD8+ T cells. In addition, infection resulted in increased antiviral function. Since infected CD8+ T cells are found in vivo, further research is required to examine the effects of HIV-1 infection on these important effector cells.

Contact Information: Karen Copeland, Tel: 613-737-8775, Email: kcopeland@ohri.ca

207

MODULATION OF HIV-1 SPLICING THROUGH SR PROTEIN OVEREXPRESSION

Craig Platt [1]; Alan Cochrane [1];
1-Department of Medical and Molecular Genetics, University of Toronto, Toronto, Canada;

Plain Language Summary: HIV-1 is a complex retrovirus that produces a 9kb primary transcript which can be spliced into a 4kb class and a 2kb class of mRNA through the use of inefficient alternative splice sites. It is crucial to the successful replication of the virus that these 3 classes of transcripts are produced in the correct ratio. Alternative splicing is controlled in part through the association of SR family proteins with splicing enhancers present in the viral RNA. Alterations in the levels of SR-related proteins present in the cell cause changes in the splicing pattern of HIV-1 and therefore render it non-replication competent.

Objectives: To identify members of the SR protein family able to alter the ratio of HIV-1 9kb, 4kb and 2kb RNA transcripts and block viral gene expression.

Methods: 293T cells were transfected with a HIV provirus and various SR-related proteins or mutants thereof. RNA and protein extracts were harvested and RT-PCR, Northern blots and Western Blots were performed on the lysates. RT-PCR primers were used such that the 9kb, 4kb and 2kb classes of RNA could be examined independently of each other.

Results: Several of the SR-related proteins tested were able to change the splicing pattern of HIV-1. Of particular interest, mutants of Tra2a and Tra2b missing the first RS domain (Tra2aDN and Tra2bDN) resulted in a very strong shift in the 2kb splicing pattern to a predominantly SD1-SA7 transcript. This results in an increase in the production of Nef, and a decrease in the production of all other viral proteins. The production of p24 was also drastically reduced (>90%) when these mutants were over-expressed.

Conclusions: Alteration of SR-related protein levels such as SRp30C, SC35, Tra2a and Tra2b can result in a change in the splicing pattern of HIV-1. This change in the splicing pattern causes reduced HIV structural protein synthesis either through a direct reduction of the encoding RNAs, or through a reduction in Rev protein required to export the 9kb and 4kb class of RNA from the nucleus.

Contact Information: Craig Platt, Tel: 416-978-2500, Email: craig.platt@utoronto.ca

208

THYMIC SUBSETS DIFFERENTIALLY DOWNREGULATE CD127 EXPRESSION UPON IN VITRO HIV INFECTION

Charlene Young [1,2]; Jonathan Angel [1,2];
1-Ottawa Health Research Institute, Ottawa, Ontario, Canada; 2-Department of Biochemistry, Microbiology and Immunology, University of Ottawa, Canada;

Plain Language Summary: Thymocytes are a subset of cells that play a major role in host immunity. 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. We hypothesis that impaired thymic function in HIV infection is due to a decrease in CD127 expression on developing thymocytes

Objectives: Thymic function is altered in HIV infection leading to a dysregulation of the thymic epithelial network and reduced thymic output. IL-7/IL-7R (CD127) signaling is a critical pathway required for the maturation and differentiation of thymocytes. Since CD127 expression is decreased on circulating CD8 cells in HIV infection we hypothesize that impaired thymic function in HIV infection is due to a decrease in CD127 expression on developing thymocytes.

Methods: Human thymocytes were obtained from children undergoing cardiac surgery and co-cultured with thymic epithelial cells. The expression of CD127 was determined by flow cytometry at various developmental stages of T-cell maturation: triple negative CD3-CD4-CD8-(TN), double positives CD3-/+CD4+CD8+(CD3DP), and single positive cells CD3+CD4+CD8-(SP4) and CD3+CD4-CD8+(SP8). Thymocytes were infected at an MOI of 0.001 with X4 (HIVIIIB), R5 (HIVBal), a dual tropic strain (HIV CS204) and a replication incompetent strain (HIV8E5) for up to 72 hours. The expression of CD127 on the various subsets was determined by flow cytometry. Changes in CD127 expression was calculated relative to expression levels of CD127 on mock infected thymocytes.

Results: CD127 was expressed on all subsets; with the highest expression being SP8 cells where up to 70% of the cells expressed CD127. In vitro HIV infection resulted in decreased expression of CD127 on CD3-DP, CD3+DP, SP4 and SP8 when infected with HIV(IIIB) and HIV(BAL). The downregulation in the CD3+DP, SP4 and SP8 subsets appeared to be transient. No downregulation in CD127 expression was seen when infected with the replication incompetent 8E5 strain.

Conclusions: In vitro HIV infection alters CD127 expression on thymocytes suggesting that HIV may play a role in impaired thymic function by altering the IL-7 responsiveness of thymocytes.

Contact Information: Charlene Young, Tel: 613-737-8160, Email: cyoung@ohri.ca

209

INTERACTIONS BETWEEN HOST CD8+ T-CELL CLONE RECEPTORS AND THE HIV-1 GLYCOPROTEIN CONFER SUSCEPTIBILITY TO INFECTION

Naveed Gulzar [1]; Anjali Shroff [1]; Daria Klonowska [1]; Bahar Buberoglu [1]; John E. Kim [2]; Karen F. Copeland [1];
1-Molecular Medicine Program, Ottawa Health Research Institute; 2-National HIV Reference Services Laboratory, Health Canada, Ottawa, Canada;

Plain Language Summary: The factors required for HIV infection of CD8+ T-cells have been poorly studied. Our objective was to examine the viral determinants required for entry of the virus in these cells. We found that HIV infection of the cells results in a modulation of two key cellular receptors. These factors may play a role in the increased infectivity and productivity of the virus in the CD8+ T-cell clones that were used in the experiments.

Objectives: To date, the role and function of CD8+ T-cells in response to HIV-1 infection has been poorly understood. Furthermore, conflicting results concerning the susceptibility of CD8+ T-cells to HIV-1 infection have been reported. Our research aims to examine whether CD8+ T-cells provide suitable targets for productive HIV-1 infection and the mechanism(s) by which HIV-1 enters CD8+ T-cells. We hypothesized that chemokine and other cellular receptors confer susceptibility to HIV-1 infection in vitro.

Methods: CD8+ T-cell clone infection was monitored by p24 ELISA and flow cytometry. DNA sequencing analysis of the HIV-1 envelope was performed by standard automated methods. The expression of CD4, CD8, CXCR4 and CCR5 receptors was assessed by flow cytometry and RT-PCR analysis. In addition, receptor blocking studies were performed using CD4, CD8 and CXCR4 monoclonal antibodies.

Results: The CD8+ T-cell clones harbored HIV-1 replication at levels 10-20 times greater than that of primary CD8+ and CD4+ T-cells. Progeny virus from these clones did not yield any significant mutations and retained the ability to infect PBMCs. Our research also demonstrated that during the course of infection, there was no up-regulation of CD4 on the surface of the T-cell clones, however, the expression of the CD8 and CXCR4 receptors decreased significantly. Interestingly, the use of antibodies to CD8 or CXCR4 abrogated viral binding and replication in the CD8+ T-cell clones.

Conclusions: The CD8+ T-cell clones served as requisite targets of HIV-1 as they supported viral infection and production at levels greater than untransformed primary CD8+ and CD4+ T-cells. Productive viral infection resulted in the down-regulation of the CD8 and CXCR4 receptors and antibodies to these receptors blocked HIV-1 infection. The enhanced binding of HIV-1 to these receptors may in part explain the ability of the CD8+ T-cell clones to support high levels of viral infection and replication. Thus, viral entry into these cells may be facilitated through access to chemokine receptors and/or other cellular receptors.

Contact Information: Naveed Gulzar, Tel: 613-737-8899 x73238, Email: ngulzar@rogers.com

210

INTRACELLULAR HIV-TAT EXPRESSION INDUCES IL-10 SYNTHESIS BY SERINE 133 PHOSPHORYLATION OF CREB-1 THROUGH THE ACTIVATION OF ERK MAPK IN HUMAN MONOCYTIC CELLS

Katrina Gee [3]; Jonathan Angel [3]; Wei Ma [2]; Sasmita Mishra [2]; Niranjala Gajanayaka [1]; Karl Parato [3]; Ashok Kumar [1,2];
1-Department of Pathology and Laboratory Medicine, Division of Virology and Molecular Immunology, Research Institute, CHEO; 2-Department of Biochemistry, Microbiology and Immunology, University of Ottawa; 3-Ottawa Health Research Institute and the Division of Infectious Diseases, Department of Medicine, Ottawa Hospital General Campus;

Plain Language Summary: Human immunodeficiency virus (HIV)-tat plays an important role in virus replication and in various aspects of host immune responses including dysregulation of cytokine production. IL-10, an anti-inflammatory cytokine, is upregulated during the course of HIV infection representing an important pathway by which HIV may induce immunodeficiency. Herein, we show that extracellular as well as intracellular tat induced IL-10 expression in normal human monoyctes and promonocytic THP-1 cells.

Objectives: The signaling pathways involved in the regulation of IL-10 production by endogenous tat remain unknown. Therefore the objectives of this study were to: 1) investigate the role of intracellularly expressed HIV tat on IL-10 production, 2) investigate the signaling pathways involved in tat-induced IL-10 production, 3) identify the transcription factors involved in tat-induced IL-10 production.

Methods: To understand the molecular mechanism underlying intracellular tat-induced IL-10 transcription, we employed a retroviral expression system to investigate the role of mitogen activated protein kinases (MAPKs) and the transcription factor(s) involved.

Results: Our results suggest that an inhibitor specific for the extracellular signal-regulated kinase (ERK1/2), PD98059, selectively blocked intracellular tat-induced IL-10 expression in THP-1 cells. Our results also demonstrate that intracellular tat induced serine 133 phosphorylation of the cyclic adenosine 3',5'-monophosphate-responsive element binding-1 (CREB-1) protein that was specifically inhibited by PD98059 as determined by IL-10 promoter analysis and gel shift assays.

Conclusions: Overall, our results suggest that intracellular HIV-tat induces IL-10 transcription by a novel signaling pathway involving ERK MAPK-dependent serine 133 phosphorylation of the CREB-1 transcription factor.

Contact Information: Katrina Gee, Tel: 737-7600 x3919, Email: kgee@uottawa.ca

211

GLOBOTRIAOSYLCERAMINDE, GB3, IS A NATURAL RESISTANCE FACTOR FOR HIV-1 INFECTION

Nicole Lund [1,2]; Darinka Sakac [1]; Clifford A. Lingwood [2,3]; Donald R. Branch [1,2,4];
1-Canadian Blood Services; 2-University of Toronto; 3-Hospital for Sick Children; 4-Toronto General Research Institute, Toronto, ON, Canada;

Plain Language Summary: Glyscosphingolipids (GSLs) are lipid (fat)-sugar conjugates within the cell membrane that are required for HIV infection. Several GSLs are able to bind to an outer surface HIV protein called gp120. We have studied one such GSL called globotriaosylceramide (Gb3) and its effect on HIV infection. When Gb3 is inserted into HIV target cell membranes in the test tube, it reduces HIV infection. In addition, HIV target cells from individuals who express higher amounts of Gb3 appear to be resistant to HIV infection. In contrast, target cells from individuals who do not express Gb3 are more susceptible to HIV infection. Our findings suggest Gb3 may provide a natural resistance to HIV infection in individuals who express high levels.

Objectives: Glycosphingolipids (GSLs) have been implicated in HIV-host cell fusion, and several bind to HIV-gp120 in vitro. In addition, inhibiting glycolipid biosynthesis blocks HIV membrane fusion. While the GSL globotriaosylceramide (Gb3) has been shown to augment HIV fusion in in vitro models, its exact role in HIV infection is not known. We previously developed a soluble analogue of Gb3, which effectively inhibits HIV membrane fusion and viral entry. We thus hypothesize Gb3 influences susceptibility to HIV infection, and its expression is able to inhibit viral fusion and entry. We have presently investigated the effects of exogenous or differentially expressed Gb3 effects on HIV-1 infection.

Methods: Exogenous Gb3 was introduced into Jurkat T-cell membranes by liposome transfer, and susceptibility to X4 HIV-1IIIB infection determined. The effects of differential Gb3 expression on HIV-1 infection were investigated using PBMCs with Gb3 accumulation (from patients with Fabry lysosomal storage disease), increased Gb3 expression (P1k blood group individuals), or lacking Gb3 (from p blood group individuals). Susceptibility of activated PBMCs from these individuals was determined using R5 HIV-1Ba-L or X4 HIV-1IIIB infection.

Results: Exogenous Gb3 transfer in Jurkat T-cells reduced productive HIV-1 infection levels by 50%, without affecting CD4 receptor and CXCR4 co-receptor expression. PBMCs from patients with Fabry disease (Gb3 accumulation) were resistant to productive R5 HIV-1 infection, but not X4 HIV-1 infection. These PBMCs showed low expression of R5 HIV-1 co-receptor, CCR5. P1k blood group PBMCs (increased Gb3 expression) have shown resistance to both R5 and X4 HIV-1 infection. PBMCs from p blood group individuals (lacking Gb3) were hypersensitive to R5 HIV-1 infection, while X4 HIV-1 infection levels were variable. Interestingly, these PBMCs showed higher levels of CCR5.

Conclusions: Our findings suggest Gb3 is inhibitory to HIV infection, and may provide natural resistance in individuals expressing high levels. Exploiting Gb3 inhibition may also present novel strategies for prevention of HIV/AIDS.

Contact Information: Nicole Lund, Tel: 416-313-4456, Email: nicole.lund@utoronto.ca

212

INHIBITION OF HIV-1 PROTEIN EXPRESSION BY SAM68DC: A STRUCTURE FUNCTION ANALYSIS

Kim Marsh [1]; Meredith McLaren [1]; Vanessa Soros [2]; Alan Cochrane [1];
1-Department of Medical Genetics and Microbiology, University of Toronto; 2-Gladstone Institute of Virology and Immunology, University of California;

Plain Language Summary: Sam68DC is a mutant human protein that was found to inhibit HIV-1 propagation. In this study we have endeavoured to determine how this inhibition occurs. The novel nature of the mechanism of Sam68DC inhibition of HIV-1 propagation may provide another strategy for anti-HIV treatment. To limit superfluous secondary effects, we first determined the minimal domains of Sam68DC required for the inhibition. Sam68DC inhibits the HIV-1 lifecycle by specifically destabilizing a subset of the viral RNAs, and thereby prevents production of the structural and enzymatic proteins of HIV-1.

Objectives: To determine the minimal domains of Sam68DC required for inhibiting HIV-1 protein expression. To use the minimal domain to determine how Sam68DC is able to inhibit HIV-1 protein expression.

Methods: To define the minimal inhibitory domain of Sam68DC, sequential deletions were made from the N- or C-terminus. Internal deletions were made based on functional domains defined in other studies. The minimal inhibitory mutant combined the internal, N- and C-terminal deletions that were still functional. Human cancer cell lines were transiently transfected with portions of the HIV-1 virus and Sam68DC or mutants thereof. Gp120 production was assayed by Western blot on the lysates, and the unspliced and spliced RNA was analysed by random amplification of cDNA ends (RACE-PAT). To control that the effects were specific to HIV-1, the effects of Sam68DC on p24 production from Rev-dependant and –independent vectors were compared. Other techniques used include: immunofluorescence and in situ hybridization.

Results: The minimal domain of Sam68DC required for inhibition is: D14(D45-54)-314. The amino acids 15-24 and 301-314 are essential for this inhibition. Our studies indicate that although Sam68DC bundles RNA at the nuclear periphery, this does not correlate with inhibition of protein production. Sam68DC can bundle RNAs which are not inhibited, and can maintain inhibition of HIV-1 RNA upon disruption of the RNA bundles. Our studies show that Sam68DC inhibits HIV-1 protein expression by specifically destabilizing the 3' end of the incompletely spliced HIV-1 RNAs. This prevents production of the HIV-1 structural and enzymatic proteins, and thereby stops the viral lifecycle.

Conclusions: We have defined the minimal domains of Sam68DC required for inhibition of HIV-1 protein expression. Sam68DC inhibits the viral lifecycle by destabilizing the 3' end of the incompletely spliced HIV-1 viral RNAs.

Contact Information: Kim Marsh, Tel: 416-978-2500, Email: kim.marsh@utoronto.ca

213

DESIGN OF VACCINE AGENTS TO ELICIT 2F5-LIKE NEUTRALIZING ANTIBODY RESPONSES AGAINST HIV

Rosemarie Mason [1]; Mark Luscher [1]; Steve Bryson [2]; Angelica Bello-Ramirez [3]; Emil Pai [2]; Lakshmi Kotra [3]; Kelly MacDonald [1,4];
1-Division of Clinical Science, University of Toronto; 2-Department of Biochemistry, University of Toronto; 3-Faculty of Pharmacy, University of Toronto; 4-Department of Microbiology, Mount Sinai Hospital;

Plain Language Summary: Neutralizing antibodies are a correlate of protective immunity against HIV and a small but increasing number of neutralizing monoclonal antibodies (nmAb) to HIV have been identified. Among these is the nmAb 2F5 which selectively binds to the envelope glycoprotein sequence ELDKWAS expressed on the surface of HIV. 2F5 potently neutralizes several different strains of HIV, however, attempts to generate vaccine agents with the ability to elicit an immune response to this portion of the virus have failed. Our ongoing project aims to use powerful tools for the visualization of the antibody structure, together with computer-aided molecular design to make new vaccine agents that can mimic the native ELDKWAS structure and give rise to 2F5-like neutralizing antibody responses.

Objectives: The aim of this study is to design synthetic molecules mimicking the 2F5 neutralizing epitope ELDKWAS.

Methods: The three dimensional structure of nmAb 2F5 bound to its epitope ELDKWAS was determined using crystallographic analysis and surface plasma resonance experiments. Structural information provided by these analyses was then used for the design and chemical synthetic of molecules (peptidomimetics) which mimic the three-dimensional structure of ELDKWAS, residue by residue, as it is bound to 2F5.

Results: Structural analysis of nmAb 2F5 bound to the gp41 peptide ELDKWAS as well as various mutants of ELDKWAS has been performed. Structural information provided from these analyses indicates the flexible and rigid regions in the three-dimensional confirmation induced onto the ELDKWAS epitope when bound by 2F5. The two most conserved functional and conformational regions among all the complexes of ELDKWAS or mutants of ELDKWAS bound to 2F5 are the Trp and Lys residues. We utilized these findings for the synthesis of molecules mimicking this induced conformation of ELDKWAS. Synthetic molecules with this predisposed conformation will be used to induce clinically effective neutralizing antibodies similar to 2F5.

Conclusions: We have used structural studies to design peptidomimetic molecules to incorporate immunologically significant features of the broadly-neutralizing antibody epitope ELDKWAS. These first-generation agents will be used to elicit antibodies in vivo that will guide the further design and refinement of the peptidomimetic agents toward the goal of producing neutralizing antibodies in vivo capable of recognizing and blocking many HIV 1 isolates and clades. Such agents will be entered in human vaccine trials.

Contact Information: Rosemarie Mason, Tel: 416-978-1605, Email: rosemarie.mason@utoronto.ca

214

INACTIVATING HIV-1 AT THE DNA LEVEL: NEW TOOL, NEW TARGET

Reza Nazari [1]; **Sadhna Joshi** [2];
1-Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, Canada; 2-Department of Medical Genetics and Microbiology, University of Toronto, Toronto, Ontario, Canada;

Plain Language Summary: The Lactococcus lactis group II intron, LI.LtrB, has been studied for its structure and potential application in many fields, including gene therapy. Modified group II introns are capable of inserting into new target DNA.

Objectives: As a novel approach to HIV-1 gene therapy, we are using the modified group II introns to inactivate the HIV-1 proviral DNA.

Methods: Two group II introns targeting nucleotides 4021 and 4069 of the sense DNA strand of HIV-1 provirus DNA were modified to contain the neo gene. E.coli cells were co-transformed with the donor plasmids expressing modified introns and the LtrA protein and the recipient plasmids containing the intron insertion sites. Insertion frequencies of the modified and unmodified introns were similar, suggesting that the modifications did not alter the mobility. Next the E.coli cells were co-transformed with the donor plasmids expressing the modified introns and pHIV (pNL4-3, an infectious HIV-1 provirus DNA clone) to allow intron insertion within the HIV-1 provirus DNA. The intron-inserted pHIV was isolated and used to transfect human 293T cells. The virus particles were collected. To assess the infectivity of these virus particles, CD4+ T lymphoid (PMI) cells were infected and checked for provirus DNA integration and progeny virus production.

Results: P24 antigen assay revealed that similar amounts of virus particles were released from the 293T cells transfected with uninserted (pHIV) or intron-inserted (pHIV-I) HIV-1 provirus DNA. The progeny virus infectivity was determined by infecting the PM1 cells. The PM1 cells exposed to intron-containing viral particles were not infected; The PCR analysis of the genomic DNA revealed the lack of HIV-1 DNA in these PM1 cells. However, DNA was present in PM1 cells infected with the control virus. The endogenous CCR5 DNA was amplified as a control, and was shown to be present in all cells. The PM1 cells exposed to intron-containing progeny virus were also viable with no syncytia formation and no HIV-1 progeny virus production until day 35-post-infection, when the experiment was stopped.

Conclusions: Since the intron insertion site is located within the integrase domain of HIV-1 pol gene, intron insertion is expected to yield non-infectious viruses. Thus, as expected, the transfected 293T cells produced similar levels of virus particles as the control. However, in the absence of a functional integrase, the provirus DNA integration did not take place in the PM1 cells that were infected with these virus particles.

Contact Information: Reza Nazari, Tel: 416-978-1256, Email: reza.nazari@utoronto.ca

215

PROSPECTIVE ANALYSIS OF ANTI-HIV IMMUNE RESPONSES AMONG HIGHLY EXPOSED HIV-1 NEGATIVE NAIROBI SEX WORKERS

Bing Li [1]; Mark Luscher [1]; Rupert Kaul [1]; Joshua Kimani [2]; Kelly MacDonald [1];
1-Division of Clinical Sciences, University of Toronto; 2-University of Nairobi, Kenya;

Plain Language Summary: Despite repeated exposure to HIV-1, some individuals remain uninfected, including highly exposed, persistently seronegative (HEPS) female sex workers. The mechanisms of protection or resistance are not clear. Studies to date have all been cross-sectional or retrospective and so causality has not been ascertain. Eight hundred ninety female sex workers were screened and 466 HIV-1 negative women were enrolled in a Azithromycin Prophylaxis Trial and were followed up regularly until year 2003. Over the study period, 35 subjects seroconverted (cases, 7.5%) and an average of 3 controls per case was selected matching with study entry date, duration of prostitution and number of clients per week. HIV-1 specific responses were examined. This is the first prospective analysis of the role of anti HIV-1 cellular immune responses in mediating protection from subsequent HIV infection.

Objectives: Try to analyze prospectively the role of anti HIV-1 cellular immune responses in mediating protection from subsequent HIV infection among exposed seronegative female sex workers in Nairobi.

Methods: HIV-1 specific cytotoxic T lymphocyte responses and proliferative activities were examined using IFNgamma ELISpot and [H]3-thymidine proliferation assays with PBMCs stimulated with defined HIV-1 epitope pools (DE) or/and 15-mer peptide pools to cover the whole HIV-1 genome.

Results: Comparison of demographic, behavioral factors and incident infectious diseases among cases and controls showed that condom use was significantly associated with remaining HIV negative, and type 2 Herpes infection was significantly associated with HIV seroconversion. HIV-1 specific cellular responses were detected in both seropositive and seronegative subjects over the study period.

Conclusions: 1.Responses to HIV peptides were frequent in seronegative individuals in this cohort of HIV-1 exposed commercial sex workers (40-50%). 2. Preliminary analysis of the data suggest a correlation between IFNgamma response to HIV-1 Gag and accessory genes and seroconversion in this study. Proliferative responses did not correlate with seroconversion. 3. Herpes type 2 infection is strongly associated with subsequent seroconversion. 4. Logistic regression analysis incorporating known risk factors (i.e. herpes, syphilis, condom use etc) will be performed to further assess the independent relative risk.

Contact Information: Bing Li, Tel: 416-946-3732, Email: Bing.li@utoronto.ca

216

ASSESSING SELECTIVE PRESSURES ON THE SEQUENCE OF AN IMMUNODOMINANT HIV CTL EPITOPE

Natasha Christie [1,2]; Mark A. Luscher [2]; David Willer [2]; Colin Kovacs [3]; Kelly S. MacDonald [1,2,4];
1-Dept. of Immunology, University of Toronto, Toronto ON ; 2-Division of Clinical Sciences, University of Toronto, Toronto ON; 3-Canadian Immunodeficiency Research Collaborative, Toronto ON; 4-Dept. of Microbiology, Mt. Sinai Hospital, Toronto ON;

Plain Language Summary: This project focuses on immune cells called cytotoxic T lymphocytes (CTLs) that recognize small fragments (epitopes) from proteins that make up the human immunodeficiency virus (HIV). Immunodominant epitopes are recognized by a particularly large number of CTLs within a single person, and by a large number of people within a population. They are often suggested to be the best epitopes to include in the design of candidate HIV vaccines. Here we investigate a broadly-recognized epitope called SLYNTVATL (SL9), to test the idea that not all immunodominant HIV epitopes evoke fully functional CTLs. Understanding which responses are most beneficial is crucial in designing HIV vaccines.

Objectives: The goal of this project is to quantify opposing selective pressures acting on the sequence of this epitope. Our objectives are two fold: 1) To investigate the sequence constraints imposed on this particular epitope sequence by viral fitness requirements. 2) To assess naturally occurring SL9 epitope sequence variation in vivo as a measure of immune pressure on the epitope sequence.

Methods: To determine replicative defects associated with point mutations throughout the epitope, HIV plasmid clones incorporating synonymous and non-synonymous mutations in the SL9 epitope region have been constructed. These constructs were transfected into cell culture and subsequently viral viability was determined by mono-infection p24 assays. Furthermore, in order to document variation of this epitope sequence in vivo, single-copy proviral DNA from HIV+ patient PBMCs was isolated using a quantitative limiting dilution PCR approach and the resulting amplicons were sequenced. These patients were screened for reactivity to the epitope using IFN-g ELISpot assays in order to compare sequence sets from SL9-reactive and SL9-unreactive patients.

Results: Mono-infection viral replication assays indicate that synonymous mutations in this epitope region do not impact viral infectivity. Gag sequences from patients show mutations predominantly at non-anchor residues of this epitope. When comparing patient groups based on their IFN-g reactivity to the SL9 epitope, those lacking responses had more mutations within the epitope.

Conclusions: Mutations in the SL9 region of Gag do not appear to impair RNA processing or trafficking during the lifecycle of HIV. Studies of HIV variant sequences in vivo reveal the presence of variant SL9 sequences in both comparison groups. Trends indicating more variant sequences at both the genomic and protein level in the SL9 non-reactive group may indicate previous CTL escape. Studies are underway to define the immunological reactivity to autologous variants of the epitope.

Contact Information: Natasha Christie, Tel: 416-978-1605, Email: natasha.christie@utoronto.ca

217

INTERFERON-GAMMA-DEPENDENT HYPERACTIVATION OF THE STAT1 TRANSCRIPTION FACTOR IN MONOCYTES FROM HIV+ PATIENTS

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

Plain Language Summary: Monocytes/macrophages are cells capable of killing microbial pathogens and play a critical role in inflammation and the immune response. Their activity is strictly controlled by growth factors of the immune system called cytokines. We studied whether the impairment of monocyte/macrophage function in HIV-positive patients may be the result of defects in their responsiveness to certain cytokines.

Objectives: Cytokines (IFN-γ, IL-10, GM-CSF, and IL-4) regulate the phagocytic, anti-microbial, and antigen presenting function of monocytes/macrophages in large part via the Janus kinase (Jak) / Signal Transducer and Activator of Transcription (STAT) signal transduction pathway. Therefore, our objective was to evaluate the capacity of these cytokines to induce the Jak/STAT signaling pathway in HIV-infected patients.

Methods: Peripheral blood mononuclear cells (PBMC) were obtained from HIV-negative controls and two groups of HIV-positive patients. Group 1 included HIV-positive patients off therapy for > 6 months while group 2 consisted of patients on sustained highly active anti-retroviral therapy (HAART) for >1 year. PBMC were stimulated with IFN-γ, IL-10, GM-CSF, or IL-4. The cells were then stained with antibodies specific for the monocyte marker CD14, activated (tyr-phosphorylated) STAT1, 3, 5, and 6 proteins, and cytokine receptor chains. Expression of these molecules was determined by flow cytometric analysis.

Results: Monocytes from all patients were capable of inducing tyr-phosphorylated STAT6 (P-STAT6) in response to IL-4, P-STAT5 in response to GM-CSF, and P-STAT3 in response to IL-10. There were no clear differences in responsiveness among the three groups of patients (HIV-negative, HIV-positive off therapy, HIV-positive HAART) in the case of IL-4, GM-CSF and IL-10 stimulation. However, in the case of IFN-γ stimulation, the STAT1 transcription factor was significantly hyperinduced in HIV-positive patients off therapy compared to HIV-negative and HAART patients. Interestingly, the upregulation in P-STAT1 occurred despite equivalent IFN-γ receptor α and β chain expression levels.

Conclusions: In contrast to the other cytokines tested, IFN-γ-dependent STAT1 activation was clearly upregulated in the monocytes from patients off therapy compared to patients on HAART and HIV-negative controls. STAT1 hyperactivation was not due to enhanced IFN-γ receptor expression levels, suggestive of a mechanism downstream of cell surface receptor expression. The biological impact and the molecular mechanisms responsible for IFN-γ-induced STAT1 hyperactivation are not clear at present. However, this phenomenon may contribute to monocytes dysfunction by predisposing these cells to apoptosis and/or affecting their phagocytic activity.

Contact Information: Marko Kryworuchko, Tel: 613-737-7600 XT 2312, Email: MKryworuchko@cheo.on.ca

218

DUAL ROLE OF IL-10 IN HIV INFECTION: MOLECULAR MECHANISMS RESPONSIBLE FOR THE ENHANCEMENT OF HIV REPLICATION IN DENDRITIC CELLS AND ITS INHIBITION IN MACROPHAGES

Ali Akbar Rahim Rahimi [1,2]; Charlene Young [1]; Masoud Ghorbani [2]; Marko Kryworuchko [1,2]; Ashok Kumar [1,2];
1-Department of Biochemistry, Microbiology and Immunology, University of Ottawa; 2-Division of Virology, Research Institute, Children's Hospital of Eastern Ontario;

Plain Language Summary: HIV attacks the immune system, resulting in a progressive illness that leaves the infected individual vulnerable to opportunistic infections and cancers. HIV/AIDS is fatal. No cure or vaccine exists and new treatments are very costly. Therefore, additional modalities are needed to achieve disease containment and virus elimination. One attractive approach is to use cytokines with anti-viral activities, such as Interleukin-10 which plays a key role in HIV immunopathogenesis. It has been shown to inhibit HIV replication in monocytes and monocyte derived macrophages (MDMs). In contrast, IL-10 enhances HIV replication in dendritic cells. These observations illustrate the complexity of the role of IL-10 in HIV infection. Further investigations are needed to understand the molecular mechanism by which IL-10 regulates HIV replication.

Objectives: We have shown the molecular mechanism by which IL-10 exerts its inhibitory and stimulatory effect on the expression of cell surface markers. Moreover, for the first time we have shown a novel role for STAT1 and PI3K in IL-10-induced CD14 expression in human monocytic cells. We hypothesized that IL-10 may employ distinct signalling cascades and transcription factors for its inhibitory and stimulatory effects on HIV replication and based on our and the other studies we aimed: 1. To elucidate the signalling pathways, particularly those involving PI3K, MAPKs, and STAT1, responsible for the stimulatory effects of IL-10 on HIV replication in dendritic cells. 2. To investigate the role of signalling pathways, in particular, the JAK/STAT3 signalling cascade, responsible for the inhibitory effects of IL-10 on HIV replication in human macrophages.

Methods: HIV-1 propagation, Monocyte Isolation, in vitro production of MDMs and monocyte derived dendritic cells (MDDs), Flow cytometry analysis, HIV-1 p24 ELISA, RT-PCR, cDNA Microarray techniques.

Results: We have shown that monocytes in presence of M-CSF or GM-CSF + IL4 differentiate into macrophages and dendritic cells, respectively. As a model system we have propagated a clinical strain of HIV-1 (CS-204) by inoculation of the virus on a human myeloid cell line and have made a stock of the virus at 40 ng/ml. The stock virus was applied to infect the monocytes, MDMs, and MDDs to show the involvement of the aforementioned signalling pathways. On the other hand genes, which are involved in IL-10 effect on monocytes, are under investigation by using cDNA microarray techniques.

Conclusions: The treatment of monocytes with growth factors provided reliable in vitro model systems to study HIV-1 replication in macrophages and dendritic cells. The signalling molecules thus identified may represent targets for novel therapeutic interventions.

Contact Information: Ali Akbar Rahim Rahimi, Tel: 613-737-7600 x3919, Email: arahi080@uottawa.ca

219

DEVELOPING VACCINE CONSTRUCTS TO ELICIT A POTENT HUMORAL AND MUCOSAL NEUTRALIZING RESPONSE AGAINST HIV-1

Sumiti Jain [1]; Kenneth L. Rosenthal [1];
1-Centre for Gene Therapeutics, Department of Pathology and Molecular Medicine, McMaster University, Hamilton Ontario, Canada;

Plain Language Summary: This project involves the generation of vaccines that elicit an antibody responses against a specific target on the HIV-1 glycoprotein. Two different vaccine delivery systems were administered in mice via two different routes in different combinations. Preliminary results show that a good systemic immune response can be elicited. In future studies we will determine the mucosal response and the functionality of these antibodies in preventing HIV-1 infection in vitro.

Objectives: The ultimate goal of these studies is to develop and test vaccines that will elicit potent neutralizing antibody responses, both mucosally and systemically, against two specific epitopes in the membrane proximal region (MPR) of the HIV-1 glycoprotein gp-41: ELDKWAS and NWFDIT.

Methods: The MPR sequence was inserted into the gag gene of HIV-1 Clade A at the C-terminus. The expression of this transgene in plasmid DNA and replication-incompetent recombinant adenovirus constructs generates a virus like particle, expressing the ELDKWAS and NWFDIT epitopes. Female C57BL/6 mice were immunized with a homologous [pDNA+CpG] prime-boost regiment or a heterologous [pDNA+CpG] prime followed by an adenovirus boost regiment. The [pDNA+CpG] formulation was administered intra-muscularly into each hind limb followed by electroporation of the muscle to increase uptake, whereas the recombinant adenovirus was administered intra-nasally. Serum was collected from these mice over two months and was tested in indirect ELISAs to measure systemic IgG/IgA responses specific to the ELDKWAS and NWFDIT epitopes.

Results: In initial studies, the groups immunized with [pDNA+CpG] as a homologous prime-boost, both ELDKWAS and NWFDIT-specific IgA and IgG responses were measured in the serum. The best overall response elicited was the ELDKWAS-specific IgG, with a 5000-times end point dilution titre during the peak response period. NWFDIT-specific IgA was undetectable and the best NWFDIT-specific IgG response during the peak period was titred at a 1800-fold end-point dilution. Groups of mice that were primed with [pDNA+CpG] and boosted with recombinant adenovirus generated a similar serum antibody profile, however the overall levels of antibodies was higher. The peak IgG antibody response against ELDKWAS was at a 8000-fold end-point dilution and at 7500 against NWFDIT.

Conclusions: These preliminary results indicate that the vaccine constructs successfully elicit systemic IgG/IgA responses against these known neutralizing epitopes. In future studies we will determine the mucosal antibody response generated by measuring the ELDKWAS and NWFDIT specific responses in mice vaginal washes and fecal samples. We will also determine the functionality of the systemically and mucosally elicited antibodies by assessing their ability to prevent infection via classical neutralization and transcytosis-inhibition assays.

Contact Information: Sumiti Jain, Tel: 905-525-9140 x22494, Email: jains4@mcmaster.ca

220

DISRUPTION OF CYTOKINE SIGNALING IN T CELLS FROM HIV+ PATIENTS: ROLE IN PATHOGENESIS

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

Plain Language Summary: T cells are vital to the cellular immune response and thus play a major role in controlling HIV replication and preventing the development of AIDS. The maintenance of these cells requires that they respond properly to growth and regulatory factors of the immune system called cytokines. We demonstrated that a subset of CD4 and CD8 T cells from HIV-positive patients fail to integrate certain cytokine-specific growth signals. This may contribute to the impairment of cell-mediated immunity observed over the course of chronic infection with HIV.

Objectives: Cytokines transmit proliferation, survival, and differentiation signals to cells in large part through the Janus kinase (Jak) / Signal Transducer and Activator of Transcription (STAT) signalling pathway. Therefore, we evaluated the capacity of cytokines important in T cell growth and differentiation [Interleukin (IL)-2, IL-4, IL-7, IL-10, and IL-15] to activate this pathway.

Methods: Peripheral blood mononuclear cells (PBMC) were obtained from HIV-positive patients as well as HIV-negative volunteers. PBMC were stimulated ex vivo with the mentioned cytokines and the cells stained with antibodies specific for CD4, CD8 and activated (tyr-phosphorylated) STAT5, STAT3 and STAT6 proteins. STAT activation levels in CD4 and CD8 T cells were analyzed by flow cytometry.

Results: IL-2 and IL-15 induced STAT5 phosphorylation (P-STAT5) in CD4 T cells but there was a clear separation of cells into P-STAT5-negative and P-STAT5-positive populations to similar proportions in HIV-negative and HIV-positive patients. A similar stratification was observed in response to IL-7 but the proportion of P-STAT5-negative cells was significantly higher in HIV-positive patients compared to HIV-negative controls. In CD8 T cells from HIV-infected patients, although clearly inducing P-STAT5, IL-2 and IL-15 stimulation revealed a P-STAT5-negative population, which was not detected in HIV-negative subjects. This P-STAT5-negative population was observed in the CD8 T cells from all HIV-positive patients studied, irrespective of HAART. In response to IL-7, P-STAT5-negative cells were observed in both HIV-positive and HIV-negative patients. However, their proportion was higher in HIV-infected patients. In contrast, IL-10-induced P-STAT3 and IL-4-induced P-STAT6 activation was not distinguishable from HIV-negative controls.

Conclusions: The P-STAT5-negative and P-STAT5-positive populations observed in CD4 T cells may be a reflection of their naïve and memory cell phenotypes. In CD8 T cells, the P-STAT5-negative population may represent replicatively senescent cells that arise due to the chronic antigenic stimulation that occurs during HIV infection, thus contributing to the eventual insufficiency of the CD8 T cell response.

Contact Information: Marko Kryworuchko, Tel: 613-737-7600 x2312, Email: MKryworuchko@cheo.on.ca

221

SUBCELLULAR LOCALIZATION AND FUNCTIONAL ACTIVITY OF P-GP IN BRAIN CELLULAR TARGETS OF HIV-1 INFECTION: ROLE IN ANTIRETROVIRAL DRUG RESISTANCE

Karlo Babakhanian [1]; Reina Bendayan [1];
1-Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy, University of Toronto;

Plain Language Summary: In the central nervous system (CNS), HIV-1 infection occurs early during infection and infects primarily microglia, the immune cells of the brain, and to a lesser extent, astrocytes. Release of cytokines and chemokines by infected microglia may result in neuronal and astrocytic dysfunction termed HIV encephalitis (HIVE). For effective treatment of HIVE, anti-HIV drugs have to permeate the blood-brain barriers (BBB) and reach their site of action (i.e., microglia, astrocytes). Brain microvessel endothelium serves as a major component of the BBB and express proteins such as P-glycoprotein (P-gp) that pump substrate drugs such as protease inhibitors used in highly active antiretroviral therapy (HAART), from the brain extracellular fluid into the blood. In addition to cell surface, subcellular localization (on the nuclear and cytoplasmic vesicle, Golgi apparatus membranes) could result in low anti-HIV drug concentrations at its site of action (i.e., nuclei, cytoplasm). We hypothesize that P-gp expressed in brain microvessel endothelial cells and microglia may result in low drug concentrations at cellular targets of HIV-1 infection due to its localization not only at the cell membrane but also at subcellular sites.

Objectives: To investigate the localization, expression and activity of subcellular P-gp in primary cultures of human brain microvessel endothelial cells (HBEC), as well as rat brain microvessel endothelial (RBE4) and glial (microglial and astrocytes) cell lines.

Methods: Western blot analysis was undertaken in nuclear membrane fractions isolated from RBE4 and microglia cell lines. Subcellular localization of P-gp was investigated by immunogold electron microscopy and fluorescent microscopy. Both studies used P-gp monoclonal C219 antibody.

Results: Western blot analysis detected a single band of appropriate size for P-gp expression at the nuclear membrane of RBE4 and microglia cells. Immunocytochemical analysis at the electron microscope revealed P-gp along the plasma membrane, caveolae, coated vesicles and nuclear envelope of RBE4, microglia and primary cultures of astrocytes. Fluorescence immunocytochemistry suggested protein localization at the nuclear membrane of RBE4 cells. To investigate if the protein retains its function at the subcellular level, transport studies using specific P-gp probes are presently in progress.

Conclusions: Localization of P-gp at subcellular sites could alter drug concentrations in the nucleus as well as the cytosol, two target sites for anti-HIV drug action. Drug transporter subcellular localization and activity involved in the sequestration of drugs could lead to the development of new strategies that would result in improved drug accumulation in the cytoplasm and nucleus, sites of anti-HIV drug action.

Research supported by Ontario HIV Treatment Network, Ontario Ministry of Health, and Canadian Institutes of Health Research.

Contact Information: Karlo Babakhanian, Tel: 416-946-7523, Email: carl__12@yahoo.com

222

SCREENING FOR HIV-ASSOCIATED ANAL CANCER: TEST CHARACTERISTICS OF ANAL CYTOLOGY AND ONCOGENIC HPV FOR THE DETECTION OF HIGH-GRADE DYSPLASIA

Irving Salit [1]; Jill Tinmouth [1]; Alice Lytwyn [2]; Janet Raboud [1]; William Chapman [1]; Teresa Darragh [3]; Barbara Winkler [4]; Marie Sano [1];
1-Univ. of Toronto, Toronto, ON, Canada; 2-McMaster Univ., Hamilton, ON, Canada; 3-UCSF, San Francisco, CA; 4-Quest Diagnostics, Teterboro, NJ.;

Plain Language Summary: Anal cancer occurs at high rates in the presence of HIV. We initiated a cancer screening program using Pap smears and anoscopy. Many subjects were found to have advanced pre-cancerous changes. High-resolution anoscopy was the best method for detecting these changes.

Objectives: We initiated an anal cancer screening study in HIV+ men using anal cytology, HPV detection and high-resolution anoscopy with directed anal biopsy. The aim was to determine the test characteristics of anal cytology and oncogenic HPV for detection of histologic high-grade anal intra-epithelial neoplasia (AIN 2/3).

Methods: Subjects were HIV+ men with anal receptive intercourse. Samples for anal cytology were collected by rotating a swab in the anal canal and processing by ThinPrep™. Oncogenic HPV was determined using Hybrid Capture™. Anal cytology and biopsies were independently assessed by at least 2 blinded pathologists and analyses done using these consensus diagnoses. The reference standard was consensus diagnosis of AIN 2/3.

Results: Results are presented on 246 pt. visits (median age=44, CD4=403, viral load <50, 89% on HAART). Anal cytology was abnormal in 73%: HSIL in 7%, low-grade changes (LSIL) in 50% and ASCUS in 16%. Anal biopsies were abnormal in 71%: AIN 2/3 in 28% and AIN 1 in 43%. The sensitivity (Sn) of any abnormality on the anal cytology in detecting AIN 2/3 was 84% and the specificity (Sp) was 32%. Negative predictive value (NPV) was 84%, Positive predictive value (PPV) was 33%. Abnormal anal cytology missed only 11/70 (16%) AIN 2/3 lesions. HSIL on anal cytology was not strongly predictive of AIN 2/3. Of 18 pts. with HSIL on anal cytology, only 12 (67%) had AIN 2/3; Sn was 17% and Sp was 97%. Oncogenic HPV was found in 86% of pts. The presence of HPV had Sn of 99%, Sp of 19%, NPV of 97% and PPV of 28%. Detection of HPV missed only 1/67 (1.5%) AIN 2/3.

Conclusions: High rates of anal dysplasia have been detected. Abnormal anal cytology was sensitive but not specific in detecting AIN 2/3. Oncogenic HPV detection had similar performance to anal cytology.

Contact Information: Irving Salit, Tel: 416-340-3697, Email: irving.salit@uhn.on.ca

223

EXPLORING THE MEANING OF "DISABILITY" FOR ADULTS LIVING WITH HIV/AIDS: PRELIMINARY FINDINGS AND FUTURE DIRECTIONS

Kelly O'Brien [1,2,3]; Ahmed Bayoumi [1,2]; Aileen Davis [2,4]; Carol Strike [5,6]; Nancy L. Young [2,7];
1-Centre for Research on Inner City Health, St. Michael's Hospital, Toronto, ON; 2-Department of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON; 3-Department of Physical Therapy, University of Toronto, Toronto, ON; 4-Toronto Rehabilitation Institute, Toronto, ON; 5-Centre for Addiction and Mental Health, Toronto, ON; 6-Department of Psychiatry, University of Toronto, Toronto, ON; 7-Hospital for Sick Children, Toronto, ON;

Plain Language Summary: Four focus groups were conducted to determine the meaning of "disability" from the perspective of adults living with HIV. Health-related challenges experienced may be physical, psychological or social in nature. Types of health-related challenges (or disability) that adults living with HIV experience included: fatigue, difficulty initiating and maintaining personal relationships, loss of self-esteem, mental health challenges, work and stigma. Factors that might influence these health-related challenges were: the uncertain and episodic nature of HIV, participants' perception of their health status, the trade-off of experiencing the deteriorating effects of HIV and living with the side effects of the medications, HIV and aging, and coping strategies such as participants' outlook on their illness and maintaining a healthy lifestyle. More interviews with adults living with HIV are needed to further explore the concept of "disability".

Objectives: To determine what "disability" means from the perspective of adults living with HIV.

Methods: We conducted focus groups with men and women living with HIV who self-identified as having experienced an "episode" of illness attributed to HIV. We asked participants to describe the health-related challenges they experience as a result of living with HIV, the areas of their life that are affected, and how these challenges impact their overall health. We audiotaped discussions for later verbatim transcription. We identified broad emerging themes via open coding and facilitated using N6!

Results: Twelve men and eleven women living with HIV participated in four focus groups. The median number of years participants were living with HIV was 8 (interquartile range: 9 years). Sixteen participants were taking antiretrovirals and 13 indicated their lowest CD4 count was <200 cells/mm3. Participants conceptualized "disability" as multi-dimensional, often spanning physical, mental and social domains of health. The health-related challenges experienced centred around six major themes: fatigue, difficulty initiating and maintaining personal relationships, loss of self-esteem, mental health challenges, work, and stigma. Other common themes emerged from participants' experiences that appeared to mediate or influence their challenges: the uncertain and episodic nature of HIV, participants' perception of their health status, the trade-off between the potential deteriorating effects of HIV and living with the adverse effects of antiretrovirals, HIV and aging, and coping strategies such as participants' outlook on their illness and maintaining a healthy lifestyle.

Conclusions: "Disability" experienced by adults living with HIV appears to be multi-dimensional in nature, with health-related challenges affecting physical, mental and social life domains. Other factors such as coping strategies and the unpredictable and episodic nature of HIV may influence one's experience and perception of "disability". Additional interviews are required to further investigate the relationship between "disability" and its influential factors.

Contact Information: Kelly O'Brien, Tel: 416-978-0565, Email: kelly.obrien@utoronto.ca

224

HIV/AIDS AND AEROBIC EXERCISE: RESULTS OF AN UPDATED COCHRANE COLLABORATION SYSTEMATIC REVIEW

Kelly O'Brien [1,2]; Stephanie Nixon [2]; Richard Glazier [1,3]; **Anne-Marie Tynan** [1];
1-Centre for Research on Inner City Health, St. Michael's Hospital, Toronto, ON; 2-Department of Physical Therapy, University of Toronto, Toronto, ON; 3-Department of Health Policy, Management and Evaluation, University of Toronto, ON;

Plain Language Summary: A Cochrane Collaboration systematic review was performed to determine the effects of aerobic exercise interventions on CD4 counts, viral load, heart and lung conditioning and psychological status in adults living with HIV/AIDS. Among the ten studies that met inclusion criteria, results from meta-analyses demonstrated statistically significant improvements in depressive symptoms and potentially clinically important improvements in cardiopulmonary fitness among exercisers compared to non-exercisers. In conclusion, performing aerobic exercise, or a combination of aerobic and progressive resistive exercise is safe and may lead to improvements in cardiopulmonary fitness and psychological status for adults living with HIV/AIDS.

Objectives: To examine the safety and effect of aerobic exercise interventions on immunological and/or virological, cardiopulmonary and psychological parameters in adults living with HIV/AIDS.

Methods: A systematic review of literature on HIV/AIDS and exercise was performed from 1980 to August 2003 according to Cochrane Collaboration protocol. Inclusion criteria included randomized controlled trials comparing aerobic exercise interventions with no aerobic exercise interventions or another exercise treatment modality performed at least 3 times/week, for duration of at least 4 weeks among adults (18 years of age of older) living with HIV/AIDS. Abstracts were reviewed independently by two investigators to determine study eligibility. Data were abstracted from studies that met inclusion criteria using standardized data abstraction forms. Methodological quality of included studies was assessed. Meta-analysis was conducted using random effects models whenever possible.

Results: Ten studies met inclusion criteria and eleven meta-analyses were performed. Meta-analyses compared outcomes of CD4 count, CD4 percentage and viral load (immunological / virological status), maximum oxygen consumption (VO2max) (cardiopulmonary status) and depression-dejection subscale of the Profile of Mood States (POMS) (psychological status). Main results indicated that aerobic exercise was associated with significant improvements in depressive symptoms, no change in CD4 count, CD4 percentage or viral load, and a non-significant trend towards improvements in VO2max among exercisers compared to non-exercisers. Greater improvements in VO2max were found among heavy intensity exercisers compared to moderate intensity exercisers.

Conclusions: Performing aerobic exercise or a combination of aerobic and progressive resistive exercise at least 3 times/week for at least 4 weeks may lead to significant improvements in psychological status for adults living with HIV/AIDS and potential clinically important improvements in cardiopulmonary fitness. Findings are limited to participants who continued to exercise. Aerobic exercise appears to be safe and may be beneficial for adults living with HIV/AIDS who are medically stable.

Contact Information: Kelly O'Brien, Tel: 416-978-0565, Email: kelly.obrien@utoronto.ca

225

INTERPROFESSIONAL LEARNING IN REHABILITATION IN THE CONTEXT OF HIV: A CONCEPTUAL FRAMEWORK OF EXISTING HIV CURRICULA FOR HEALTH CARE PROFESSIONALS

Kelly O'Brien [2,3]; **Gillian Bone** [1,3]; Elisse Zack [1]; Deb Cameron [4]; Christopher Sulway [5]; Janet Wu [5];
1-Canadian Working Group on HIV and Rehabilitation; 2-Centre for Research on Inner City Health, St. Michael's Hospital, Toronto, ON; 3-Department of Physical Therapy, University of Toronto, Toronto, ON; 4-Department of Occupational Therapy, University of Toronto, Toronto, ON; 5-St. Michael's Hospital,Toronto, ON;

Plain Language Summary: A conceptual framework of existing HIV curricula for health professionals was developed to inform the development of an interprofessional educational program for rehabilitation professionals on HIV/AIDS. The framework consists of four components based on whether curricula were interprofessional or uniprofessional, and whether curricula were specific to rehabilitation professionals or more broadly included other health care professionals. Implementation of any newly developed curriculum will help increase the knowledge and capacity of rehabilitation professionals so that they may better serve people living with HIV/AIDS in Canada.

Objectives: To highlight existing HIV curricula and educational resources in order to inform future interprofessional curriculum development for the education of rehabilitation professionals on rehabilitation in the context of HIV/AIDS.

Methods: This review was conducted as part of a larger project conducted by the Canadian Working Group on HIV and Rehabilitation (CWGHR) aimed at increasing the capacity of rehabilitation professionals to respond to the rehab needs of people living with HIV/AIDS through the development of new interprofessional curriculum, resources and partnerships. Existing HIV education curricula and resources implemented with current and future health professionals in Canada and the United States were identified. A variety of databases were searched and a National advisory committee, members of CWGHR and the CWGHR Education and Practice Advisory Committee were consulted.

Results: Characteristics of existing HIV curricula varied depending on whether curricula were interprofessional or uniprofessional, and whether curricula were specific to rehabilitation professionals (occupational therapists, physical therapists and speech-language pathologists) or more broadly included other health care professionals. A conceptual framework of Existing HIV Curricula for Health Care Professionals was developed. This framework consists of four intersecting components that represent different types of HIV curricula including: A) interprofessional HIV curricula specific to rehabilitation professionals, B) HIV curricula specific to rehabilitation professionals with no particular focus on interprofessional education, C) interprofessional HIV curricula for health care professionals that may include but is not specific to rehabilitation professionals and D) HIV curricula more broadly for health care professionals who may or may not include rehabilitation professionals. Examples of curricula within each component of this framework are demonstrated.

Conclusions: A range of existing HIV curricula exists that may be used to inform future curriculum development for rehabilitation professionals. Future development, implementation and evaluation of an interprofessional education curriculum will help to increase knowledge and capacity among future and existing rehabilitation professionals so that they may better meet the rehabilitation needs of people living with HIV/AIDS in Canada.

Contact Information: Gillian Bone, Tel: 416-513-0440 x235, Email: gbone@hivandrehab.ca

226

HIV SPECIALISTS' INVOLVEMENT, PERCEPTIONS AND ISSUES IN REHABILITATION: RESULTS OF A NATIONAL CANADIAN SURVEY

Catherine Worthington [2]; Ted Myers [1]; **Kelly O'Brien** [1,4]; Rhonda Cockerill [3]; Stephanie Nixon [4]; Tarik Bereket [1];
1-HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto, Toronto, ON; 2-Faculty of Social Work, University of Calgary, Calgary, AB; 3-Department of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON; 4-Department of Physical Therapy, University of Toronto, Toronto, ON;

Plain Language Summary: A national postal survey was conducted to investigate HIV specialists' involvement with rehabilitation and perceptions of rehabilitation issues for people living with HIV/AIDS (PHAs) in Canada. The largest percentages of the referrals made are to community-based ASOs and social workers for assistance with social participation restrictions. In conclusion, HIV specialists currently provide limited rehabilitation-related services for PHAs, however, they refer to a range rehabilitation services. There is a need for more collaborative practices among health care professionals to better meet the rehabilitative needs of PHAs.

Objectives: To investigate HIV specialists' involvement with rehabilitation and perceptions of rehabilitation issues for people living with HIV/AIDS (PHAs) in Canada.

Methods: A national postal survey was conducted with HIV specialists drawn from national association lists supplemented with snowball sampling. The survey was constructed with a national advisory committee including PHAs and HIV and rehabilitation professionals.

Results: Among the HIV specialists, the response rate was 63%, with 214 eligible surveys produced. Respondents included nurses, physicians, social workers, pharmacists, psychologists, and dieticians who had worked in an HIV clinical setting within the past year. Respondents averaged 16 years in practice, and had seen a mean of 53 HIV positive clients within the last month. Ninety percent were from metropolitan or urban areas. Sixty-two percent indicated that under half of their HIV caseload was rehabilitation-related, where rehabilitation was defined as services and activities that address or prevent impairments, activity limitations, and participation restrictions. Seventy-five percent indicated that their profession was 'very important' in the rehabilitation of PHAs. Ninety-four percent agreed or strongly agreed that rehabilitation professionals who provide service for PHAs need specialized training, and only 44% agreed or strongly agreed that rehabilitation professionals currently possess adequate knowledge and skills to assess and treat PHAs. Within the last year, 86% had referred HIV positive clients at least once to social workers, 85% to community-based AIDS service organizations, 50% to physiotherapists, 35% to occupational therapists, and 32% to physiatrists. The most important rehabilitation issues in the context of HIV were seen to be income supports (85% indicated 'very important'), prevention (83%), chronic poverty (81%), housing (80%), employment (76%), and stigma (74%).

Conclusions: HIV specialists currently provide limited rehabilitation-related services for PHAs, and refer them to a range of rehabilitation services. Respondents felt community-based supports are crucial for PHAs. There is a need for more collaborative practices among health care professionals to better meet the rehabilitative needs of PHAs.

Contact Information: Kelly O'Brien, Tel: 416-978-0565, Email: kelly.obrien@utoronto.ca

227

HAND HYGIENE PRACTICES AMONG DENTISTS, SURGEONS, NURSES AND DENTAL HYGIENISTS IN CANADA: A MAJOR CONCERN FOR IMMUNOSUPPRESSED PATIENTS

Gillian McCarthy[1,2]; Michael John[4,5,6]; Kenneth Harris[3,7];
1-Department of Epidemiology and Biostatistics, Schulich School of Medicine & Dentistry, UWO; 2-Department of Dentistry, Schulich School of Medicine & Dentistry, UWO; 3-Department of Surgery, Schulich School of Medicine & Dentistry, UWO; 4-Department of Microbiology and Immunology, Schulich School of Medicine & Dentistry, UWO; 5-Department of Medicine, Schulich School of Medicine & Dentistry, UWO; 6-Clinical Microbiology and Infection Control, London Health Sciences Centre; 7-Surgery, London Health Sciences Centre;

Plain Language Summary: The necessity for improvements in infection control and containment in healthcare facilities has been highlighted by the emergence of new pathogens and drug resistant strains of micro organisms. Patients who are immunosuppressed, including those with HIV disease/AIDS are particularly vulnerable to infection. The most important procedures for preventing transmission of infection are hand washing or hand disinfection (HHPs) but previous investigations have shown only partial compliance among healthcare workers (HCWs).

Objectives: The objective of this investigation was to investigate compliance with HHPs among dentists, surgeons and dental hygienists in Canada; and among nurses in Ontario.

Methods: HHPs of HCWs in Canada were investigated using mailed surveys of stratified random samples of dentists (n= 6440), surgeons (n=4000) and hygienists (n= 5900) in Canada; and nurses in Ontario (n=5810). Dillman's guidelines for administration of mailed surveys were used. The proportions of respondents who always used HHPs before treatment and after removal of gloves were estimated. HHPs of surgeons in the clinic or office environment (not the OR) were investigated. Data were weighted and analysed using SPSS/PC+.

Results: Response rates were 66% (dentists), 60% (nurses), 56% (surgeons) and 56% (hygienists). When anticipating exposure to blood or potentially infectious body fluid, routine glove use was reported by 95% of dentists, 70% of surgeons, 84% of nurses and 100% of hygienists. The percentages of respondents who always used HHPs before treatment and (after glove removal) were: Dentists, 76 (63); Surgeons in the clinic/office, 73 (70); Nurses, 71 (59); Dental hygienists, 80 (70). Reasons for poor compliance with routine HHPs among nurses included insufficient time (22%), no access to sinks or hand disinfectants (12%) and dermatitis (9%).

Conclusions: HHPs require improvement in all healthcare groups studied especially after degloving. Nurses reported the lowest rates of hand washing or disinfection. Many HCWs think that gloves protect their hands so they do not need to wash or disinfect hands after glove removal. However contamination of gloved hands occurs frequently as a result of cuts, punctures or microperforations in the gloves; and cross contamination will only be avoided if effective HHPs are used after degloving. The major obstacles to HHPs among nurses were lack of time and limited access to sinks or disinfectants – these modifiable factors should be urgently addressed.

Funding for these studies was received from Health Canada (NHRDP), the Medical Research Council of Canada, the Ontario HIV Treatment Network, and the Canadian Institutes of Health Research.

Contact Information: Gillian McCarthy, Tel: 519-661-2111, Email: Gillian.McCarthy@Schulich.uwo.ca

227B

ACCESS TO ELECTIVE SURGERY FOR PATIENTS WITH HIV AND OTHER BLOODBORNE PATHOGENS IN CANADA

Gillian McCarthy[1,2]; Ken Harris[3,4,5];
1-Dentistry, Schulich School of Medicine & Dentistry,UWO; 2-Department of Epidemiology and Biostatistics, Schulich School of Medicine & Dentistry, UWO; 3-Postgraduate Education, Schulich School of Medicine & Dentistry, UWO; 4-Department of Surgery, Schulich School of Medicine & Dentistry, UWO; 5-Department of Surgery, London Health Sciences Centre.;

Plain Language Summary: Healthcare workers who perform invasive procedures are at risk of exposure to HIV and other bloodborne pathogens (BBPs). Many are reluctant to provide treatment to patients infected with HIV, hepatitis B virus (HBV) or hepatitis C virus (HCV). Previous studies of surgeons' attitudes related to surgical procedures on HIV patients have not included a comprehensive national investigation of attitudes among surgeons in different subspecialties. Access to elective surgery for patients living with HIV in Canada was investigated using a confidential mailed survey of a random sample of 4000 surgeons, stratified by subspecialty.

Objectives: The objectives were to estimate the proportions of surgeons in Canada who (1) were willing to perform elective surgery on patients with AIDS, HIV, HBV, HCV or those in high risk groups; (2) who would refuse to treat HIV patients; (3) To investigate the best predictors of refusal or willingness to perform elective surgery on HIV patients.

Methods: A national mailed survey of a random sample of surgeons (n=4000), stratified by subspecialty with three follow-up attempts. Dillman's guidelines for administration of mailed surveys were used. Weighted data were analyzed using chi-square tests and multiple logistic regression (MLR).

Results: The response rate adjusted for non-delivery was 56%. The proportions of surgeons who were willing to perform elective surgery on infected patients were: HIV, 86%; AIDS, 81%; HBV or HCV, 92%. Willingness to operate on patients in high risk groups ranged from 93-97%: IV drug abusers, 93%; patients from countries where BBPs are endemic, 94%; men who have sex with men, 95%; and patients who received blood/ blood products between 1979-1985, 97%. MLR showed that the best predictors of willingness to perform elective surgery on HIV patients were subspecialty (general surgery or obstetrics/gynecology), lack of concern related to safety/staff fears, and ethical responsibility to treat HIV patients. Eight per cent of respondents reported that they would refuse to perform elective surgery if indicated on patients with HIV: Subspecialists reporting the highest rates of refusal were plastic surgeons (14%)and cardiac surgeons (12%); those reporting the lowest rates of refusal were vascular or thoracic surgeons and opthalmologists (5%). MLR indicated that the best predictors of refusal to treat were lack of ethical responsibility and concerns about safety/staff fears.

Conclusions: Improved training and professional development courses emphasizing ethics and safer surgical practices may improve access to elective surgery for patients with HIV.

Contact Information: Gillian McCarthy, Tel: 519-661-2111, Email: Gillian.McCarthy@Schulich.uwo.ca

228

INFECTION RATES IN HIV-HCV AND HCV PATIENTS TREATED WITH INTERFERON ARE SIMILAR AND NOT RELATED TO NEUTROPENIA

Curtis Cooper [1,2,3]; **Saif Al-Bedwawi** [1,2]; **Craig Lee** [1,2,3]; **Gary Garber** [1,2,3];
1-University of Ottawa; 2-The Ottawa Hospital Division of Infectious Diseases; 3-The Ottawa Health Research Institute;

Plain Language Summary: Infections are a complication of HCV drug therapy. It is not known if the risk for this is increased in those living with HIV. This analysis suggests that it is not. HCV drug therapy causes the number of infection fighting blood cells (neutrophils) to fall. The size of the reduction in neutrophils does not predict the risk of infection.

Objectives: Infectious complications of interferon-based HCV therapy in HIV-HCV co-infection are not well described. The correlation to interferon-induced neutropenia is unclear.

Methods: All recipients of interferon-based HCV therapy followed at The Ottawa Hospital Viral Hepatitis Clinic between June 2000 and May 2005 were identified from a SPSS 11.0 clinical database containing patient characteristics and laboratory data. All infectious complications identified by staff or reported by patient during the period of interferon exposure and one month after were identified by chart review. No patients received G-CSF.

Results: In total, 214 patients received 246 courses of therapy (6880 person-weeks of therapy). 28 HIV infected patients received 35 courses of therapy (913 person-weeks of therapy). 11 infectious complications in HIV-HCV patients were recorded (1.2 infections/ 100 person-weeks of therapy) which was similar to HIV negative patients (1.0 infections/ 100 person-weeks of therapy). The mean time to infection was 10 weeks of therapy (17 weeks in HIV negative, p=0.07). Infections included: 40% respiratory, 16% cutaneous, 15% oral cavity; 12% genitourinary, 12% gastrointestinal. 15% of infections were fungal (thrush-6, cutaneous-4) in nature. The proportion of infection types did not differ between HIV-HCV and HCV patients. No AIDS defining illnesses were identified and no infections required hospitalization and/or discontinuation of therapy in those with HIV. HIV status, age, sex, race, stage and grade of biopsy, and type of interferon were not correlated with infection rate by Cox regression analysis. Neutrophil counts declined from a baseline mean of 3800 cells/μL (SD 1700) to a nadir of 1900 cells/μL (SD 1100) by week 8 of therapy. The total, fungal and bacterial infection rates did not correlate with nadir neutrophil count or size of decline from baseline. The total infection rate was not greater for those with nadir counts <1000 cells/μL (0.83/ 100 person-weeks of therapy) or <750 cells/μL (0.71/100 person-weeks). Baseline neutrophil count, nadir count <1000 cells/μL, and occurrence of infectious complication were not related to AZT use.

Conclusions: Although the onset may be more rapid in HIV, overall infection rates are similar between HIV-HCV and HCV patients selected for HCV antiviral therapy. Neutrophil count is not correlated with infection rate in recipients of interferon-based HCV therapy. Interferon dose reduction and/or G-CSF dosing in those with neutropenia is not supported by this analysis.

Contact Information: Curtis Cooper, Tel: 613-737-8924, Email: ccooper@ottawahospital.on.ca

229

PATTERNS OF DOSAGE-ADJUSTMENTS FOR RIFABUTIN-ANTIRETROVIRAL DRUG INTERACTIONS

Laura Park-Wyllie [1,2]; Ahmed Bayoumi [1,3,4,5]; Anne Holbrook [6,7]; Lehana Thabane [6,7]; Tony Antoniou [2]; Deborah Yoong [8]; Derek Kam [1]; Mitchell Levine [6,7];
1-Centre for Research on Inner City Health, St.Michael's Hospital; 2-Department of Family and Community Medicine, St. Michael's Hospital; 3-Division of General Internal Medicine, St. Michael's Hospital, Toronto; 4-Department of Medicine, University of Toronto; 5-Department of Health Policy, Management, and Evaluation, University of Toronto; 6-Centre for Evaluation of Medicines, St. Joseph's Hospital; 7-Department of Clinical Epidemiology and Biostatistics, McMaster University; 8-Positive Care Clinic, St. Michael's Hospital;

Plain Language Summary: Dosage adjustments are recommended when rifabutin is co-administered with currently available antiretrovirals so that therapeutic concentrations of these agents are maintained. However, information regarding the frequency of dosage adjustment during combined use and associated clinical outcomes is currently lacking.

Objectives: To evaluate the pattern of drug dosage adjustment practices for interacting rifabutin – antiretroviral drug combinations.

Methods: A retrospective cohort study of participants enrolled in the HIV Ontario Observational Database (HOOD) was performed. Participants who were prescribed rifabutin and potent antiretroviral CYP450 inhibitors (saquinavir, indinavir, nelfinavir, ritonavir, amprenavir, lopinavir/ritonavir, delavirdine) or potent antiretroviral CYP450 inducers (efavirenz, nevirapine) were examined. In the exposure group, dosages of either rifabutin or the interacting antiretroviral had been adjusted according to recommendations from standard HIV drug interactions sources. Participants in whom dosages were not made served as the control group. Treatment efficacy and adverse event outcomes were compared between the two groups to identify whether an association existed between the exposure and antiretroviral efficacy, antiretroviral toxicity or rifabutin-related efficacy and toxicity.

Results: We identified 147 patients (93% male) who had received an interacting rifabutin–antiretroviral drug combination between 1995-2002. Dosages adjustments were made in 18 (12%) participants, and dosages were not adjusted in 129 (88%) participants. Of the patients not receiving dosage adjustments, the majority of combinations involved saquinavir (n=57) or indinavir (n=55). Contraindicated combinations occurred in 46% (60/129) of the unadjusted drug combinations. When comparing the frequency of dosage adjustments according to the availability of evidence describing a particular drug interaction, 27% (n=35/129) of the occurrences occurred despite the availability of the information on the drug interaction. Non-adjusted combinations were taken by patients for an average of 141 days per person. There were viral load measurements available for 16 patients. The mean log change in viral load in these patients were -0.63 vs -0.34 in the dosage adjusted and unadjusted groups, respectively. (p=0.31). There were too few documented adverse events to compare these outcomes between the groups.

Conclusions: This study demonstrates the uptake of dosage-adjustment practices for rifabutin-antiretroviral drug interactions according to the availability of the evidence. However, there remain about one-quarter of patients who do not receive recommended dosage-adjustments despite the available evidence. This may suggest the need for continued education and efforts to increase access to information pertaining to drug interactions and relevant dosage adjustment. Further research should look at viral and clinical outcomes that result from dosage-adjustment practices.

Contact Information: Laura Park-Wyllie, Tel: 416-864-6060 x6790, Email: parkwylliel@smh.toronto.on.ca

230

A SYSTEMATIC REVIEW OF CURRENT PRACTICES IN THE MEASUREMENT OF HIV-RELATED DIARRHEA

Jill Tinmouth [1]; Gabor Kandel [2]; George Tomlinson [3]; Sharon Walmsley [3]; Hillary Steinhart [3]; Richard Glazier [4];
1-Department of Medicine, Sunnybrook and Women's College Health Sciences Centre; 2-Department of Medicine, St. Michael's Hospital; 3-Department of Medicine, University Health Network; 4-Department of Family and Community Medicine, St. Michael's Hospital;

Plain Language Summary: Review of the literature on clinical trials of HIV-related diarrhea found that common sense measures of bowel movement frequency, form and duration were used to define presence of diarrhea while bowel movement frequency was most often used to assess response to treatment.

Objectives: To conduct a systematic review of measures used in clinical trials of HIV-related diarrhea was conducted.

Methods: Medline was searched from 1966 to November 2003 for clinical trials in HIV-related diarrhea. The sample was restricted to articles in which the primary objective was to evaluate an intervention. Data were abstracted from the articles pertaining to the type of trial, the therapeutic intervention, the definition of diarrhea and the definition of a response to the therapy. For the latter two items, stool frequency, stool form, duration of diarrhea, stool weight, grading scales, microbiology tests and overall global assessment were considered. Proportions of articles using these parameters are reported.

Results: The search strategy identified 286 articles, of which 38 met our inclusion criteria. The majority of trials were prospective; 22 were open-label and 12 were controlled trials. “Other drug” was studied most frequently (16 trials); in this category, octreotide (10 trials) was most often evaluated. Most commonly, presence of diarrhea was defined using stool frequency (20 trials, 53%), stool form (16 trials, 42%) and/or duration of diarrhea (26 trials, 68%); often, more than one characteristic was used. In trials using frequency, 12 of the 20 used a cut-off of 2 or more BMs/d to define diarrhea. A change in stool frequency (22 trials, 58%) was most often used to measure the response to the therapeutic intervention. Seven of these trials used reduction to less than 3 BMs/d to define response. Seven other measures were commonly used to determine response.

Conclusions: In practice, study investigators most frequently used the parameters of stool frequency, form and duration of diarrhea to define the presence of HIV-related diarrhea. Response to therapy was most often measured using change in the number of BMs/d. The high proportion of articles using one of 7 other measures suggests a lack of consensus regarding measures of response. No validated tools to define presence of diarrhea or response to therapy were identified. Further work is needed to develop such measures and should incorporate the dominant parameters identified in this systematic review as they are representative of expert opinion.

Contact Information: Jill Tinmouth, Tel: 416-480-5910, Email: jill.tinmouth@sw.ca

231

THE PERFORMANCE OF VARIOUS INSTRUMENTS IN THE MEASUREMENT OF HIV-RELATED DIARRHEA

Jill Tinmouth [1]; George Tomlinson [2]; Gabor Kandel [3]; Sharon Walmsley [3]; Hillary Steinhart [3]; Richard Glazier [4];
1-Department of Medicine, Sunnybrook and Women's College Health Sciences Centre; 2-Department of Medicine, University Health Network; 3-Department of Medicine, St. Michael's Hospital; 4-Department of Family and Community Medicine, St. Michael's Hospital;

Plain Language Summary: Various ways to measure HIV-related diarrhea were studied. It was found that self-report of bowel movement (BM) frequency overestimated prospective measurement of BM frequency. Combining BM frequency and form was the best way to measure diarrhea.

Objectives: To assess various measures of HIV-related diarrhea.

Methods: HIV+ subjects with self-reported diarrhea were studied in 2 ways. In part 1, all subjects (n=48) retrospectively reported (RR) stool frequency & form (categories: 1 = formed to 5 = watery) and completed a prospective (PR) 7 day stool chart of stool frequency & form using the Bristol Stool Form Scale (BSFS) [1 (hard) to 7 (watery)]. In part 2, diarrhea was assessed in a subgroup (n=20) using 4 measures: 8 hr stool weight (SWt), diarrhea symptom score (0 = none to 5 = severe) (DSx), stool frequency, stool form using the BSFS. For part 1, correlation was assessed with Spearman's correlation coefficient. For part 2, models were used to determine whether stool frequency or form best predicted SWt and DSx.

Results: For the overall group, the median (range) age was 42 yrs (20 – 62). Thirty-nine subjects (81%) were on HAART; median CD4 was 390 cells/mm3 (20 – 1110) and 20 (42%) had viral load < 50 copies/mL. In part 1, the median stool frequency by RR was 4 (1 – 18) BM/d and the median stool form category was 4. Using PR, the median number of BMs/d was 3.5 (1 – 10.1) and the median BSFS score was 5.6 (2.3 – 6.7). The absolute difference in frequency using the two measures was 1.4 BMs/d (95% CI: 0.7 – 2.1). Correlation between stool frequency measured by RR and PR was substantial ($r_s = 0.62$, $p < 0.0001$) while stool form correlated poorly ($r_s = 0.16$, $p = 0.26$). In part 2, the SWt was 94g/8hr (0 – 426 g), the DSx was 1.5 (0 – 5), the BSFS score was 5.5 (2 – 7) and the median number of BMs/8 hr was 1 (0 – 7). Whether SWt or DSx was used as the reference standard, models using both stool frequency and form performed best.

Conclusions: In part 1, self-report of frequency overestimated frequency measured prospectively. This result may be due to regression to the mean or subjects' inflation of their estimates; it is of interest as subject self-report of these parameters is often used to determine eligibility for trials in HIV-related diarrhea. In part 2, stool frequency and form were good predictors of diarrhea relative to two different reference standards.

Contact Information: Jill Tinmouth, Tel: 416-480-5910, Email: jill.tinmouth@sw.ca

232

A COMPARISON OF REPORTING OF ADVERSE DRUG EVENTS (ADES) IN QUESTIONNAIRES TO EVENTS RECORDED BY CHART REVIEW

Janet Raboud [1,2]; Elizabeth Phillips [3]; Maia Lesosky [4]; Sharon Walmsley [1,2]; Ahmed Bayoumi [2,5];
1-Division of Infectious Disease, University Health Network, Toronto, Ontario; 2-University of Toronto, Toronto, Ontario; 3-University of British Columbia, Vancouver, British Columbia; 4-Mount Sinai Hospital, Toronto, Ontario; 5-St. Michael's Hospital, Toronto, Ontario;

Plain Language Summary: Individuals attending the Toronto Hospital Immunodeficiency Clinic filled out a self-administered questionnaire about the frequency, severity and chronicity of common adverse drug events among individuals taking HAART therapy. Rates and types of adverse drug events reported on the questionnaires were compared to data collected by chart review as part of the HIV Ontario Observational Database.

Objectives: ADEs occur frequently among individuals taking HAART therapy and are the most common reason for discontinuing HAART in the first year of treatment. The purpose of this study is to compare rates and types of ADEs obtained by chart extraction to those on self-administered surveys.

Methods: HIV Ontario Observational Database (HOOD) participants attending the Toronto Hospital Immunodeficiency Clinic completed a self administered questionnaire on up to 3 occasions. Information was collected on frequency, severity and chronicity of ADEs including diarrhea, nausea, fatigue, changes in body shape, etc. Questionnaire data were compared to HOOD data where ADEs are obtained by chart review.

Results: 66 participants completed the questionnaires. The median age was 42, 85% male, 59% MSM, 41% heterosexual transmission, median 9 years since diagnosis. 68% had viral load < 50 copies/mL, median CD4 was 430. 95% of participants were on an NRTI, 65% on a PI and 46% on an NNRTI. The most common ongoing ADEs were diarrhea (44%), dry skin (42%), difficulty sleeping (42%) and changes in body shape (41%). Of 384 ADEs reported, 295 (77%) were reported on the questionnaire only, 33 (9%) in HOOD only and 56 (15%) were reported in both. The ADE most commonly reported in HOOD was rash (35%). The ADEs least likely to be recorded in HOOD were confusion, fever, dry skin, headache and numbness in hands and feet (all < 10%). The likelihood of an ADE being reported in HOOD did not depend on the severity or frequency of the event.

Conclusions: ADEs were more likely to be reported on questionnaires than recorded from chart extractions. Patients may be more likely to report an ADE in response to a prompt than to volunteer it independently. Our study is unable to determine whether the decreased frequency of recorded symptoms in the cohort study is due to faults in report, recording, or extraction but argues strongly for supplementing chart extracted data with direct questionnaires.

Contact Information: Janet Raboud, Tel: 416-586-8852, Email: raboud@mshri.on.ca

233

A NOVEL QUANTITATIVE P24 CAPTURE ASSAY FOR THE HYBRID FLOW APPLICATION PLATFORM (HYFAP)

Sylvie Faucher [1]; Alice Sherring [1]; Michèle Bergeron [1]; Paul Sandstrom [1]; Francis Mandy [1];
1-National HIV and Retrovirology Laboratories, Public Health Agency of Canada, Ottawa, Canada;

Plain Language Summary: A novel assay for the detection of HIV-1 p24 antigen was developed for a new generation of multi-tasking flow cytometers adapted to cellular and bead-based assays. This new p24 antigen assay performed as well as the commercial Perkin Elmer kit for the detection of HIV-1 purified p24 antigen.

Objectives: Protein and antibody bead arrays offer an alternative to ELISA and Western blotting. The simplicity, cost-reduction and high-throughput of these assays are the foremost advantages over conventional assays. In line with the view that a multi-tasking platform could be used to monitor HIV infected patients, a p24 antigen capture immunoassay was developed for the HyFAP, a flow cytometry system compatible with cellular and multiplex bead applications.

Methods: A quantitative HIV-1 p24 antigen capture immunoassay was developed using Luminex coupling beads and commercially available anti-p24 antibodies. Four commercial monoclonal antibody preparations were screened for their capacity to capture recombinant and native detergent solubilized HIV-1 p24 antigen (Perkin Elmer). The detection was done using biotinylated anti-p24 (HIV-1) polyclonal antibodies and streptavidin-PE. The analysis was done using the Luminex System.

Results: One of the four monoclonal antibody preparations tested showed a markedly better capture of HIV-1 recombinant p24 antigen on beads. The same monoclonal antibody was also the only one to bind native detergent solubilized p24 antigen. The assay showed very good reproducibility and performed well in presence of Triton X-100, the detergent used in commercial p24 antigen assays. In quantitative assays, the bead-based p24 assay showed a detection limit below 6 pg/mL, similar to that of the Perkin Elmer kit (4.3 pg/mL).

Conclusions: A novel bead-based HIV-1 p24 antigen capture assay using fluorescent beads was developed for the HyFAP. The assay was simple, fast and performed very well when detecting detergent solubilized p24 antigen.

Contact Information: Sylvie Faucher, Tel: 613-941-8856, Email: sylvie_faucher@phac-aspc.gc.ca

234

SPECIAL IMMUNOLOGY SERVICES (SIS) CLINIC PATIENT DEMOGRAPHICS 1991-2004

David Free [1]; **Debbie Sheehan** [1,2]; Marcia Nauta [2,3]; Abraham Ture [1];
1-Faculty of Nursing, McMaster University; 2-City of Hamilton Public Health and Community Services Department ; 3-Special Immunology Services Clinic, Hamilton Health Sciences;

Plain Language Summary: The Special Immunology Services (SIS) Clinic provides care to HIV positive patients in Hamilton, Ontario. The goal of this research project was to analyze SIS patient chart data for the years 1991 – 2004, comparing findings with published Ontario HIV data for the same time period. Key findings from the chart audit include: a shift to more female patients and more patients from HIV-endemic countries. There was a 50% increase in referrals to SIS since 2002. The poster summarizes recommendations for the SIS Clinic based on the chart audit results.

Objectives: The Special Immunology Services (SIS) Clinic provides care to HIV positive patients and is located within Hamilton Health Sciences, a tertiary care teaching hospital serving south-central Ontario. The multidisciplinary clinic provides HIV, STI, and Hepatitis testing; counselling; treatment; and patient education. The goal of this project was to analyze SIS patient data for the years 1991 – 2004, comparing findings with published Ontario HIV data for the same time period.

Methods: A retrospective chart review of all SIS patient records (N=1348) was conducted. A chart audit tool was adapted for this project based on an instrument previously used for the same purpose. Exclusion criteria included records prior to 1991(N=271), all (HIV) negative patients (N=90), and patients who did not come for their initial appointment (N=110). Frequency and cross tabulation analyses were performed on the remaining records (N=931).

Results: The majority of the SIS clinic HIV+ patient referrals are from the regions of Hamilton (53.5%) and Niagara (18.9%). There was a 50% increase in HIV+ SIS referrals seen between 2002 and 2004. The proportion of male patients referred to SIS decreased over time relative to females ($p<0.001$). The SIS clinic patient risk factors were similar to the Ontario data. In both groups, men who have sex with men (MSMs) are the most represented group followed by heterosexuals, intravenous drug users, endemic/immigrants, and transfusions. Significant changes have occurred in MSM (decrease from 41.2% in 1991 to 31.9% in 2004) and endemic country (increase from 3.9% in 1991 to 31.9% in 2004) risk factors in the SIS patients over time ($p<0.001$). Similar trends also occurred in Ontario.

Conclusions: The demographics of HIV infection are changing in SIS patients and Ontario. The sharp increase in new patients from endemic countries starting in 2002 is likely due to the change in Canadian legislation which mandated HIV testing for all immigrants. The recent increase in SIS patient referrals has implications for future clinic staffing & budget. The observed patient demographic trends will assist SIS clinic staff in targeting prevention/education services and directing research efforts.

Contact Information: David Free, Tel: 905-546-2424 x3286, Email: dsheehan@hamilton.ca

235

MOTIVATION FOR PARTICIPATING IN A NOVEL THERAPEUTIC HIV VACCINE TRIAL (CTN173): AN UPDATE

Louise Balfour [1]; John Kowal [1]; Amy Silverman [1]; Georgio Tasca [1]; Cecile Tremblay [2]; Jean-Pierre Routy [3]; Jonathan Angel [1];
1-Ottawa Hospital - General Campus; 2-CHUM, Montreal; 3-Montreal Chest Hospital;

Plain Language Summary: The goal of this psychology-sub study was to help us better understand what psychological factors motivate people to participate in HIV vaccine research and what types of concerns people might have about participating. The second goal of this research was to examine how patients' mood and quality of life might be affected by participating in this type of vaccine study.

Objectives: Objectives: Understanding HIV patients' motivation and concerns about participating in novel therapeutic vaccine trials is important. Potential social and personal risks and benefits should be carefully weighed by patients when they enroll. Patients who feel better prepared or more informed are more likely to adhere to their treatments. The present study is a psychological sub-study of a larger, multi-site therapeutic HIV vaccine trial. The main focus of this psychological sub-study is to describe HIV patients' motivation for participating and to monitor patients' mood, coping, and quality of life throughout the study.

Methods: Methods: Eligible participants were at least 18 years-old, have documented HIV infection, have an "undetectable" HIV viral load (< 50 copies/ml) for >2 years and a CD4 nadir >250 cells/uL, and currently be taking highly active antiretroviral treatment. All patients completed an 11-item vaccine motivation scale at study baseline. Data collection for the larger clinical trial is ongoing. All patients enrolled in the larger study agreed to participate in the psychology-sub-study.

Results: Results: Preliminary results (N=28) indicate that most vaccine trial participants (> 78%) report low social risk concerns (e.g., fears of rejection or discrimination by others) and high hopes for potential social benefits (e.g., being one step closer to developing an effective HIV vaccine). Most study participants (96%) are motivated by personal benefits (e.g., to learn updated information about HIV), and 81% acknowledge that they have accepted some level of personal risk (e.g., the therapeutic vaccine may cause some side-effects).

Conclusions: Conclusions: Preliminary results from this study suggest that patients who enroll in a novel therapeutic HIV vaccine trial are initially highly motivated to participate because they feel that potential social and personal benefits to participating outweigh potential personal risks. At study follow-up, patients' baseline motivation will be correlated with their mood and adherence to the treatment protocol.

Contact Information: Louise Balfour, Tel: 613-737-8037, Email: lbalfour@rottawahospital.on.ca

236

A SYSTEMATIC REVIEW OF THE EFFECTIVENESS OF BEHAVIOURAL INTERVENTIONS TO IMPROVE ADHERENCE TO ANTIRETROVIRAL THERAPY IN HIV/AIDS

Sergio Rueda [1,2]; Laura Park-Wyllie [1,2]; Richard Glazier [1,2]; Ahmed Bayoumi [1,2]; Anne-Marie Tynan [1]; Tony Antoniou [1]; Sean B. Rourke [1,2];
1-St. Michael's Hospital; 2-University of Toronto;

Plain Language Summary: Strict adherence to antiretroviral therapy is required to derive maximal benefit and to ensure that today's treatments remain effective for as long as possible. Some behavioural interventions have a significant impact on improving adherence, but there is a need for standardization and methodological rigour in the conduct of adherence trials. Further research is required before any specific adherence improving strategy can confidently be incorporated into standard clinical practice.

Objectives: To conduct a systematic review of the research literature on the effectiveness of behavioural interventions to improve adherence to antiretroviral therapy in HIV/AIDS.

Methods: A systematic search of the core databases was performed from January 1996 until May 2005. Randomized Controlled Trials examining the effectiveness of behavioural interventions to improve the adherence to HAART were considered for inclusion. Only those studies that measured adherence at a minimum of six weeks were included. Study selection, quality assessments, and data abstraction were performed independently by two reviewers.

Results: Study heterogeneity with respect to differing populations, interventions, outcomes, and length of follow-up did not allow for meta-analysis. We included 19 studies involving 2,159 PHAs. Sample sizes ranged from 22 to 367. Study duration ranged from a single session to a variable number of sessions delivered over one year. Many of the interventions involved the provision of an educational component to improve adherence and often addressed strategies to overcome barriers to adherence and the development of problem-solving skills. They ranged from simple interventions (e.g., the provision of reminder devices) to complex interventions (e.g., cognitive-behavioural therapy delivered by licensed psychologists). Eleven of the 19 studies demonstrated a statistically significant advantage associated with the described adherence intervention. The advantage associated with adherence outcomes does not seem to translate into the more clinically relevant outcome of viral suppression. Only 4 out of 12 studies that reported virological or immunological results found a significant effect associated with the intervention. The studies had several methodological shortcomings.

Conclusions: There is a need for standardization and methodological rigour in the conduct of adherence trials. Some interventions have a significant impact on improving adherence. Further research is required before any specific adherence improving strategy can confidently be incorporated into standard clinical practice.

Contact Information: Sergio Rueda, Tel: 416-864-6060 x6485, Email: ruedas@smh.toronto.on.ca

237

AN EVALUATION OF DYNAL T4 QUANT KIT FOR CD4 T-CELL ENUMERATION USING INNOVATION FROM ONTARIO TO LED CONVERT A LIGHT MICROSCOPE TO EPIFLUORESCENCE

Francis Mandy [1]; Michele Bergeron [1]; Marco Angelini [2]; Peter Pennefather [3];
1-HIV Immunology Laboratory, Public Health agency of Canada; 2-Fraen Corporation, Milan, Italy; 3-Departement of Pharmacology, University of Toronto;

Plain Language Summary: Affordable CD4 T-cell methods are in great demand to monitor individuals with HIV on ART. Using an invention from Ontario, it is possible to reduce the cost of CD4 T-cell monitoring for small rural labs. This report describes an evaluation study for such low cost manual technology.

Objectives: There is a massive global demand for the acceleration of treatment of HIV infection hence the need for affordable CD4 T-cell counting. There is a need for affordable and reliable assays at remote clinics in Africa and Asia. Fluorescent microscopy with commercial kits is an option but often it is too expensive and difficult to sustain at rural locations.

Methods: The T4 Quant kit is a relatively inexpensive and simple CD4 T-cell kit for fluorescent microscopy. It uses an immunomagnetic cell separation technique for isolating CD4 T-cells. Nucleus are counted using a fluorescent stain. An AxioStar, Zeiss light microscope was converted to fluorescence for this evaluation. Battery powered LED illumination was added with optical filters to work with acridine orange. The excitation source was a 3 watts Royal Blue Luxeon LED with peak wavelength @ 450nm. Backlight (red) is generated with a 3 Watts Red Luxeon LED with peak wavelength @ 635nm. The converted portable microscope's cost remained under $3000.00. For evaluation purposes this microscope was equipped with a C mount to obtain digital images. The results were recorded from both microscopes and compared to each other and to flow cytometric results.

Results: 16 HIV positive patient samples were evaluated with all methods. The values tested by flow were in the range between 77 and 811 CD4 T-cell counts per µL. SD was 2.5 between the two microscopic methods the upper limit was 3.8 and the lower limit was -6.0. Both methods were compared to the predicate flow cytometry method using Bland Altman statistics. The values generated with the low cost microscope compared well with results from both the predicate and the high end microscopy.

Conclusions: The preliminary results indicate that it is possible to replace a conventional relatively expensive epifluorescent microscope requiring line AC voltage with much lower cost instrument without compromising the quality of the Dynal kit's performance. Based on these preliminary results a more in depth multi-site evaluation should be performed.

Contact Information: Francis Mandy, Tel: 613-957-0174, Email: Frank_Mandy@phac-aspc.gc.ca

238

BLOOD MITOCHONDRIAL GENE EXPRESSION (CCOI) IS DECREASED IN NEONATES BORN TO HIV-INFECTED MOTHERS TREATED WITH HAART DURING PREGNANCY

Hélène Côté [1]; John Forbes [1,2]; **Ari Bitnun** [3]; David Burdge [2]; Evelyn Maan [2]; Adriana Costei [3]; Izabelle Gadawski [1]; Janet Raboud [4]; Stanley Read [3]; Susan King [3];
1-Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver; 2-Children's & Women's Health Centre of British Columbia, University of British Columbia, Vancouver; 3-Division of Infectious Diseases, Hospital for Sick Children, University of Toronto, Toronto; 4-University Health Network, University of Toronto, Toronto, Canada;

Plain Language Summary: There is concern that exposure to anti-HIV drugs in utero may have deleterious effects on energy metabolism in babies. In order to assess for this possibility we performed blood tests on infants born to HIV-infected women who were exposed to anti-HIV medications with infants born to HIV-uninfected women not exposed to these medications within 3 days of birth.

Objectives: Highly active antiretroviral therapy (HAART) has been associated with mitochondrial DNA (mtDNA) depletion. Infants born to HIV-infected antiretroviral-treated pregnant women have been noted to have evidence of mitochondrial toxicity such as elevated serum lactate. We investigated whether whole blood mtDNA or mtRNA depletion occurs in neonates exposed to antiretroviral therapy in utero.

Methods: Blood samples were collected at day 1-3 of age from HIV-uninfected neonates born either to HIV-infected HAART-treated mothers (subjects N=26) or HIV-uninfected mothers (controls N=22). mtDNA/nuclear DNA ratio and mtRNA (CCOI/beta-actin) levels were quantified and compared between groups using the wilcoxon rank sum test. The relationships between the length of drug exposure in utero and 1-month lactate vs mtDNA and mtRNA were investigated using Spearman and Pearson correlation.

Results: HIV-infected mothers had received HAART for a median of 18 weeks [IQR 14-31] of their pregnancies, as well as intrapartum IV zidovudine (AZT). Their infants received standard prophylactic AZT. Three HIV-infected mothers used drugs of addiction and 2 were on methadone during pregnancy while 5 were co-infected with HCV. There was no difference between the two groups with respect to APGAR score at 1min - 8 [8-9] vs 9 [8-9] (P=0.17), but neonates born to HIV-infected women had lower birth weight (3102±429 vs 3536±473 g, P=0.002) and shorter gestation time (38.7±1.7 vs 39.7±1.3 w, P=0.014). Blood mtDNA levels were similar in subjects and controls (median mtDNA/nDNA [IQR] = 128 [115-156] vs 128 [100-154], P=0.60). By contrast, mtRNA levels were lower in subjects than controls (5.0 [3.8-8.8] vs 13.2 [4.5-26.3], P=0.052). The length of exposure to HAART in utero (since 1st, 2nd or 3rd trimester) showed no correlation with mtDNA (R=0.33, P=0.18) or mtRNA (R=0.17, P=0.51). Lactate at 1 month was marginally positively correlated with neonate mtDNA levels (R=0.41, P=0.085, N=19). The few subjects exposed to stavudine and/or didanosine in utero (N=4) tended to have lower mtDNA than those exposed to other nucleoside reverse transcriptase inhibitors (117 [113-124] vs 134 [117-154], P=0.20) and higher mtRNA (13.6 [8.1-35.2] vs 4.9 [3.2-7.3], P=0.18) although these differences did not reach statistical significance.

Conclusions: Based on these preliminary results, at 1-3 days of age, before extensive post-natal exposure to AZT, HIV uninfected neonates showed no evidence of blood mtDNA depletion, but tended to have lower mitochondrial gene expression.

Contact Information: Ari Bitnun, Tel: 416-813-7654 x3362, Email: ari.bitnun@sickkids.ca

239

DURATION AND OUTCOMES OF HIV ANTIRETROVIRAL THERAPY DIFFER BETWEEN HIV-HCV AND HIV-HBV CO-INFECTED PATIENTS

Curtis Cooper [1,2,3,4]; Courtney Cohoon [4]; Dave Mackie [4];
1-University of Ottawa; 2-Division of Infectious Diseases; 3-The Ottawa Hospital; 4-Ottawa Health Research Institute;

Plain Language Summary: The evaluation of HIV drug therapy in those with chronic viral hepatitis is usually done on groups combining both HIV-HCV and HIV-HBV co-infected people. This analysis suggests that these two groups have very different characteristics and that the liver reactions to treatment are not similar. We conclude that HIV drug therapy in HIV-HCV and HIV-HBV patients should be assessed separately.

Objectives: The combination of HIV-HCV and HIV-HBV patients to assess HAART outcome in those with viral hepatitis is common but may not be appropriate.

Methods: Clinical, laboratory, and virologic results pertaining to HAART regimens initiated at The Ottawa Hospital Immunodeficiency Clinic between January 1, 1994 and December 31, 2004 were assessed by computerized database analysis (SPSS 11.0) in all HIV-HCV and HIV-HBV co-infected subjects.

Results: By univariate Cox regression, HCV versus HBV (OR=1.8, p<0.001), history of injection drug use (OR 2.0, p<0.001), CD4 < 200 cells/μL (OR=1.2, p<0.001) and alcohol abuse while on HAART (OR 1.3, p<0.01) predicted earlier HAART discontinuation. History of injection drug use remained significant by multivariate analysis (OR 1.6, p<0.02). Regimens were discontinued specifically for hepatotoxicity in 3% of HIV-HBV co-infected and 5% of HIV-HCV co-infected ($\chi 2$, p=NS). Liver enzymes increased from baseline to month 3 in HCV (mean 9 IU/mL). In contrast, liver enzymes declined from baseline to month 3 in HBV (mean -15 IU/mL). Enzymes were similar to baseline for both HCV and HBV by month 12.

Conclusions: Antiretroviral treatment durations differ between HBV and HCV. This is unlikely to be a direct result of differences between viruses and more to do with the burden of substance abuse and differing psychosocioeconomic characteristics of those with HIV-HBV and HIV-HCV. Although the frequency and severity of HAART-related clinically relevant liver toxicity is similar, patterns of liver enzyme changes following the initiation of HAART differ between HCV and HBV. It is likely not appropriate to combine HIV-HCV and HIV-HBV co-infected subjects together for analysis when evaluating HAART outcomes in those with chronic viral hepatitis.

Contact Information: Curtis Cooper, Tel: 613-737-8924, Email: ccooper@ottawahospital.on.ca

240

COMPARTMENTALIZED ACTIVATION OF CMV IN THE MALE GENITAL TRACT IS ASSOCIATED WITH DISPROPORTIONATE SHEDDING OF HIV IN SEMEN.

Prameet Sheth [1]; Ali Danesh [1,4]; Anthony Sheung [1]; Colin Kovacs [2]; Roberta Halpenny [2]; Kelly MacDonald [1,3]; Tony Mazzulli [3]; David Kelvin [4]; Rupert Kaul [1];
1-Department of Medicine, University of Toronto, Canada; 2-Canadian Immunodeficiency Research Collaborative inc, Toronto, Canada; 3-Mt Sinai Hospital, Toronto, Canada; 4-Division of Experimental Therapeutics, Toronto General Research Institute, Toronto, Canada;

Plain Language Summary: Globally, most HIV transmission results from contact with HIV-infected semen. Although levels of HIV in semen are usually lower than in blood, some men shed disproportionately high amounts of HIV in semen, and may be at a higher risk of transmitting to their partner(s). We hypothesized that this might be related to local reactivation of CMV or herpes, both of which are common, chronic genital infections in HIV-infected men.

Objectives: To evaluate the influence of compartmentalized CMV and HSV-2 reactivation on HIV shedding and the inflammatory milieu in semen.

Methods: Blood and semen samples were collected from 26 HIV infected therapy-naïve men. Blood and semen viral loads were measured using the Versant HIV RNA 3.0 Assay (bDNA), and cytokine profiles were evaluated using the Becton Dickinson cytokine bead array. HSV-2 IgG serology was performed and levels of CMV and HSV-2 DNA in semen were evaluated using the Artus Gmbh QPCR kit.

Results: Within each of the blood and semen compartments, levels of several inflammatory cytokines were highly interrelated, but there was no relationship between compartments. For instance, IL6 levels in semen were positively correlated with semen IFNg, IL8, IL12 and TNFa (all $p \leq 0.1$), and blood IL6 with their levels in blood (all $p \leq 0.01$). However, semen IL6 was not correlated with IL6 or the other inflammatory cytokines in blood (all $p < 0.5$). HIV shedding in semen was associated with semen inflammatory cytokines IL6, IL8, IL12 and IFNg ($p \leq 0.05$). All men were CMV seropositive, and 17/26 participants were shedding CMV in semen. Semen HIV levels exceeded blood in 9/26 (35%) of therapy-naive men, and disproportionate shedding was strongly associated with compartmentalized semen CMV reactivation (OR 10.5; $P < 0.01$). Overall, semen levels of HIV and CMV were closely correlated ($r = 0.5$; $P < 0.01$), independent of blood HIV viral load and CD4+ T-cell count.

Conclusions: HIV-1 shedding in semen is strongly correlated with compartmentalized semen inflammation. Reactivation of common, persistent viral co-infections may be an important mediator of both semen inflammation and HIV shedding. Strategies to prevent primary or recurrent viral co-infections may be important in reducing sexual transmission of HIV.

Contact Information: Prameet Sheth, Tel: 416-946-7054, Email: prameet.sheth@utoronto.ca

241

REHABILITATION PROFESSIONALS' KNOWLEDGE, ATTITUDES AND PRACTICE ISSUES ON HIV/AIDS: RESULTS OF A NATIONAL CANADIAN SURVEY

Kelly O'Brien [1,4]; Catherine Worthington [2]; Ted Myers [1]; Rhonda Cockerill [3]; Stephanie Nixon [4]; Tarik Bereket [1];
1-HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto, Toronto, ON; 2-Faculty of Social Work, University of Calgary, Calgary, AB; 3-Department of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON; 4-Department of Physical Therapy, University of Toronto, Toronto, ON;

Plain Language Summary: A national postal survey was conducted with rehabilitation professionals to describe their knowledge, attitudes and practice issues with people living with HIV/AIDS (PHAs) in Canada. Almost two thirds of respondents indicated they never knowingly served a PHA. Less than one third had received training in HIV/AIDS as part of their rehabilitation degree. Very few felt that rehabilitation professionals possess the knowledge and skills to assess and treat PHAs. In conclusion, despite the role that rehabilitation professionals have to play in the care and treatment of PHAs, only a minority currently serve HIV/AIDS clients highlighting a need for further education in this field.

Objectives: To describe rehabilitation professionals' knowledge, attitudes and practice issues with people living with HIV/AIDS (PHAs) in Canada.

Methods: A national postal survey was conducted with rehabilitation professionals (occupational therapists, physical therapists, speech-language pathologists, and physiatrists) randomly sampled from national and provincial mailing lists. The survey was constructed with a national advisory committee including PHAs and rehabilitation and HIV professionals.

Results: The overall response rate was 74%, with 1058 usable surveys produced. The majority of the respondents were female (88%) and averaged 14 years in practice. Only 27% had received training in HIV/AIDS as part of their rehabilitation education. Sixty-one percent indicated that they had never knowingly served an HIV positive client. Of these, 27% indicated that they would like to work with this client group (27% would not, and 46% were unsure). Of the 39% who had knowingly served an HIV positive client, the mean number of PHAs served in the past year was 4. The majority indicated that their profession was somewhat (40%) or very important (46%) for this population, but only 19% agreed that rehabilitation professionals currently possess adequate knowledge and skills to assess and treat PHAs. Fifty-three percent disagreed that serving PHAs is more demanding than serving clients with other chronic illnesses or conditions, and 50% agreed that many rehabilitation professionals are uncomfortable with the idea of working with PHAs. Forty-one percent indicated that there were service barriers specific to HIV that might prevent PHAs from having their rehabilitation needs met.

Conclusions: Despite the role that rehabilitation professionals have to play in the care and treatment of people living with HIV, only a minority currently serve HIV/AIDS clients. There is a need for further education and service development in this field.

Contact Information: Kelly O'Brien, Tel: 416-978-0565, Email: kelly.obrien@utoronto.ca

242

FRAMINGHAM RISK SCORES AND CAROTID ARTERY THICKNESS IN THE CANADIAN HIV VASCULAR STUDY

Marek Smieja [1]; Eva Lonn [1]; Fiona Smaill [1]; Lynn Kelleher [1]; Shelley Schmidt [1]; Sandy Smith [1]; Kevin Gough [2]; John Gill [3]; Sylvie Trottier [4]; Marianne Harris [5];
1-McMaster University, Hamilton; 2-University of Toronto, Toronto; 3-University of Calgary, Calgary; 4-Universite de Laval, Quebec; 5-University of British Columbia;

Plain Language Summary: Heart disease is an important long-term consequence of combination anti-retroviral treatment. However, as current studies cannot precisely establish the relative contribution of individual risk factors, use of the Framingham Risk Score is recommended by most experts. We examined how well this risk score predicts the extent of atherosclerosis, as measured by high resolution ultrasound of the carotid arteries amongst 244 Canadian HIV-positive subjects.

Objectives: Anti-retroviral treatment increases the incidence of future myocardial infarction, but we remain unclear as to whether the Framingham Risk Score adequately captures the extent of asymptomatic atherosclerosis in HIV-positive subjects. Our objective was to examine how closely these risk scores were associated with carotid artery thickness.

Methods: HIV-positive subjects aged 35 years or older, attending university-affiliated clinics in five Canadian centers, were recruited into a prospective study of cardiovascular risk. We completed baseline ultrasound examinations in 295, and one-year follow-up in 192. 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). Amongst 244 people analyzed to date, we sought an association between carotid IMT and the Framingham Risk Score, which includes assessment of age, gender, smoking, total and HDL cholesterol, and systolic blood pressure.

Results: Mean (SD) age was 46.2 (8.1) years; 91.0% were men; and 41.4% were current smokers. Carotid IMT was 0.82 (0.24) mm. Framingham scores were aggregated according to the Canadian Consensus Guidelines into low (<10%/10 year risk), intermediate (10-19%) or high risk (>20%). 66.9% were low risk, 26.7% were intermediate risk, and 6.4% were high risk. Framingham Risk Score predictions for 10-year cardiovascular risk were strongly associated with carotid IMT (Beta=0.087 per category change, R=0.54, P<0.001), but explained only 29% of the variance. The individual variables age, gender, smoking, total HDL cholesterol, systolic blood pressure and statin exposure explained 56% of the variance.

Conclusions: The Framingham Risk Score was strongly associated with the extent of carotid artery thickness among HIV-positive subjects, but explained only half of the variance compared with the individual risk factors. This suggests that the risk score will need a different weighting of the individual coronary risk factors to better reflect atherosclerotic risk among people with HIV.

Contact Information: Marek Smieja, Tel: 905-521-6143, Email: smiejam@mcmaster.ca

243

APPROPRIATENESS OF ANTIRETROVIRAL THERAPY AT INITIATION OF TREATMENT FOR HIV IN ONTARIO: 2004

Anita Rachlis [1,2,3]; **Christopher Jones** [1]; Carol Swantee [1,4]; Keyi Wu [4];
1-Ontario HIV Treatment Network; 2-University of Toronto; 3-Sunnybrook and Women's College Health Sciences Centre; 4-Ontario HIV Laboratory;

Plain Language Summary: This study demonstrated that the specific combinations of antiretrovirals prescribed by Ontario physicians in 2004 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 2004 when initiating patients on treatment for established HIV infection were aligned with practice guidelines.

Methods: The 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 2004 were analyzed to determine their consistency with the Preferred, Alternative and/or Not Recommended combinations recommended by the March 23, 2004 version of the US Department of Health and Human Services' *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents.* Also, any drug or drug combination that could not be matched with any DHHS category was deemed an outlier.

Results: For 2004, of 552 initiations, 312 (56.5%) were Preferred combinations and an additional 143 (25.9%) were Alternative combinations. Combinations that were either Not Recommended or Should Not Be Offered At Any Time represented 11.6% (64) of all initiations in 2004.

Conclusions: For 2004, a large majority (82.4%) of initiating antiretroviral regimens prescribed by HIV-treating physicians in Ontario were aligned with DHHS's recommendations for Preferred and Alternative combinations of drugs.

Contact Information: Christopher Jones, Tel: 416-569-0799, Email: cjones@management-tools.ca

244

NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) IN HIV VERSUS NON-HIV: DIFFERENCES IN METABOLIC AND NUTRITIONAL PARAMETERS

Saira Mohammed [1,2]; Johane Allard [1]; Ellie Aghdassi [1]; Ghazal Avand [1,2]; Morris Sherman [1]; Jenny Heathcote [1]; Irving Salit [1];
1-Department of Medicine, University Health Network, Toronto, Canada; 2-Department of Nutritional Sciences, University of Toronto, Toronto, Canada;

Plain Language Summary: NAFLD is becoming a common condition in the general population as it is closely associated with the features of the metabolic syndrome (e.g. obesity) which pose as risk factors of NAFLD and are linked to insulin resistance, a pathogenic factor in NAFLD. In the HIV population, HIV drugs may pose as a potential risk factor of NAFLD as well leading to metabolic abnormalities.

Objectives: The purpose of this study was to compare parameters of metabolic syndrome and nutritional status between HIV-positive (HIV+) and non-HIV male patients.

Methods: Fourteen HIV+ and eighteen non-HIV male subjects, with ultrasound/liver biopsy-proven NAFLD and with 1.5 times elevated liver enzymes, not taking antioxidant supplements and with alcohol consumption of less than 2 drinks per day were compared for dietary intake (7-days food record), physical activity (7-day activity log), blood biochemistry (glucose, insulin, c-peptide, HOMA, HbA1c and lipid profile) and anthropometric measurements [body mass index (BMI), arm muscle area (AMA), waist circumference and skinfold measurements]. Body composition was assessed by bioelectrical impedance analysis (BIA). Data were compared by unpaired t-test and Mann-Whitney test with significance considered if $P<0.05$.

Results: The mean age was similar (HIV+: 44.1+/-1.4 VS non-HIV: 45.5+/-3.1 yr, p=0.675). BMI, waist circumference, and total body fat estimated from skinfold thicknesses were lower whereas AMA was higher in HIV+ than in non-HIV (BMI: 26.3+/-0.5 VS 29.8+/-1.1 kg/m2, p=0.004; waist circumference: 92.3+/-1.7 VS 99.9+/-3.0 cm, p=0.042; total body fat: 46+/-2% VS 56+/-2%, p=0.0001; AMA: 62.7+/-3.9 VS 41.2+/-4.4 cm2, p=0.001) respectively. Physical activity and energy intakes were higher in HIV+ than in non-HIV (Physical activity: 8.4+/-1.8 VS 3.8+/- 0.9 units of exercise/day, p=0.048; total energy intake: 29.1+/-2.8 VS 21.3+/-2.5 kcal/kg, p=0.045) respectively. In general, macronutrient and micronutrient intakes were not different between the 2 groups. Insulin resistance (IR) parameters were similar (HOMA: HIV+: 6.1+/-1.1 VS 11.3+/-6.0, p=0.286). Serum triglyceride (TG), and C-peptide were higher whereas serum HDL and LDL levels were lower in HIV+ than non-HIV (TG: 2.8+/-0.5 VS 1.7+/-0.2 mmol/l, p=0.044; C-peptide: 1136+/-124 VS 402+/-92 pmol/l, p=0.0001; HDL: 0.97+/-0.05 VS 1.25+/-0.08 mmol/l, p=0.010; LDL: 2.3+/-0.2 VS 3.1+/-0.3 mmol/l, p=0.032) respectively.

Conclusions: Despite similar insulin resistance parameters and NAFLD, HIV+ patients had greater activity levels and leaner body mass. This suggests that HIV drugs, chronic infection, and dyslipidemia rather than lifestyle habits contribute to the first hit, IR, of the two-hit hypothesis on the pathogenesis of NAFLD. This study is funded by the Ontario HIV Treatment Network.

Contact Information: Saira Mohammed, Tel: 416-918-3235, Email: saira.mohammed@utoronto.ca

245

DIETARY INTAKE OF MALE SUBJECTS WITH HIV INFECTION: COMPARISON WITH THE DIETARY REFERENCE INTAKE

Elaheh Aghdassi [1]; Irving Salit [1]; Lillia Fung [2]; Johane Allard [1];
1-Department of Medicine, The University Health Network, The Toronto General Hospital, Toronto, Canada; 2-Department of Nutritional Sciences, The University of Toronto, Toronto, Canada;

Plain Language Summary: The purpose of this study was to compare the dietary intake of HIV-infected male patients with the recommendations and dietary reference intake set for young adults by World Health Organization. Sixty-six male subjects recorded their dietary intake for 7 days. Patients on HIV medications had a trend toward a higher energy intake that was accounted for by a higher saturated fat (bad fat) and monounsaturated fat intake. In those who had at least one abnormality either in their blood or body appearance, there was a trend toward a higher intake for energy, %dietary fat and vitamin E compared to those with no abnormalities. These results indicate that although the dietary intake of HIV+ subjects may be adequate to meet the energy needs, the macronutrient composition and intake of several of the micronutrients are inadequate in many patients. Dietary abnormalities are more prominent in those receiving ART and in those with metabolic abnormalities. Dietary counseling should part of patient care in the HIV+ population

Objectives: To compare the dietary intake of HIV-infected male patients with the recommendations and dietary reference intake set for young adults by World Health Organization.

Methods: Sixty-six HIV+ subjects in a tertiary hospital clinic were instructed to record their intake for a period of 7 days. The subjects had a mean age of 43.9 ± 1.1y, BMI: 24.6±0.4kg/m2, 57 were receiving antiretroviral therapy (ART) and 40 had at least one metabolic abnormality (blood lipid profile, glycemia and/or lipodystrophy).

Results: The mean energy intake was 2316.93±65.23 kcal/d that was adequate to meet the energy needs. Percentage of energy from fat, saturated fat, carbohydrates, and proteins were 33%, 11%, 48% and 19%, respectively. Average fiber intake was 21.57±1.08 g/d. Although these values were close to the recommendations, 60.6% of subjects had intake of fat exceeding the recommended 30% of intake, 53% had SFA intake exceeding the recommended 10%, 24.2% had protein intake below the recommended 15%, 57.6% had cholesterol intake exceeding the recommended intake of <300 mg/d and 71.2% had fiber intake below the minimum recommended intake of 25 g/d. Daily intakes of vitamins C, E, D and minerals calcium and zinc were suboptimal in 37.9%, 95.5%, 59.1%, 75.8% and 40.9% respectively. Patients on ART, had a trend toward a higher energy intake (ART: 2352±73 vs Naïve: 2094±107 kcal/d, p=0.06) that was accounted for by a higher saturated fat (ART: 28.3±1.5 vs Naïve: 22.4±2.5 g/d, p=0.06) and monounsaturated fat intake (ART: 30.2±1.4 vs Naïve:23.1±2.2, p=0.015). In those experiencing at least one metabolic abnormality there was a trend toward a higher intake for: energy (2391±90 vs 2202±87, p=0.14), %dietary fat (35±1 vs 29± 2, p=0.03) and vitamin E (9.18±0.76 vs 6.87±0.42 mg/d, p=0.011) compared to those with no abnormalities.

Conclusions: These results indicate that although the dietary intake of HIV+ subjects may be adequate to meet the energy needs, the macronutrient composition and intake of several of the micronutrients are inadequate in many patients. Dietary abnormalities are more prominent in those receiving ART and in those with metabolic abnormalities. Dietary counseling should be an integral part of patient care in the HIV+ population.

Contact Information: Ellie Aghdassi, Tel: 416-340-4413, Email: ellie.aghdassi@uhn.on.ca

246

HIV-MEDIATED DECREASE OF IL-12 P40 PRODUCTION MAY BE THE RESULT OF INHIBITION OF BOTH P38 AND JNK KINASE, LEADING TO DYSFUNCTIONAL PROMOTER ACTIVITY

Fiona Frappier [1,2]; Jonathan Angel [1,2];
1-Department of Microbiology and Immunology, University of Ottawa; 2-Molecular Medicine Program, Ottawa Health Research Institute;

Plain Language Summary: Infection with HIV is characterized by deficient cell-mediated immunity both in response to the virus itself as well as to secondary pathogens. The dysfunctional immune response following infection with HIV is multifaceted and is characterized primarily by a significant decrease in CD4 T cell numbers. In addition, the cell function of the remaining CD4 T cells is compromised due to an inadequate signaling environment. The signaling molecule IL-12 is critical for appropriate CD4 T cell function. Infection with HIV significantly decreases production of IL-12 and is thought to be an important contributing factor to the loss of cell-mediated immunity. Thus further understanding how IL-12 is produced and how HIV affects this production may lead to the identification for new therapy targets.

Objectives: IL-12 is critical for the generation of cellular immune responses, but the signaling pathways that lead to its production are not well characterized. In HIV infection, IL-12 synthesis is impaired and may contribute to the associated immunodeficiency. We have previously shown that HIV directly inhibits IL-12p40 gene transcription in monocytic cells and alters binding to the NFkB, AP-1, Sp-1 and Ets-2 sites of the p40 promoter and inhibits phosphorylation of the upstream MAP kinases (MAPK) signaling molecules p38 and JNK. Further delineating the mechanisms by which HIV inhibits IL-12 synthesis will provide important insight into the immunopathogenesis of HIV infection.

Methods: To investigate the role of the relevant MAPK, p40 was quantified using ELISA in LPS stimulated cells in the presence and absence of MAPK inhibitors (SB203580 for p38, PD98059 for MEK/ERK1/2 and SP600125 for JNK). Electromobility shift assays and luciferase assays were performed to determine whether MAPK inhibition altered p40 promoter activity.

Results: In uninfected monocytes, inhibition of p38 and JNK decreased LPS-induced p40 protein production; consistent with previous results, inhibition of ERK had no effect on p40 production. Both the p38 and the JNK inhibitors decreased AP-1 and Sp-1 binding activity while only the JNK inhibitor reduced NFkB binding.

Conclusions: Decreased production of IL-12 observed in HIV infected monocytes is a result of inhibition p38 and JNK MAPK signalling in response to LPS stimulation. Inhibiting MAPK function leads to dysfunctional nuclear factor binding to Sp-1, NF-kB and AP-1 as well as decreased p40 promoter activity and IL-12 production. Understanding the mechanism by which HIV alters this signaling pathway may lead to novel approaches in the treatment of HIV infection.

Contact Information: Fiona Frappier, Tel: 613-737-8160, Email: ffrappier@ohri.ca

247

IN SITU LOCALIZATION OF P-GLYCOPROTEIN (P-GP) IN HUMAN AND RAT BRAIN: RELEVANCE TO THE TREATMENT OF HIV-1 INFECTION IN THE BRAIN

Reina Bendayan [1]; Patrick Ronaldson [1]; Moise Bendayan [2];
1-Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada; 2-Department of Pathology and Cell Biology, Faculty of Medicine, University of Montreal, Montreal, PQ, Canada;

Plain Language Summary: Despite recent advances in HAART, treatment of HIV-1 infection of the brain remains difficult, possibly due to the fact that anti-HIV drugs do not enter the brain very well. The entry of anti-HIV drugs into the brain may be limited by drug export pumps [i.e., P-glycoprotein (P-gp)] at the interface between the brain and the blood [i.e., the blood-brain barrier (BBB)]. The goal of this research was to examine the location of P-gp at the BBB in order to understand how this export pump may limit the brain entry of anti-HIV drugs. We observed that P-gp is present in all brain cells at the BBB (i.e., endothelial cells, astrocytes, pericytes), suggesting that all of these cells may play a role in restricting the entry of anti-HIV drugs into the brain.

Objectives: HIV-1 encephalitis (HIVE), a chronic neurodegenerative condition, may result from HIV-1 infection of the central nervous system (CNS). Although highly active antiretroviral therapy (HAART) has been successful in reducing systemic viral load in HIV-1 seropositive patients, HIVE remains refractory to drug therapy, possibly due to the poor permeation of anti-HIV drugs into the brain. Accumulation of anti-HIV drugs such as the HIV-1 protease inhibitors in the CNS can be highly restricted by ATP-dependent, membrane-bound efflux transport proteins such as P-gp, at the blood-brain barrier (BBB). Previous studies have documented gene and protein expression of P-gp in brain microvessel endothelial cells. However, the exact localization of P-gp at the BBB remains controversial. While several studies have localized P-gp at the luminal membrane of brain microvessel endothelial cells (Beaulieu et al. 1997; Virgintino et al. 2002), others have identified the abluminal membrane as the primary location (Schlachetzki and Pardridge, 2003).

Methods: In the present study, we examined the cellular/subcellular distribution of P-gp, in situ, in rat and human brain tissue, using high-resolution quantitative immunogold cytochemistry at the electron microscope level. The P-gp monoclonal antibody C-219 was used in these studies. We also examined the functional activity of P-gp at the abluminal side of the BBB in cortical rat astrocytes using rhodamine 123, a fluorescent dye and well-established P-gp substrate.

Results: P-gp localized to both the luminal and abluminal membranes in human and rat capillary endothelial cells as well as in adjacent astrocytes and pericytes suggesting that all the cellular components of the BBB may participate in restricting brain permeability of xenobiotics. Furthermore, P-gp was distributed subcellularly along the nuclear envelope and in caveolae, cytoplasmic vesicles, Golgi complex and rough endoplasmic reticulum in endothelial cells. Rhodamine 123 accumulation was significantly enhanced (1.8-fold) in the presence of P-gp inhibitors (i.e., cyclosporine A, PSC833, GF120918), suggesting P-gp mediated efflux activity in astrocytes, a major component of the abluminal side of the BBB.

Conclusions: Our data provide evidence for the localization of P-gp throughout the entire BBB suggesting that all the cellular components of the barrier may participate in restricting brain permeability of pharmacological agents including anti-HIV drugs. Further work is needed to elucidate P-gp activity at subcellular sites.

Supported by CIHR and the OHTN. PTR is supported by an OHTN Studentship Award.

Contact Information: Patrick Ronaldson, Tel: 416-946-7523, Email: ptronaldson@sympatico.ca

248

DEVELOPMENT OF A RURAL ARV CLINIC WITHIN A NATIONAL TREATMENT PROGRAM IN BOTSWANA

Cheryl Arneson [1];
1-Contract Consultant, African Comprehensive HIV/AIDS Partnerships, Botswana;

Plain Language Summary: This presentation will outline the components of the Botswana National Program and specifically the development of one rural site. It will demonstrate the ability to provide medication and treatment despite the challenges of staffing, physical environment, bureaucracy and geography.

Objectives: Describe the successes and challenges to the development of a HIV treatment clinic in a rural African setting.

Methods: Clinic was developed using interactive teaching and mentoring from outside HIV experts over a six month period. Local staff were integral to the design, implementation and sustainability of each site.

Results: Program outcomes, ongoing challenges and updated statistics will be presented.

Conclusions: Despite many challenges, successful HIV ARV treatment programs can be developed in even the most rural settings. Ongoing assessment and government support will be necessary for maintaining quality and sustainability.

Contact Information: Cheryl Arneson, Tel: 416-320-4011, Email: Yippeenurse@hotmail.com

249

BARRIERS AND FACILITATORS TO ADHERENCE OF ANTIRETROVIRAL MEDICINE: A SYSTEMATIC REVIEW EXAMINING DEVELOPED AND DEVELOPING NATION PATIENTS-REPORTED ISSUES

Edward Mills [1,2]; Jean Nachega [3]; Sonal Singh [3]; Beth Rachlis [4]; Ping Wu [5]; Chris Gill [6]; Curtis Cooper [7];
1-Centre for International Human Rights Law, University of Oxford; 2-Dept. of Clinical Epidemiology & Biostatistics, McMaster University; 3-Bloomberg School of Public Health, Johns Hopkins University; 4-UBC Centre for Excellence in HIV/AIDS; 5-Dept. of Epidemiology, London School of Hygiene & Tropical Medicine; 6-Center for International Health and Development, Department of International Health, Boston University School of Public Health; 7-Division of Infectious Diseases, Dept. of Medicine, Ottawa University;

Plain Language Summary: Adherence to HAART is the greatest predictor of treatment success. We aimed to determine what barriers and concerns exist for patients in preventing good adherence. We additionally examined whether barriers reported by patients in developing nations were similar to patients in developed nations. We used an experimental methodology which we developed. We systematically reviewed the literature and identified all qualitative studies assessing patients reported barriers and facilitators. We then searched the literature for all surveys of patients asking these same questions. We included 37 qualitative studies and 47 surveys. Important barriers reported in both economic settings are listed below (scientific abstract). We found that important barriers to adherence are consistent across multiple settings and countries and that interventions are required to offset patient concerns so as to promote adherence.

Objectives: Adherence to Highly Active Antiretroviral Therapy medication is the greatest predictor of treatment success and mortality for patients who have access. We aimed to systematically review the literature to determine patients reported barriers and facilitators to adhering to antiretroviral therapy

Methods: We searched 8 electronic databases from inception to June 2005. We retrieved studies conducted in settings in both developed and developing nations. Both qualitative and quantitative studies were included. We independently, in duplicate, extracted information on barriers and facilitators reported in qualitative studies addressing adherence. We then examined all survey studies addressing barriers and facilitators to adherence. In order to place the findings of the qualitative studies in a generalizable context, we pooled the surveys.

Results: We included 37 qualitative studies and 47 studies using a quantitative methodology. Seventy-two studies (35 qualitative) were conducted in developed nations, while the remaining 12 (2 qualitative) were conducted in developing nations. Important barriers reported in both economic settings included: fear of disclosure; concomitant substance abuse; forgetfulness; suspicions of treatment; regimens that are too complicated; number of pills required; decreased quality of life; work and family responsibilities; falling asleep, and; access to medication. Important facilitators reported by patients in developed nation settings included: having a sense of self-worth; seeing positive effects of antiretrovirals; accepting their seropositivity; understanding the need for strict adherence, making use of reminder tools, and; having a simple regimen. In surveys presenting proportions, only 6 barriers occurred at statistically different proportions across the economic dividers: suspicions about treatment; concerns about unknown side effects, dislike of the taste, size and frequency of doses, uncertainty about treatment progress and feeling they were healthy enough were all more prevalent in developed nations. Concerns about financial pressures were more prevalent in developing nations.

Conclusions: We found that important barriers to adherence are consistent across multiple settings and countries. Clinicians should use this information to engage in open discussion with patients to promote adherence and identify barriers and facilitators within their own populations.

Contact Information: Edward Mills, Tel: 416-951-8530, Email: emills@ccnm.edu

250

RESOURCE ALLOCATION FOR HIV/AIDS: THE CASE OF KWADUKUZA

Arielle Lasry [1]; Gregory S. Zaric [2]; Michael W. Carter [1];
1-Healthcare Resource Modelling Lab, University of Toronto; 2-Richard Ivey School of Business, University of Western Ontario;

Plain Language Summary: The current HIV prevalence rate in the municipality of KwaDukuza, South Africa, hovers around 33% for a population of 170,000. We conducted 40 interviews to understand the manner in which funds are being allocated towards HIV/AIDS interventions in KwaDukuza. We establish the types of political and social constraints faced by decision-makers when allocating resources to HIV/AIDS programs. Given the tremendous gap between actual HIV funding and requirements, improved knowledge of resource allocation can minimize the serious and pervasive societal repercussions of the AIDS epidemic. Our research aims to suggest strategies for improving the HIV/AIDS resource allocation process in KwaDukuza.

Objectives: The case study aims to analyze the manner in which funds are currently being allocated towards HIV/AIDS interventions in KwaDukuza, document the logic underlying these decisions, and formulate guidelines for an improved resource allocation process.

Methods: The data collection for the case study was completed over a six-week period during the months of March and April 2005 in KwaDukuza. During this time, 40 key informant interviews were conducted. Following approval from the key informant, interviews were recorded. The total recording time was 26 hours and the interviews were transcribed. The interview questions were developed as open-ended as possible to allow respondents to fully communicate the complexity of their resource allocation problems and constraints. Content analysis software was used to categorize the information obtained from the interview transcriptions.

Results: Results suggest that there is no standard, formal procedure for allocating funds towards HIV/AIDS interventions. Resource allocation decisions in the context of HIV, are made in an environment subject to social, ethical and political pressures from numerous bodies including donor organizations, advocacy groups and public health officials.

Conclusions: Awareness of resource allocation practices and the factors that influence these practices can enhance the decision-making process and lead to a more effective distribution of HIV/AIDS funding. While these guidelines do not eliminate the social and political constraints under which funding decisions are made, they provide an opportunity understand their impact on health outcomes.

Contact Information: Arielle Lasry, Tel: 514-680-3903, Email: arielle@mie.utoronto.ca

251

WORLD HEALTH ORGANIZATION QUALITY-OF-LIFE ASSESSMENT OF HIV-POSITIVE ADULTS IN KIGALI, RWANDA

Robert Burgoyne [1,2]; Andrea Sharp [1]; Edmund Lambert [3]; Alex Hakuzimana [4];
1-Toronto General Hospital; 2-Department of Psychiatry, University of Toronto; 3-University Teaching Hospital of Kigali; 4-Treatment and Research AIDS Centre (TRAC) HIV Clinic of Kigali, Rwanda;

Plain Language Summary: A quality-of-life measure was completed by adults living with HIV and a comparison group of HIV-negative adults in Rwanda. Quality-of-life as rated by Rwandan PHA was mostly similar to that of the HIV-negative Rwandans and other studies of PHA, but poorer in some ways compared to the non-ill general global population. The measure was partially sensitive to illness factors.

Objectives: Assess quality-of-life as perceived by adults living with HIV in Kigali, Rwanda using the World Health Organization's Quality of Life Brief-Form module (WHOQOL-BREF), compare results to global general population norms and previous HIV-related studies in other parts of the world, and assess the scale's ability to detect differences according to health status.

Methods: The WHOQOL-BREF was administered to 250 HIV-positive adults and 50 HIV-negative comparison controls attending the TRAC HIV Clinic of Kigali, Rwanda. Mean ratings of the four domains: Physical, Psychological, Social and Environmental were compared to norms as well as the results of two HIV-related research reports from Taiwan and Italy. Discriminant validity was also evaluated: independent samples t-tests to assess differences according to HIV serostatus, self-reported health status and CD4 cell count; one-way ANOVA to assess differences across WHO HIV stage.

Results: Environmental ratings were significantly lower for both the HIV+ and HIV- subgroups compared to norms for well populations and other HIV populations (Italian, Taiwanese), while Psychological domain ratings appeared similar to or better than the latter comparison groups. The HIV+ subgroup Physical and Social domain ratings were lower compared to well population norms but consistent with the Italian and Taiwanese comparison groups. Ratings were significantly poorer for the HIV+ compared to HIV- adult Rwandans on the Physical domain ($p = .00$). For the HIV+ overall those who perceived themselves to be ill had poorer ratings in the Psychological ($p = .00$) and Social ($p = .01$) domains compared to those perceiving themselves as being healthy. For those with CD4 count ≤ 200 cells/μL, Physical domain ratings were poorer ($p = .00$) while Social domain ratings were inexplicably better ($p = .01$; but moderate effect size of 0.5) compared to those with CD4 count > 200. The Physical and Environmental domains were sensitive to disease stage differences.

Conclusions: The WHOQOL-BREF instrument was inconsistent in detecting differences in health-status variables among Rwandan adults living with HIV. The Environmental domain may reflect locale-specific factors other than issues related to HIV.

Contact Information: Robert Burgoyne, Tel: 416-340-4800 x8609, Email: bob.burgoyne@uhn.on.ca

Health Services And Access To Care

252

ACCESS TO DENTAL HYGIENE SERVICES FOR HIV PATIENTS IN CANADA

Cecilia Aragon [1]; Gillian McCarthy [1,2]; Larry Stitt [3];
1-Dentistry, Schulich School of Medicine and Dentistry; 2-Epidemiology and Biostatistics, Schulich School of Medicine and Dentistry; 3-Epidemiology and Biostatistics, Schulich School of Medicine and Dentistry;

Plain Language Summary: It has been found that dentists, surgeons, and nurses can be reluctant to treat patients with HIV. Hygienists have a major role in the provision of oral care for patients with HIV who are vulnerable to severe periodontal disease. However, there are a few comprehensive reports of dental hygienists' attitudes related to the provision of treatment for people living with HIV. This study investigated access to dental hygiene services for patients living with HIV in Canada.

Objectives: This study investigated access to dental hygiene services for patients living with HIV in Canada.

Methods: A survey was mailed to a stratified random sample of dental hygienists licensed by their Provincial Colleges in Canada (N=5,900). A modification of Dillman's guidelines for administration of mailed surveys was used with two additional mailings to non-respondents. Frequencies, proportions and means were calculated for all response variables. Comparisons between groups were done using Pearson's chi square analyses. Multiple logistic regression analyses were used to identify the best predictors of willingness to treat and refusal to treat patients with HIV. Data were analyzed using SPSS/PC+.

Results: The response rate was 56%. Nine percent of respondents reported that they would refuse to treat patient infected with HIV. Multiple logistic regression analyses indicated that the best predictor of refusal to treat was lack of ethical responsibility to provide treatment for patients living with HIV.
Ninety-one percent of hygienist participating in this study reported willingness to treat patients infected with HIV. The best predictor of willingness to treat was ethical responsibility.

Conclusions: The percentage of dental hygienists who reported refusal to treat patients with HIV was lower than the proportion of dentists (16%) who reported refusal to treat in an earlier national study (n=6,440). In the study of dentists, lack of ethical responsibility was also the best predictor of refusal to treat HIV patients. These findings confirm the need to promote professional ethics in the undergraduate and professional development dental programs. It is also important to ensure that more compassionate and ethical applicants to dental and dental hygiene programs are selected for training.

Contact Information: Cecilia Aragon, Tel: 519-661-2111 x81539, Email: cecilia.aragon@schulich.uwo.ca

253

AN ENVIRONMENTAL SCAN OF CANADIAN AND INTERNATIONAL SUPPORT POLICIES AND PROGRAMS FOR PEOPLE WITH HIV AND OTHER EPISODIC DISABILITIES

Eileen McKee [1];
1-Canadian Working Group on HIV and Rehabilitation;

Plain Language Summary: The unpredictable nature of HIV and other episodic disabilities, such as multiple sclerosis, mental illness and cancer, presents challenges to active labour force participation, stable income and social inclusion as fluctuations occur in a person's ability to participate. The Canadian Working Group on HIV and Rehabilitation (CWGHR) undertook an international review of workplace and income support policies and programs, both public and private, in order to identify the disincentives for people with HIV and other episodic disabilities and address the disincentives to labour force participation, while ensuring income and benefit supports when not able to work.

Objectives: The objective was to identify effective models, policies, programs that facilitate the optimal labour force engagement, as well as provide disability income and other support when not able to work, for people with HIV and other episodic disabilities. The recommended models will be costed and will provide the basis for creating workable models that allow for the flexibility for people with HIV and other episodic disabilities to participate in the labour force. With multi-sector engagement and collaboration, these models will then be implemented and evaluated at several pilot sites across Canada.

Methods: A multi-sector national advisory committee developed key guiding principles for policies and programs to be recommended. The researchers engaged in key informant interviews, developed an annotated bibliography and analyzed Canadian, U.S., British, European and Australian policy that then resulted in comprehensive recommendations for the Canadian context.

Results: Many of the criteria for effective integration of labour force participation and income support were found in German and Dutch models. Common themes of effective models included: multi-sector coordination; flexibility to accommodate episodic participation in the labour force; income and benefit support when disability did not allow for labour force participation. The final report includes recommendations for incorporating aspects of these models into the Canadian market system. These suggestions are focused on both the private and public sector and on potential directions for the work plans that will be created to better enable persons with episodic disabilities to function in the workforce in a supportive environment.

Conclusions: Further research is needed to determine the effectiveness of models, or components thereof, that are effective in other jurisdictions when implemented in the Canadian context.

Contact Information: Eileen McKee, Tel: 416-513-0440 x234, Email: emckee@hivandrehab.ca

254

ENHANCING PARTNER NOTIFICATION PROCEDURES: THE UTILITY OF SOCIAL NETWORK ANALYSIS IN STI AND HIV PREVENTION

Emily Meadows [1]; John Wylie [2,3]; Ann Jolly [1,4];
1-University of Ottawa, Ottawa, ON; 2-Cadham Provincial Laboratory, Manitoba Health, Winnipeg, MB; 3-University of Manitoba, Winnipeg, MB; 4-Division of Modeling and Projections, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, Ottawa, ON;

Plain Language Summary: In Canada, rates of sexually transmitted infections (STIs) have increased considerably over the past decade. Although successful control programs have been implemented, the observed increase in rates suggests that STI prevention programs are not targeting individuals most at risk of acquiring a STI. As such, recent studies have focused on characterizing these high-risk populations to provide the basis for the development of targeted programs. These results have important implications for STI prevention, including HIV. Specifically, results of this study indicate the utility of using enhanced control programs combined with an emerging technique to examine these populations. This approach to disease prevention may be useful in other regions.

Objectives: Since 1997, Canada has witnessed an upsurge in the incidence of bacterial sexually transmitted infections (STIs). This increase in STI incidence suggests general population level control programs may not be reaching the section of the population responsible for the spread of STIs - core groups. Core groups are highly interconnected groups of individuals with rapid partner change and infection. Social network analysis (SNA) can be used to characterize core groups. SNA is a technique used to analyze a group of individuals connected by relations with one another. The objective of this study, unique in its scope, was to examine the transmission of STIs within core groups in Manitoba using both traditional epidemiology and SNA.

Methods: Routine partner notification data was collected from 8,476 individuals diagnosed with, or exposed to a STI. This data was supplemented with more detailed information on symptoms, sexual behaviours and proxy information on sexual contacts collected from 857 individuals. Groups of individuals connected directly or indirectly through sexual relationships were identified, and their profiles described.

Results: A total of 2,508 distinct groups were identified, ranging in size from 2 to 33 individuals. There were 1,192 cases naming no partners. Sixty percent of the groups consisted of two members only, 23% of three members, 11%, 5% and 1% of 4-5, 6-10 and greater than 11 members, respectively. Larger groups (size ≥ 15) contained more individuals diagnosed with gonorrhea and syphilis, and contained more repeat cases and individuals with repeat nominations. Further analysis revealed that members were involved in the sex trade and drug use. Unique to this dataset, was the identification of same sex partnerships, 31% of larger groups exhibiting this feature. Three different types of groups were identified, containing individuals which differed demographically and clinically.

Conclusions: At a time when public health funding is scarce, a greater understanding of disease transmission patterns within core groups will clearly aid in the development of targeted education and prevention programs for all STIs including HIV. These results indicate that the use of enhanced partner notification procedures combined with social analytic techniques is warranted. Furthermore, they provide the initial characterization needed for the development of these programs.

Contact Information: Emily Meadows, Tel: 613-562-5800 x871, Email: emeadows@uottawa.ca

255

A MODEL TO ASSESS COMMUNITY CAPACITY TO DELIVER INTEGRATED PREVENTION, CARE, TREATMENT INFORMATION AND SUPPORT SERVICES

Geoff Lawrence [1,2]; **Michael Bailey** [1]; Darien Taylor [1];
1-Canadian AIDS Treatment Information Exchange, Toronto, Canada; 2-Ontario Institute for Studies in Education, Toronto, Canada;

Plain Language Summary: In an effort to develop an integrated model of HIV/AIDS services that have traditionally isolated prevention, support and treatment, a national project involving the Canadian AIDS Treatment Information Exchange (CATIE) and seven pilot communities across Canada was initiated.

Objectives: 1) To develop a model to assess organizational and community capacity to deliver integrated services. 2) To define and implement an HIV information training program aimed to increase treatment information capacity, specific to each site. 3) To increase participation of other community organizations throughout Canada in an integrated approach to HIV prevention, care, treatment and support.

Methods: Through national consultations with pilot communities and key experts in community-based HIV/AIDS treatment information, a consensus-driven, participatory tool for assessing community capacities to deliver integrated services was developed. This tool was pilot tested in two communities, refined, and delivered in the five remaining pilot communities. An HIV treatment information training based on needs derived from the HIV treatment information needs and capacity assessment is in development. Sites will select staff, volunteers and representatives from community organizations to attend workshops on HIV treatment-related topics specific to their community. The train-the-trainer format allows for continuous peer-driven HIV 101 training within organizations.

Results: The assessment tool developed to evaluate community capacity to deliver integrated HIV/AIDS services included several dimensions: organizational infrastructure/culture, leadership, service coordination and collaboration, knowledge, skills and required information. The diversity among the pilot communities required the tool to be flexible. This tool will be used to develop customized training and organizational development models in each community and later becoming a portable model for national use. It has assisted in defining core treatment information modules to be taught using a train-the-trainer teaching approach. Findings from these trainings will serve as a formative evaluation for ongoing national HIV treatment information trainings. The trainings have also defined community HIV treatment information areas to be developed in collaboration with CATIE.

Conclusions: While assessment of community capacity remains poorly defined and difficult to study, this project has resulted in a specialized vision of community capacities to deliver integrated HIV treatment programs. This participatory research process developed a transferable community capacity assessment tool to be used to define capacity building needs for developing integrated HIV/AIDS services.
Using a train-the-trainer model, the HIV treatment information trainings address the challenge of building and sustaining organizational treatment information capacity, given staff and volunteer turnover.

Contact Information: Darien Taylor, Tel: 416-203-7122 x250, Email: dtaylor@catie.ca

256

TESTING PATTERNS AND DEMOGRAPHIC DATA FROM THE FIRST HIV-RELATED SOCIAL EPIDEMIOLOGICAL STUDY IN TORONTO'S EAST AFRICAN COMMUNITIES

Kimberly Gray [1]; Liviana Calzavara [1,2]; Esther Tharao [3]; Nancy Ramuscak [1]; Ann Burchell [1]; Ted Myers [1,2]; Robert Remis [1,2]; Carol Swantee [4]; Catherine Chalin [2];
1-HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto; 2-Department of Public Health Sciences, University of Toronto; 3-Women's Health in Women's Hands; 4-HIV Laboratory, Ontario Ministry of Health and Long-Term Care;

Plain Language Summary: EAST is the first epidemiological study of the prevalence and correlates of HIV-related attitudes and behaviours in Ontario of immigrants from countries where HIV is endemic. This analysis of testing patterns indicates that the majority of participants have been tested for HIV, reflecting Canada's current immigration requirements.

Objectives: To present preliminary data from the East African Health Study in Toronto (EAST) including demographics and HIV testing patterns in Ethiopian, Kenyan, Somali, Tanazian and Ugandan communities.

Methods: 174 East Africans (of 500) have been interviewed for this cross-sectional face-to-face survey. The survey is administered by an interviewer chosen by the participant (own community or other) and covers a range of topics, including immigration history, general health issues, access and uptake of health care, HIV risk behaviours, and HIV knowledge, beliefs and attitudes. Prevalence data will be analysed when the study is complete.

Results: 17% of participants were Ethiopian, 26% Kenyan, 20% Somali, 3% Tanzanian, and 34% Ugandan. 68% were Christian and 29% Muslim. 40% were married and 55% have had children. 90% of participants reported working in the past 12 months and 57% reported a personal income < $30,000. 64% have completed post-secondary education, the mean age was 35, and 96% were born in East Africa, although only 69% were living there before Canada. 36% arrived in Canada as landed residents and 34% as refugee applicants. 44% came to Canada since 2000 and 46% have visited Sub-Saharan Africa since their arrival. 79% reported having been tested for HIV, with an average number of lifetime tests at 2.62 and 69% having been tested for immigration. 34% of testers who did not test for immigration (n=29) tested because they were prompted by another person or health professional. 79% who had never tested (n=29) stated this was because they felt healthy. 30% of participants did not agree that results of an HIV test would be kept confidential in Canada and 38% thought you had to give your name when testing.

Conclusions: This study reflects Canada's changing immigration patterns with almost half of participants coming to Canada since 2000. The majority have been tested for HIV, which is not surprising with Canada's policy of mandatory HIV testing for residency applicants, although most have had multiple tests. A third of the participants do not believe that testing can be anonymous or results would be confidential, suggesting a need for education and advocacy.

Contact Information: Kimberly Gray, Tel: 416-946-7026, Email: kimberly.gray@utoronto.ca

257

THE COMPARATIVE EFFECTIVENESS OF CASE MANAGEMENT AS AN APPROACH TO SUPPORT SERVICES AND PREVENTION FOR PEOPLE LIVING WITH HIV/AIDS (PHAS)

Janet Caswell [1]; **Winston Husbands** [1,2]; **Gina Browne** [2]; Donna Braybrook [1]; Kristy Buck [1]; Jacqueline Roberts [2]; Amiram Gafni [2];
1-AIDS Committee of Toronto; 2-Community Linked Evaluation AIDS Resource (CLEAR) Unit;

Plain Language Summary: This study seeks to determine which PHAs are likely to benefit most from working with a case manager in an AIDS service organization versus accessing support services entirely on their own initiative. We compared two groups of PHAs divided between those working with a case manager at the AIDS Committee of Toronto and those accessing services on their own at the same agency.

Objectives: This randomized trial of 78 people living with HIV/AIDS (PHAs) assessed who, with what characteristics and circumstances, benefits most from which approach to the provision of support services at an AIDS service organization (ASO) - case management compared to usual self-directed care.

Methods: Participants were prognostically stratified on their homelessness (yes/no) and being a youth (less than 30 years old, 30 years and older). PHAs from each strata were randomized to receive either self-directed use of ACT support services and any external services or self-directed care plus strengths-based case management for a 6-month period. Various instruments were used to measure mediating variables (social support, depression, coping ability and adherence to medical regimes). Outcome measures (risk behaviours, quality of life and health and social service utilization) were also assessed. Mediating variables and outcome measures were completed both at baseline as well as at the 6 month follow-up.

Results: Case management compared to usual self-directed care markedly improved the physical, social, and mental health function of female PHAs and PHAs who were very depressed at baseline. Case management was also associated with a reduction in risk behaviours among PHAs.

Conclusions: Case management for PHAs can be an effective way to increase access to services and improve the quality of life for women living with HIV and very depressed PHAs, and also to reinforce HIV prevention efforts by reducing risk-taking behaviours among PHAs. ASOs should be compensated for the savings their case management services create within the provision of services to PHAs and within the entire health care system. Case management should become a priority for policy makers and government funders when considering issues that will affect the delivery of social and health-related services to communities affected by HIV.

Contact Information: Winston Husbands, Tel: 416-340-8484, Email: whusbands@actoronto.org

Prevention Issues In The MSM Community

258

UNPROTECTED SEX AMONG MSM WHO DO NOT PARTICIPATE IN THE BAREBACK SCENE

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

Plain Language Summary: This study reports on the characteristics and beliefs of MSM who have unprotected anal sex with casual partners but do not report participating in the bareback scene or accessing bareback websites.

Objectives: To identify circuits, networks, and sites of vulnerability to HIV transmission among MSM as a foundation for developing specific, culturally-appropriate messaging that speaks to the needs of diverse sets of MSM.

Methods: Survey of 947 men attending Toronto Pride 2005.

Results: Half of the study participants who report having unprotected anal sex (UAI) with a casual male partner during the last six months do not report being part of the bareback scene and/or cruising bareback websites. Unlike men in the bareback scene, they are not associated with particular venues or circuits in the gay community. Unlike men not reporting UAI, they more often agree that: if they lose an erection, they will have sex without a condom, alcohol/drugs help them connect with other guys and make sex hotter, they like the emotional rush of pushing their limits, topping a guy makes them feel masculine and powerful, they like sex without emotional entanglements. They are less likely to report liking mutual give and take in sex. Like barebackers, they respect the wish of a partners to have sex without a condom, perceive that a lot of guys don't want to use condoms, and are more likely to be depressed about not having a relationship and give in to having sex without a condom.

Conclusions: MSM who have unprotected anal sex with casual partners but do not report participating in the bareback scene show a distinct profile when compared to those in the bareback scene or to those who consistently use condoms. Effective prevention will require making headway on the problems of losing an erection with condom use, depression, and substance use. Other indicators suggest there may be a process whereby this set of men may be more likely to transition toward the bareback scene.

Contact Information: Barry Adam, Tel: 519-253-3000 x3497, Email: adam@uwindsor.ca

259

TALK ABOUT DISINHIBITION: MANAGING ACCOUNTABILITY FOR UNSAFE SEX

Jeffrey P. Aguinaldo [1,2]; Ted Myers [1,2];
1-Department of Public Health Sciences, University of Toronto; 2-HIV Social, Behavioural, and Epidemiological Studies, University of Toronto;

Plain Language Summary: As an explanation for the apparent increase in risk behaviours and HIV infections among gay men, the (dis)inhibitory effects of drugs and alcohol have become a popular discourse among health researchers, as is evidenced by the abundance of HIV prevention studies devoted to demonstrating the relationship between substance use and unsafe sex. In the current research, we explore and develop the idea of 'disinhibition theory' as used by men talking about their sexual health practices. We suggest that 'disinhibition theory' should be viewed not simply as a resource of use to public health researchers to explain the health behaviours of gay men, but also as a resource of use to ordinary social members. Specifically, we show how talk about the widespread phenomenon of disinhibition caused by substance use is used by men to construct safer sex practices while using drugs or alcohol as normatively difficult such that they cannot be held accountable for their own previous difficulties in implementing condom use. Implications for research and HIV prevention in the field of gay men's public health will be discussed.

Objectives: To explore how men who have sex men talk about and manage accountability for previous experiences of unsafe sex practices.

Methods: Taking a social constructionist approach to language, we do not lay claims to the men's experiences or events presumed to lie beyond their talk. Instead, we are interested in the ways that self-reports are interactively managed and discursively produced. This approach emphasizes talk-in-interaction and aims to identify the social functions of discourse within its local interactional context. To accomplish this, we employ conceptual and methodological tools of conversation and discursive analysis to explore talk derived from 27 in-depth qualitative interviews from men who have sex with men. We focus on men's self-reports that public health researchers would likely take as evidence for 'disinhibition theory'. While traditional approaches to data analysis would consider this talk as evidence for the inebriating effects of substance use on unsafe sex, our analytic approach considers instead their talk as an interactional resource.

Results: Through our analysis, we demonstrate how the men can rationalize and justify previous instances of unsafe sex practices through talk about disinhibition.

Conclusions: The implications for public health and HIV prevention will be discussed in relation to the role in which HIV research is complicit in the men's discourse practices.

Contact Information: Jeffrey Aguinaldo, Tel: 416-978-1200, Email: jeffrey.aguinaldo@utoronto.ca

260

STRESS AS A RISK FACTOR FOR HIV INFECTION AMONG GAY AND BISEXUAL MEN

Ann Burchell [1]; Liviana Calzavara [1,2]; Sandra Gardner [1]; Robert Remis [1,2]; Ted Myers [1,2]; Wendy Medved [1]; Paul Corey [2]; Janet Raboud [2]; Carol Swantee [3]; & the Polaris Study Team [1];
1-HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto; 2-Department of Public Health Sciences, University of Toronto; 3-HIV Laboratory, Ontario Ministry of Health and Long-Term Care;

Plain Language Summary: Stress may lead to a greater risk of becoming infected with HIV among gay and bisexual men. Men who experienced five or more stressful life events were over three times more likely be infected than men who experienced none. In particular, HIV risk was related to problems with drugs or alcohol, or financial- or security-related stresses. The results were based on interviews with 124 men who were recently infected and 234 men who were HIV-negative.

Objectives: To determine whether stress raises the risk of HIV infection through its intermediate effect on sexual risk behaviour among gay- and bisexually-identified men in Ontario.

Methods: Participants in the Polaris HIV Seroconversion Study were recruited through Ontario's HIV diagnostic laboratory, physicians and community organizations. Recent seroconverters (cases) were documented using HIV test results. Cases were asked about stressful life events and behaviour during the period of infection (median 6, range 3-27 months) and for controls during an equivalent time period. Data from gay- and bisexually-identified men (124 cases and 234 controls) enrolled as of December 2004 were analysed. Multiple logistic regression was used to estimate odds ratios and 95% confidence intervals (CI).

Results: HIV-positive men reported more stressful life events in the time period of infection (median=3) compared to HIV-negative men (median=2, p=0.0004, Wilcoxon rank sum test). The odds of HIV infection was 3.14 times greater among men who reported five or more stressful events compared to men who reported none (95%CI 1.64, 5.98). Financial- or security-related events resulted in increased risk for infection among men aged <30 (OR=4.42, 95%CI 1.53, 12.7), but a similar association was not observed among older men. Problems due to alcohol or drugs resulted in a two-fold increase in HIV infection risk (OR=2.02, 95%CI 1.20, 3.42). Adjustment for receptive anal sex, the proposed intermediate variable in the causal pathway between stress and infection, resulted in decreased odds ratios, providing evidence of mediation.

Conclusions: Stressful life events were related to an increased risk of HIV infection, mediated (although not entirely) by receptive anal sex behaviours. That the effect of financially-stressful events on risk behaviour, and subsequently HIV infection, was predominantly among men under the age of 30, suggests that younger men may use sexual behaviour as a coping mechanism.

Contact Information: Ann Burchell, Tel: 613-526-1425, Email: ann.burchell@utoronto.ca

Community-Based Research: Shaping New Agendas

261

A NEEDS ASSESSMENT ANALYSIS: E-LEARNING TOOLS FOR HIV/AIDS RELATED EDUCATION FOR THE CANADIAN AIDS TREATMENT INFORMATION EXCHANGE

Mary Lamon [1]; **Timothy Rogers** [2];
1-Institute for Knowledge Innovation and Technology, Ontario Institute for Studies in Education; 2-Canadian AIDS Treatment Information Exchange (CATIE);

Plain Language Summary: The Canadian AIDS Treatment Information Exchange (CATIE) provides information on HIV/AIDS treatments for people living with HIV/AIDS (PHAs), their caregivers, AIDS service organizations (ASOs) and health professionals throughout Canada. This information is currently disseminated via CATIE's website (www.catie.ca), in one-to-one phone and email exchanges, through workshops, and in printed publications. Increasingly the Internet is becoming a vital source of information and the trend towards greater use of information technology in health care is increasing. The Web provides many features appealing to different individuals; convenience, anonymity, networking, and access to reliable and up to date treatment information, and recently e-learning. E-learning, the use of a variety of information and communications technologies, has tremendous potential for helping CATIE's audiences learn about treatment options, side effects, and behavioural changes promoting a healthy lifestyle. This paper reports a needs analysis on e-learning possibilities and approaches for CATIE.

Objectives: To understand the needs and readiness in Canada for using e-learning to help PHAs and their caregivers learn about HIV/AIDS treatment.

Methods: The research methodology consisted of a review of the literature on e-learning in health care, a search of the Web to assess forms of e-learning in health care, design and implementation of a print and Web-based survey of people who access CATIE's services, and surveys of CATIE staff/volunteers. It is important to note an Internet-based survey has a bias towards those individuals who already have access to and are comfortable with Internet technologies. Likewise, we assume that individuals with an interest in e-learning were more likely to notice and complete the survey.

Results: Results for both those accessing CATIE's services and for CATIE staff/volunteers were remarkably similar although for somewhat different reasons. In terms of preferred types of e-learning, un-moderated or moderated chat rooms, discussion forums or Weblogs did not appeal to either group. In part, this was because neither group was very experienced with these forms of interactions. Both groups preferred online libraries, such as CATIE already provides, and web-based tutorials with feedback tailored to individual learning needs. CATIE clients were more concerned about privacy, confidentiality and anonymity; but CATIE staff members were concerned about needs for in-staff training as well as providing learning opportunities for other ASOs.

Conclusions: There is a great deal of interest and enthusiasm in Canada for e-learning as a means to help PHAs and their caregivers learn about treatment. Some types of e-learning appear to be better suited than others for these audiences. Results from this study will be used to develop an overall strategy for e-learning for CATIE.

Contact Information: Tim Rogers, Tel: 416-203-7122, Email: trogers@catie.ca

262

PROGRAM EVALUATION AND STUDY OF THE IMPACT OF SERVICES PROVIDED BY THE ONTARIO ORGANIZATIONAL DEVELOPMENT PROGRAM

Judith Tresidder [1]; Joan Crook [2]; Gina Browne [2];
1- The Ontario Organizational Development Program; 2- Community Linked Evaluation AIDS Resource (CLEAR) Unit;

Plain Language Summary: The Ontario Organizational Development Program (OODP) was established as a funder driven program in 1995 by the Ministry of Health and Long-Term Care (MOHLTC) AIDS Bureau, and the Public Health Agency of Canada, AIDS Community Action Program (ACAP), Ontario region in response to the request of HIV/AIDS organizations for long term organizational development resources. The objective of this study was to evaluate the impact of the OODP services provided to AIDS Service Organizations (ASOs) and to examine how OODP was fulfilling its goals. The OODP is meeting its goals and is successful in providing "free" services that help ASOs better manage their organizational challenges.

Objectives: The primary study objectives were to ascertain if OODP was meeting the organizational development requirements of ASOs and to what degree OODP was fulfilling its goals. An additional objective was to determine OODP's impact on ASOs' organizational capacity. Possible future directions for OODP and other considerations were also queried.

Methods: Forty-one structured telephone interviews were conducted with ASO key informants (2000-2003), funders (past and present), consultants (2000-2003), and the Program Administrator. Additionally, other methods included data collected and analyzed from on-site evaluations, program evaluations, annual reports from 2000-2003, and request-for-assistance forms (1996-2003).

Results: The Ontario Organizational Development Program is meeting its goals and is successful (i) in providing "free" services; (ii) helping ASOs better manage their organizational challenges; (iii) providing facilitation services; and (iv) providing validation/perspective for the individual experiences of the ASO. The OODP was considered flexible, inclusive of each participant and their ideas, responsive to ASO needs, and supportive of ASO self-determination.

Conclusions: It was recommended that OODP continue to enhance their communications strategy and to build upon links with provincial programs. Several lines of inquiry for additional services and future directions were posed to OODP for their consideration.

Contact Information: Judith Tresidder, Tel: 519-822-0887, Email: judith.tresidder@sympatico.ca

263

HIV/AIDS TREATMENT INFORMATION: WHO DOES WHAT AND HOW? A SURVEY OF AIDS SERVICE ORGANIZATIONS ACROSS CANADA

Laurie Edmiston [1]; Cole Stanley [1]; Timothy Rogers [1];
1-Canadian AIDS Treatment Information Exchange (CATIE);

Plain Language Summary: HIV/AIDS treatment information (TI) is becoming increasingly complex and challenging for people living with HIV/AIDS (PHAs) and their community intermediaries to comprehend and convey. A previous environmental scan indicated that most PHAs prefer to receive their TI from local sources, highlighting the important role of the Canadian AIDS Treatment Information Exchange (CATIE) as a national resource for local ASOs. Working in partnership with the Treatment Information Network, CATIE conducted a national survey to create a comprehensive picture of ASO TI services, the treatment-related materials they use and the barriers they face in providing TI. The results will help focus efforts to address gaps and build capacities of local ASOs to enhance integration of TI into their services.

Objectives: To investigate the extent to which the network of local ASOs is developing and/or disseminating treatment information (TI) to PHAs across Canada, either as direct service or through integration into other services.

Methods: A structured telephone interview was conducted with staff from ASOs across Canada to characterize their treatment information (TI) services and treatment-related materials. The interview also probed gaps and barriers to providing TI to PHAs locally.

Results: 107 ASOs across Canada were contacted and 79 (74%) were successfully interviewed. In this representative sample: Most ASOs (85%) provide services that involve HIV treatment information (TI), ranging from a resource centre, to staff who discuss treatment with clients, to referrals; 75% of ASOs providing TI consider this an important part of their mandate. Yet only 13% have staff dedicated to TI; 91% of ASOs see CATIE as a useful resource for their staff, regardless of how much TI they provide; Nearly 200 different print resources on HIV treatment are currently used by ASOs. We have characterized them by topic, target audience, and literacy level, among other descriptors for analysis of gaps.

Conclusions: Most ASOs agree that treatment information (TI) is an important service, but are unable to dedicate staff or volunteers to its provision. Integrating TI into other services, they cite CATIE as an important resource for staff and clients. Gaps in TI include materials for positive youth and low literacy resources. Many ASOs perceive gaps in TI materials because they are unaware of the breadth of materials available, indicating the need for improved coordination and dissemination of TI materials.

Contact Information: Tim Rogers, Tel: 416-203-7122, Email: trogers@catie.ca

264

THE ACCESS PROJECT: MEETING PEOPLE WHERE THEY ARE

Ron Lirett [2]; Vivia McCalla [1]; Lisa Shishis [1]; Karina Wulf [1];
1-Casey House Hospice; 2-Dorothy Ley Hospice;

Plain Language Summary: Barriers to accessing HIV/AIDS services for underserved populations were explored. These included: 1- lack of services for women 2- fear of disclosure 3- location of services 4- lack of cultural competency 5- language barriers 6- lack of childcare services 7- lack of knowledge of services 8- lack of holistic approach 9- lack of Harm Reduction approach 10- power imbalance 11- multiple levels of discrimination experienced by PHAs based on gender, ethnocultural affiliation, sexual orientation, substance use, and socioeconomic status.

Objectives: -To assess barriers and gaps in services for women, children, aboriginal peoples, the underhoused, and people from countries where HIV is endemic

Methods: Interviews and focus groups with people having HIV/AIDS from target populations (listed above) along with service providers

Results: 3 Developments: 1-development of a partnership between Sherbourne Health Centre (formerly Wellesly HC), the Toronto People with AIDS Foundation and Casey House to provide Casey House nurses with HIV/AIDS expertise on the Sherbourne Health Bus in front of TPWAF 2-development of Healthy Voices Nursing Clinic at Voices of Positive Women in partnership with VOPW 3- development of a Childcare Program in partnership with the Theresa Group, VOPW, Philip Aziz, TPWAF, AIDS Committee of Toronto, Black Cap, Women's Health in Women's Hands

Conclusions: The services in all 3 areas have been enhanced (#s of women, children & others served & how they have been impacted by services). The underhoused may be serviced through the Sherbourne Health Bus. Health Promotion and Harm Reduction approaches underpin an effective response to PHAs on the Health Bus and through the Healthy Voices Nursing Clinic. Educational opportunities and client support for PHAs have been accessed through the Healthy VOices Nursing Clinic both in person and via telelink.

Contact Information: Colleen Kearney, Tel: 416-962-4040 x23, Email: ckearney@caseyhouse.on.ca

265

MEASURING INTEGRATION: COMMUNITY PLANNING INITIATIVE EVALUATION

Jacqueline Roberts [1]; Gina Browne [1]; Joan Crook [1]; Robin Weir [1]; Carolyn Byrne [1]; Amiram Gafni [1]; Dale Guenter [1];
1- Community Linked Evaluation AIDS Resource (CLEAR) Unit;

Plain Language Summary: As part of the AIDS Bureau's community planning initiative, the CLEAR Unit is evaluating the impact of this process on agency collaboration, partnerships, and service integration and the organizational capacity of Community-Based AIDS Organizations. The integration of the agencies participating is evaluated from the agencies' points of view in the different regions of Ontario.

Objectives: The purpose of the evaluation is to assess each agency's self perceived current and expected level of collaboration and/or service integration among agencies in order to promote dialogue and discussion in the Community Planning Group and to measure change in agency working relationships/collaboration or service integration during the community planning initiative.

Methods: This is a before and after, repeated measures design using an integration measure developed by the investigators in the CLEAR Unit. This integration measure was developed to quantify: i) Extent of integration, which permits identification of services and the number of services within a number of programs working with other services; ii) Scope of integration, which identifies for each service, the number of services that have some sort of awareness or link with others; and iii) Depth of integration, which indicates the depth of the links among all services, and each service along a continuum of involvement, which includes non-awareness, awareness, communication, cooperation and collaboration. Representatives from each service agency in the variety of sectors as identified by the local community-planning group, are asked to rate their level of integration with each of the other services on the list. Agencies identified by the local planner were asked: 'To what extent "are you" (your service) involved with the following services?' and 'To what extent "should you" (your service) be involved with the following services?'

Results: Results can be graphed, showing current and expected levels of integration for each individual agency and the total integration for the group of agencies in the different regions of Ontario. Each community's results are given back to their community-planning group.

Conclusions: These Community based organizations in each region will have a baseline quantitative measure of the integration of each agency with each other agency and the community group as a whole.

Contact Information: Jacqueline Roberts, Tel: 905-525-9140 x22293, Email: robertsj@mcmaster.ca

266

KNOWLEDGE EXCHANGE IN ACTION: THE PASS STUDY & COMMUNITY-BASED REPORTING OF ADVERSE DRUG EVENTS

Jean-Pierre Belisle [1]; Patrick Cupido [1]; Louise Binder [1]; Derek Thaczuk [1];
1-Canadian Treatment Action Council;

Plain Language Summary: CTAC, in collaboration with the BC Centre for Excellence in HIV/AIDS, pilot tested four national community-based methods for gathering information about adverse drug events (ADEs). The study assessed specific methods for collecting ADE and quality of life data from persons living with HIV. The knowledge-exchange approach of the PASS project continues: ongoing community consultations will likely yield further insights into community priorities for further advocacy and research.

Objectives: The PASS study investigated community-based methods for reporting adverse drug events (ADEs). Objectives were to evaluate four possible community-based methods for collecting ADE information, to explore qualitative methods of data collection, and to involve multiple stakeholders in a collaborative discussion about PASS reporting methods (current and investigative).

Methods: A multi-stakeholder Advisory Committee was formed to oversee the PASS project. Protocol development and implementation was carried out in partnership with researchers at the B.C. Centre for Excellence. Data on ADE experiences was gathered between November 2002 and June 2003, by means of: a national bilingual toll-free line; face-to-face interviews in major cities; a mail/fax survey; and focus groups with Aboriginal peoples. Study results have been collated; the current phase of the study focuses on knowledge exchange. Community consultations are being held across Canada to enable PHAs to comment on the study and identify areas for further advocacy.

Results: 1070 surveys were collected: 933 from on-site interviews, 97 via mail/fax, and 40 phone interviews. Focus groups were conducted with a total of 22 Aboriginal participants. Overall demographics favoured geographic regions where interviews were conducted, but otherwise largely reflected Canadian HIV/AIDS demographics. Interviews and focus groups attracted large number of responses with considerable richness of detail. Qualitative data describing PHA lived experience was collected in parallel with quantitative data about ADEs. Research results have been described in a formal research report; to facilitate community knowledge exchange, results are currently being disseminated in community-friendly written documents and through interactive consultations.

Conclusions: A wide collaboration of community stakeholders has successfully driven the PASS study. The PASS study offers a detailed human portrait that is not captured in the existing ADE reporting system. PHAs have much to report about quality of life with HIV, medications, and ADEs, which does not yield to current quantitative PASS data collection methods. The current community dissemination and consultation strategy is likely to yield further insights into community priorities for further advocacy and research.

Contact Information: Derek Thaczuk, Tel: 416-461-3304, Email: dt@readablewriting.ca

267

TORONTO TEEN SURVEY (TTS) PHASE ONE

June Larkin [1]; **Sarah Flicker** [2]; Hazelle Palmer [3]; Jason Pole [1]; Robb Travers [4];
1-University of Toronto; 2-Wellesley Central Health Corporation; 3-Planned Parenthood of Toronto; 4-Ontario HIV Treatment Network;

Plain Language Summary: Globally, half of all new HIV infections occur among youth under 25. Recent literature reveals a number of troubling factors that create fertile conditions for the spread of HIV/AIDS among Canadian youth. These include: a rise in youth sexually transmitted infections (STIs), increasing numbers of youth living at or below the poverty line, an increasing number of youth in migration, a decline in HIV/AIDS knowledge among high school aged youth. Research demonstrates that "one size fits all" prevention strategies are rarely effective. As Canadian urban centres become increasingly diverse, comprehensive and coordinated service planning and delivery strategies are necessary to meet these increasingly complex challenges. The TTS team will work with youth, service providers, researchers and policy makers to assess the current state of youth sexual health information and services and make recommendations on how to improve the system in Toronto and other diverse urban centres.

Objectives: Identify what sexual health, including HIV/AIDS, services and information are being used by diverse youth across Toronto; Identify the gaps and barriers that exist for diverse youth in accessing sexual health services and resources; Identify the factors that facilitate diverse youth's access to sexual health services and resources; Discover how diverse youth would like to see these gaps and barriers addressed; Understand what roles service providers can play in providing relevant and effective sexual health services for diverse youth.

Methods: In phase one(2004/05), a diverse group of 12 youth aged 13-17 years worked collaboratively to develop a research design, instruments and protocol. They developed a survey to determine what sexual health services are being used by youth, what barriers prevent youth from using sexual health services and what solutions are required to increase access to sexual health services. In phase two (2006/07), YAC members will administer surveys to diverse communities of youth. Analyzed survey data will be presented to focus groups of Service Providers who work with youth to solicit their feedback on the findings and their input on the development of a city-wide strategy to improve services to ensure positive sexual health outcomes for diverse communities of youth living in a large urban environment. Results will be disseminated in a variety of formats including presentations at appropriate conferences, academic and youth-oriented websites, a youth-friendly poster, a report for service providers and academic manuscripts.

Results: In phase one, the YAC developed the protocol for a city-wide youth survey. YAC were extremely vocal about sexual health issues and services in their communities. The group reflected many of the same issues identified through research including a lack of comprehensive sexual health knowledge and dissatisfaction with current resources. Sessions revealed that although youth in urban centres face similar sexual health issues, the way sexual health is understood and practiced is very different depending on the community of youth being served. Choices youth make operate within larger socio-cultural and political contexts which must be considered in effective program planning.

Conclusions: The findings have the potential to improve quality of life for Toronto youth and consequently their communities. Sexual health as a health goal aims to enhance life and relationships, and is an integral aspect of the overall health and well being of every person. Acceptance of and action for positive, responsible youth sexuality has the potential to have a great impact on our whole social fabric.

Contact Information: Susan Flynn, Tel: 416-961-0113, Email: sflynn@ppt.on.ca

Vulnerable Populations

268

HOW IMPORTANT IS NETWORK STRUCTURE IN THE TRANSMISSION OF DISEASE AMONG INJECTION DRUG USERS?

Linda Pelude [1]; George Wells [1]; Lynne Leonard [1]; John Wylie [2,3]; Ann Jolly [1,4];
1-Department of Epidemiology & Community Medicine, University of Ottawa, Ottawa, Ontario; 2-Cadham Provincial Laboratory, Manitoba Health, Winnipeg, Manitoba; 3-University of Manitoba, Winnipeg, Manitoba; 4-Division of Modelling and Projections, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, Ottawa, Ontario;

Plain Language Summary: Networks connect everything from the World Wide Web (a virtual network); the Internet (a physical network); Hollywood actor, scientific collaboration and sexual contact networks (social networks). These networks obey universal laws despite their diverse origins and are called scale-free, a structure where a few individuals or "hubs" have many connections. In a scale-free disease transmission network, hubs have a large number of connections. Once hubs are infected a virus is easily spread. The possibility that injection drug using (IDU) networks may be scale-free has important implications for prevention programs and the sustained transmission of HIV and HCV among IDUs.

Objectives: Complex networks share similar architectures independent of the nature of the elements that comprise the network. In other words, the WWW (virtual network), Internet (physical network), Hollywood actor, scientific collaboration and sexual contact networks (social networks) all obey universal laws despite their diverse origins. These networks have been shown to be scale-free, a structure in which the majority of individuals have a small number of connections while few have many. Their distributions follow a power law ($y = Cx^{-a}$) in which the constant a, is called the exponent of the power law. An exponent < 3 indicates a scale-free network. Results indicate that less infectious viruses can spread easily in scale free networks. We explored whether the structure of injection networks of IDUs may be scale-free.

Methods: The data came from a cross-sectional pilot study (2000), of 157 Winnipeg IDUs. Scale-free networks are characterized by power law behaviour in the tail of the cumulative distribution and a value for the exponent < 3. We plotted the cumulative distribution of the frequency of injection over a 1- year period on a graph with logarithmic axes. A curve was fitted to the entire distribution and then to the tail-end of the distribution using nonlinear regression methods. The exponent was determined using both least squares: and Maximum Likelihood Estimation (MLE) method.

Results: The data follow a straight line in a log-log plot of the tail-end of the distribution, consistent with a power law. The exponent (a) derived using least squares methods = 1.275 and using MLE = 2.4, both <3. If the exponent is less than 3, then there will always be some individuals with a high enough number of contacts to spread infection. Participants who injected greater than 2,640 times in one year (those in the tail end of the distribution) were significantly more likely to be aboriginal ($p = 0.011$), have an income > $40,000 ($p = 0.007$), have injected at a hotel in the past 12 months ($p = 0.039$); and have at least one member of their network who injected daily ($p = 0.014$).

Conclusions: Interventions directed at changing the scale-free network structure are required to reduce the transmission of HIV/HCV among IDUs. Interventions should include educating high frequency injectors, targeted contact tracing of high frequency injectors; or implementing prevention (NEP) programs or safer injection facilities at or near hotels frequented by those in the tail-end of the distribution.

Contact Information: Linda Pelude, Tel: 613-327-0157, Email: pelude@sympatico.ca

269

PERFORMED ETHNOGRAPHIES ON HIV/AIDS AND PREVENTION

Tara Goldstein [1,2,3,] **Joanne Murray-Ormandy** [1,2]; Gabrielle Zilkha [1,2]; Emma Ardal [1,2]; Sarah Switzer[1,2]; Marie Richer[1,2,]; Nidhi Punyarthi[1,2]; Melissa Chance [1,2]; Teisha Thompson [1,2];
1-Gendering Adolescent AIDS Prevention Project (GAAP); 2-Women and Gender Studies Institute (WGSI), University of Toronto; 3-The Ontario Institute for Studies in Education, University of Toronto (OISE/UT);

Plain Language Summary: In response to the need for more creative approaches to connect HIV research and awareness-creation, the Gendering Adolescent AIDS Prevention (GAAP) project has used performed ethnography as an alternative to more traditional methods of HIV/AIDS education. By performed ethnography, we mean a way of disseminating research findings through performance—a medium more accessible to youth than scholarly publications.

Objectives: The objectives of this project were: to explore the value of using performed ethnography as an HIV-prevention strategy for youth, and to explore more creative and youth-accessible approaches to HIV/AIDS education.

Methods: We used data from 17 focus groups with diverse youth in Ontario and 2 focus groups of our own for three sessions of reflective writing. The reflective writing was used to create scripts for monologues and short plays.

Results: The performances that resulted critically engage with complex topics pertinent to diverse audiences such as the "othering" of HIV/AIDS, contradictory gender roles and risk behaviour, heterosexism and the silencing of safe sex information for women having sex with women, HIV/AIDS and family, the importance of solidarity across marginalized communities and the colonialist shaping of stereotypical black male youth sexuality and risk behaviour.

Conclusions: Performed ethnography is a dynamic medium accessible to youth from a wider sector of society. It has the potential to create an awareness of HIV/AIDS that is grounded in everyday experiences and to equip youth with possible tools to deal with HIV/AIDS in a wide variety of situations.

Contact Information: Joanne Murray-Ormandy, Tel: 416-979-3186, Email: gaap_yab@yahoo.ca

270

THE SHADOW EPIDEMIC: HIGH RATES OF HEPATITIS C VIRUS INCIDENCE AMONG WOMEN AND MEN IN OTTAWA WHO INJECT DRUGS

Lynne Leonard [1]; Christine Navarro [1]; Nicholas Birkett [1]; Robert Remis [2];
1-Department of Epidemiology and Community Medicine, University of Ottawa, Ottawa, Ontario, Canada.; 2-Department of Public Health Sciences, University of Toronto, Toronto, Ontario, Canada.;

Plain Language Summary: People living with both HIV and hepatitis C virus (HCV) infection face particular challenges. The treatment for each disease and the way that the disease affects people's health is complicated by the presence of the other disease. As most cases of HCV are among women and men who inject drugs we studied HCV infection among women and men in Ottawa who inject drugs to see what behaviours may be contributing to the high rates of HCV infection among this group. We interviewed 506 active injection drug users and found that more than half of them were living with HCV infection and we found that the rate at which new HCV infections were occurring was extremely high. We concluded that HCV is spread much more rapidly among this population than HIV and since nearly all the IDUs had accessed the local needle exchange programme (NEP) we recommend that NEPs increase their harm reduction activities to help IDUs understand how they can catch HCV through drug injection activities.

Objectives: Co-infection with HIV and hepatitis C virus (HCV) adversely affects the clinical course of each and poses considerable treatment challenges. The majority of Canadian HCV cases are among women and men who inject drugs (IDUs); however, HCV is comparatively understudied among IDUs. To provide direction to respond to increasing rates of HIV-HCV co-infection, this study examined factors associated with HCV seroconversion.

Methods: From October 2002 to January 2003, 506 street-recruited IDUs completed personal baseline interviews and saliva testing for HIV and HCV antibodies. Participants were eligible for follow-up interviews every six months.

Results: Baseline HCV prevalence was 57.3% (95% CI: 52.8, 61.8). Among 92 baseline HCV-negative participants completing at least one follow-up interview, 17 seroconversions were observed. Overall HCV incidence density was 25.0/100 PYs (95% CI: 13.1, 36.9), much higher than overall HIV incidence density at 2.3/100 PYs (95% CI: 0.1, 4.5). Although not statistically significant, incidence among men was over three-fold higher than among women. 77% of seroconverters had a history of incarceration; 35% had injected with used needles; and 35% had shared injecting equipment in the six months preceding their last interview. The majority (82%) reported obtaining most new needles from Ottawa's needle exchange programme (NEP) during the follow up period; 88% reported accessing NEP services for more than one year. Notably, none of the seroconverters tested HIV-positive at baseline and none seroconverted to HIV-positive.

Conclusions: HCV was acquired much more rapidly than HIV by this group of Ottawa IDUs. Sustained interventions and resource provision to reduce injection with used needles and other injection equipment are needed to reduce HCV-related harm and thereby the occurrence of HIV-HCV co-infection. Given the high level of NEP use, these findings also indicate that NEPs are well positioned to raise awareness of HCV risk and to scale-up their HCV prevention activities.

Contact Information: Lynne Leonard, Tel: 613-562-5800 x8286, Email: lleonard@uottawa.ca

271

NEEDLE EXCHANGE PROGRAM CLIENTS IN HAMILTON, ONTARIO: HEALTH STATUS AND HEALTH AND SOCIAL SERVICE UTILIZATION

Suzanne Newmark[1]; Murray Jose[2]; Valine Vaillancourt[1]; Oman Huhad[1]; Denise Mousseau[1]; Betty Anne Thomas [3]; Dale Guenter [4];
1-Van/Street Health Program, Public Health and Community Services, City of Hamilton; 2-Executive Director, The Toronto People With AIDS Foundation; 3-Executive Director, The AIDS Network, Hamilton, ON; 4-Department of Family Medicine, McMaster University, Hamilton, ON;

Plain Language Summary: The Needle Exchange Program (NEP) in Hamilton funded 50% by the City of Hamilton and 50% by the Ministry of Health and Long-Term Care through its public health branch and is a collaborative effort between the City of Hamilton, Public Health and Community Services, The AIDS Network of Hamilton, Halton, Haldimand, Norfolk, and Brant and Wesley Urban Ministries. A major focus of the NEP program is to address the broad health and social needs of the clientele and provide services such as sterile syringes, education, and referral to health and social services delivered through fixed sites and a mobile service.

Objectives: To understand the self-perceived health status of clients of Hamilton's Needle Exchange Program (NEP), and to describe their level of use of health and social services.

Methods: An inter-agency steering committee of service providers planned the research agenda and interpreted data. Clients were invited to participate in the study through personal invitation at either the clinic site or the mobile van service between April and August, 2004. Trained interviewers administered a 30 minute questionnaire.

Results: One-hundred twenty-nine participants were recruited: half were under the age of 40, 31% female, 28% married or in common-law relationship, half had completed high school or higher level education, and 93% were Canadian citizens. Almost half started injecting before the age of 20. They were relatively stable geographically, with half having lived in the same city for their entire life and half in their own house or apartment. There was a high rate of disability, with 26% receiving some form of disability payments, 16% employed and 84% claiming they had health problems. The highest reported health problems were Hepatitis C (43%), mental health (26%) and chronic pain (22%). Quality of life scores on the MOS-HIV were lower in all health domains than Canadian normative data. Only 5.4% said they have HIV. Ninety-two percent had valid health coverage and 65% had a personal doctor. Forty-two percent worried about food "a good bit of the time" to "all of the time". Food banks, emergency departments and physicians were among the health and social services used frequently.

Conclusions: Clients of the NEP suffer from a high burden of disease and low quality of life due to a wide range of health issues. They also access health and social services from a variety of points. The NEP is in an opportune position to facilitate effective coordination of service.

Contact Information: Suzanne Newmark, Tel: 905-546-3597, Email: snewmark@hamilton.ca

272

PSYCHOLOGICAL VULNERABILITY IN INDIVIDUALS AFFECTED BY HIV PREDICTS POOR PSYCHOLOGICAL AND PHYSICAL OUTCOMES: A LONGITUDINAL STUDY

Sarah Rubenstein [1,2]; William Lancee [2,3]; Sean Rourke [1,2,4]; Douglas Saunders [2];
1-St. Michael's Hospital; 2-University of Toronto; 3-Mt. Sinai Hospital; 4-Ontario HIV Treatment Network, Toronto, Canada;

Plain Language Summary: We found that people who had either negative beliefs about themselves or who felt insecure in relationships had more depressive, anxious, and physical symptoms, as well as more life stressors and poor social support. It will be important to identify individuals with these vulnerabilities and make use of appropriate interventions to improve their mental and physical quality of life.

Objectives: Various theories have been proposed about differential psychological vulnerability, including developmental theories about attachment, separation, and the formation of psychopathology. Research in the area of psychosomatic medicine also suggests an association between attachment style and physical illness, with stress as a mediator. Firstly we hypothesized that individuals living with HIV who were "psychologically vulnerable" at the outset of the study would be more likely to experience depressive and anxious symptoms as well as physical symptoms over the course of the study period. Secondarily we investigated whether life stressors and social support mediated the relationship between psychological vulnerability and the psychological and physical outcomes.

Methods: Eighty-two individuals living with HIV participated in a study investigating adherence to HAART; they were followed for up to 9 months and received up to 14 assessments. Measures were the Revised Adult Attachment Scale (RAAS), Dysfunctional Attitude Scale (DAS), Provision of Social Relations Scale (PSRS), Responses to Stressful Life Events scale (RSLES), State-Trait Anxiety Inventory (STAI), Beck Depression Inventory (BDI), and a 21-item physical symptoms inventory. We defined psychological vulnerability or lack of resilience as scoring above 35 on the RAAS or above 120 on the DAS, indicative of insecure attachment and/or negative expectations about oneself.

Results: At baseline, 55% of participants were classified as having low resilience. Focusing on anxiety, the average cumulative STAI score of the low-resilience group was significantly higher than that of the high-resilience group (18.45 SD=10.6 versus 9.57 SD=8.6; $F(1,80)=16.74$, $p<.001$). Similar results were obtained for BDI and physical symptoms (respectively $F(1,80)=14.65$, $p<.001$ and $F(1,80)=5.50$, $p<.05$). After controlling for resilience, the effects of variance in life stressors averaged over time was a significant predictor of depressive and physical symptoms, but not of anxiety. However once the top four outliers were removed, these associations became non-significant. After controlling for resilience, the effects of variance in social support averaged over time became insignificant.

Conclusions: Not only did people with low resilience have poor psychological and physical outcomes, they were also more likely to experience stressful life events and be lacking in social support. It will be important to identify individuals with this vulnerability and utilize appropriate interventions to improve their mental and physical quality of life.

Contact Information: Sarah Rubenstein, Tel: 416-864-6060 x6483, Email: rubensteins@smh.toronto.on.ca

273

ADOLESCENT SEXUAL RISK BEHAVIOUR AMONG YOUTH IN THE CANADIAN CHILD WELFARE SYSTEM: RELATIONSHIP TO GENDER AND PREVIOUS CHILD SEXUAL ABUSE (CSA)

Carolyn James [1]; Trevor Hart [1]; Tiziana Fulco [1]; Karen Roberts [1];
1-Department of Psychology, York University, Toronto, Canada;

Plain Language Summary: Currently, there are over 80,000 children and youth in the child welfare system in Canada, with this number having increased by 60% in the last five years (National Youth in Care Network, 2005). Youth in the child welfare system are more likely to have witnessed violence, experienced financial disadvantage, and been victim to various and numerous acts of abuse and neglect (Barth, 1990). To date, there has been little research on sexual risk behaviours and sexual health outcomes in this population, and to our knowledge, no published research on Canadian child welfare system youth. The present study suggests that being sexually abused is associated with increased sexual risk behaviours among youth in the child welfare system.

Objectives: The present study examines the relationship of childhood sexual abuse (CSA) and gender to sexual risk behaviours in adolescence among youth in the Canadian child welfare system.

Methods: A random sample of youth between the ages of 14 and 17 were examined as part of the Maltreatment and Adolescent Pathways (MAP) study, an epidemiological longitudinal study of youth in the child welfare system in Toronto.

Results: Most youth (61%) had ever engaged in sexual intercourse. Of the youth who had ever had intercourse, the average age of first intercourse was 13.65 (SD = 1.66), and the majority of youth (86%) reported using a condom at first intercourse. Girls were significantly more likely than boys to have ever been sexually abused (39% versus 13%; χ^2 (1) = 9.75, p = .002). However, there were no significant gender differences in any sexual risk behaviours. Having experienced forced sex was related to engaging in certain risky sexual behaviours. Of youth who had ever had intercourse, youth who had experienced CSA involving forced sex were more likely to have had sex with an unknown partner in the last 12 months (42% versus 17%; χ^2 (1) = 4.94, p = .026), and were more likely to have ever had anal sex (41% versus 7%; χ^2 (1) = 11.61, p = .001).

Conclusions: These findings suggest that severity of sexual abuse may predict risky sexual behaviours among child welfare youth. In addition, Canadian children's aid agencies should provide sexual health counselling to their youth, with an emphasis on youth who have been sexually abused.

Contact Information: Carolyn James, Tel: 416-615-2750, Email: cjames2@yorku.ca

274

FACTORS ASSOCIATED WITH HEPATITIS C INFECTION AMONG ONTARIO INMATES

Nancy Ramuscak [1]; Liviana Calzavara [1,2]; Ann Burchell [1]; Sue Raymond; Carol Swantee [3]; Ted Myers [1,2]; Peter Ford [4]; Angela Francis [3];
1-HIV Social, Behavioural & Epidemiological Studies Unit, Faculty of Medicine, University of Toronto, Toronto, Canada; 2-Department of Public Health Sciences, Faculty of Medicine, University of Toronto, Toronto, Canada; 3-HIV Laboratory, Central Public Health Laboratory, Ontario Ministry of Health and Long Term Care, Toronto, Canada; 4-Department of Medicine, Queen's University, Kingston, Canada;

Plain Language Summary: Previous research shows that inmates are at high risk for HIV and Hepatitis C (HCV) infection. The Ontario Remand Study captured a “snap-shot” of the number of inmates infected with HIV and/or HCV admitted to 13 jails, detention centres or youth centres (called remand centres) across Ontario in 2003-2004. 16.5% of adult males and 29.7% of adult females were infected with HCV, whereas 1.6% of adult males and 1.7% of adult females were infected with HIV. Those infected with HCV were more likely to be older, have been previously incarcerated, have ever injected drugs, have injected in the past year, and have injected drugs with a needle after someone else had used it. This information can be used to help provide education and prevention messages that are targeted towards those inmates most at risk for infection.

Objectives: To examine prevalence and factors associated with HCV infection among adult Ontario inmates.

Methods: The Ontario Remand Study was a voluntary, anonymous cross-sectional prevalence study of HIV and HCV infection among adults and young offenders admitted to select remand facilities across Ontario in 2003-2004 (n = 1,877). Participants were asked to provide a saliva specimen for HIV and HCV antibody screening and answer a brief, interviewer-administered risk survey. Gender-weighted logistic regression was used to determine independent factors associated with HCV infection among adult inmates.

Results: The HCV prevalence rate among adult males was 16.5% (95%CI 14.4-18.6) and 29.7% among adult females (95%CI 24.4-34.9). Among IDUs, HCV prevalence was 54.3% (95%CI 49.7-59.0) and among non-IDU was 4.4% (95%CI 3.1-5.6). Of those infected with HCV (n=285), 35% did not report being diagnosed with HCV. Rates of HIV infection were 1.6% for adult males and 1.7% for adult females.
Factors significantly associated with HCV infection were: being older (OR=1.06, 95%CI 1.04-1.08), having a history of previous incarceration (OR=4.47, 95%CI 1.70-11.75), having ever injected drugs (OR=12.65, 95%CI 7.68-20.84), having injected drugs in the past year (OR=1.85, 95%CI 1.11-3.07), and having injected with a used needle (OR=2.07, 95%CI 1.24-3.43).

Conclusions: Adult inmates in Ontario have a high prevalence of HIV and HCV, compared to the general population. Education programs and prevention messages should target inmates most at risk for infection, as well as encourage inmates to be tested. Early diagnosis is important to ensure proper medical care and treatment for those infected, and to reduce further transmission.

Contact Information: Nancy Ramuscak, Tel: 416-978-1224, Email: nancy.ramuscak@utoronto.ca

275

EVIDENCE-BASED HARM REDUCTION FOR WOMEN AND MEN WHO INJECT DRUGS

Lynne Leonard [1]; **Emily Medd** [1]; **Joyce Seto** [1]; Emily Meadows [1];
1-HIV Prevention Research Team, Department of Epidemilogy and Community Medicine, University of Ottawa, Ottawa, Ontario, Canada;

Plain Language Summary: The HIV- and HCV-related risks associated with the multi-person use (sharing) of needles to inject drugs have been well documented and used as a basis for needle exchange programmes. The risks associated with sharing other equipment used in drug preparation such as cookers to mix and heat the drug into a solution that can be injected, filters to stop undissolved particles of the drug entering the vein and water to mix with the drug or to rinse syringes after use are less well known. This lack of knowledge is a concern as injection drug users (IDUs) share these items more frequently than needles. We reviewed over 200 published studies that examined the HIV- and HCV-related risks associated with sharing drug preparation equipment. It is clear from the evidence in these articles that IDUs who share cookers, filters, swabs and water may be at risk of getting infected with HIV and with the virus that causes hepatitis C infection and so we recommend that IDUs are helped to understand these risks and are provided with these items of drug preparation equipment along with sterile needles.

Objectives: Injection with a needle and syringe which has previously been used by another injection drug user (IDU) who is living with HIV or hepatitis C virus (HCV) infection is the most effective injection practice for acquiring these viruses. Items of equipment used in drug preparation (e.g., cookers, filters or cottons, swabs, mixing or rinse water) are less efficient reservoirs of contaminated blood than the enclosed syringes used for drug injection. As such, each time a piece of previously-used drug preparation equipment is used, the HIV- and HCV-related risk may be lower. However, studies have found that IDUs share drug preparation equipment more frequently than needles. The more frequent re-use of these items suggests that the potential HIV- and HCV-related risks associated with sharing preparation equipment may be of equal concern. The objective of this paper is to examine virologic and epidemiologic evidence documenting the potential HIV- and HCV-related risks of preparing drugs for injection with equipment that may have been used or is being used by another injection drug user.

Methods: A search of medical and social science electronic databases for articles published in English investigating HIV- and HCV-related risk associated with cookers, filters or cottons, swabs and mixing and rinse water revealed over 200 relevant articles. Further information was obtained from the websites of harm reduction-related organizations and those organizations providing services to, and drug preparation equipment for, IDUs.

Results: Laboratory-based studies documented the presence of HIV antibodies and HIV DNA on used cookers, on used filters and in used rinse water. HCV RNA was detected on used cookers, used filters, used swabs and in used rinse water. Epidemiologic studies among IDUs documented increased HIV prevalence associated with sharing cookers and filters. The practices of sharing cookers and filters were found to be significant independent predictors of HCV seroconversion and the practice of sharing rinse water elevated the risks for HCV seroconversion.

Conclusions: Scientific evidence clearly demonstrates potential HIV- and HCV-related risks associated with the multi-person use of injection equipment other than needles and supports its distribution as a component of intervention programmes to reduce the harm associated with injection drug use.

Contact Information: Lynne Leonard, Tel: 613-562-5800 x8286, Email: lleonard@uottawa.ca

276

FROM STIGMA & SILENCE TO SUPPORT: PERSPECTIVES OF HIV+ PARENTS FROM SUB-SAHARAN AFRICAN & THE CARIBBEAN

Beverley J. Antle [1]; Simone Shindler [2]; **Tutsirai Makuwaza** [1]; Megan Porter [2]; Anna Laziri [2];
1-The Hospital for Sick Children, Toronto, Canada; 2-The Teresa Group, Toronto, Canada;

Plain Language Summary: This study focuses on the experiences of parents living with HIV/AIDS in Ontario who are from Sub-Saharan Africa and the Caribbean. The intersections between navigating cultural differences, parenting, managing a life-threatening illness and dealing with the resulting stigma and fear create complex situations which service providers in communities need to understand in order to develop appropriate services.

Objectives: To learn the challenges of parents coping with their sera-positive status as well as the demands of parenting in a different culture; To learn whether and how parents disclose to their children and others about their status; To illuminate parents' perception of HIV/AIDS supports within the community and helpful strategies.

Methods: This qualitative study uses both grounded theory and participatory research methodologies. An advisory committee comprising service providers and consumers is key in guiding the research in all its stages. In-depth interviews were conducted with parents, primarily mothers. Transcriptions of these interviews were analyzed using a constant comparison method to formulate a robust and meaningful understanding of parent's experiences.

Results: For all parents the goal of coming to Canada has been to find a place of hope and the opportunity of a better life, yet the reality has been the experience of difficulties and stresses, the most significant of which has been the positive diagnosis of HIV. a) HIV is devastation: Stigmatization leads to isolation, and is a barrier to employment, productivity and living an enriched life. There is an additional stigma attached to black persons, particularly from Africa. b) Parenting: Parenting with HIV leads to a great need to protect children from discovering about illness and from stigma. The absence of traditional support systems means Canada becomes a difficult place to socialize and discipline children according to one's own culture. c) Disclosure: Parents feel it is their duty to protect children and they have no wish to impose worry on others. Fear of stigma negatively impacting the whole family is a huge barrier to disclosure. d) HIV/AIDS services: These are places of acceptance, encouragement and education, where sharing pain makes life better. Some however, see many services as culturally insensitive.

Conclusions: Myths and misconceptions give rise to stigma, which makes living with HIV/AIDS a devastation. Stigma permeates all aspects of parents' lives, negatively impacting mental health and affecting decisions in relationships with children. Support services are helpful but need to be more responsive to diverse cultural needs and to become better co-ordinated to reduce either overlap or gaps.

Contact Information: Beverley Antle, Tel: 416-813-6788, Email: beverley.antle@sickkids.ca

277

THE 2005 SEXUAL HEALTH PROMOTION RESEARCH NEEDS ASSESSMENT FOR MSM IN CANADA: UTILIZATION OF RESEARCH AND CHALLENGES FOR KNOWLEDGE TRANSFER

Tarik Bereket [1]; Ted Myers [1]; Dan Allman [1,8]; Barry Adam [2]; René Lavoie [3]; Tom Lampinen [4]; Rick Marchand [5]; Liviana Calzavara [1]; John Maxwell [6]; Shaleena Theophilus [7];
1-HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto; 2-University of Windsor; 3-COCQ-Sida, Montreal; 4-B.C. Centre for Excellence in HIV/AIDS, and University of British Columbia; 5-Community-Based Research Centre, Vancouver; 6-AIDS Committee of Toronto; 7-Canadian AIDS Society; 8-Centre for Research on Families and Relationships, The University of Edinburgh;

Plain Language Summary: To assist in the development of a national toll-free telephone survey, a national research needs assessment was undertaken. The main goal of this developmental study was to identify both new and ongoing areas of research need that would provide useful information for future community development and sexual health promotion programming for MSM. This study utilized a web-based platform to assess the sexual health promotion research needs of MSM throughout Canada. ASOs, Community AIDS Organizations (CAOs), and/or members of the Canadian AIDS Society which deal with men's issues participated, with a 64% response rate. The main highlights related to the utilization of research and challenges for knowledge transfer are discussed.

Objectives: To understand how Canadian research is used and the specific challenges for knowledge transfer in order to focus future research for community development and sexual health promotion for MSM.

Methods: The study utilized a web-based platform (www.msm-health.ca) nationwide. AIDS Service Organizations (ASOs), Community AIDS Organizations (CAOs), and/or members of the Canadian AIDS Society which deal with men's issues participated. The questionnaire, available both in English and French, was widely disseminated to a total of 130 organizations, with a 64% response rate, showing the overall project interest across Canada. The study sought responses from persons in organizations responsible for sexual health promotion for MSM. Ineligible ASOs included networks, hospices, organizations dealing with women or children's needs exclusively, and ASOs with no prevention programs for MSM; comprising 31% of the total sampling frame. In addition to responses to the survey, extensive follow-up telephone consultations with sexual health educators for MSM and other key informants from ASOs were conducted across the country. The information obtained is primarily quantitative, and descriptive in nature.

Results: A majority of ASOs responding (64%) use findings from national, provincial or local Canadian studies to assist in MSM programming. Of these who utilize research findings, 60% use for behavioural risk reduction programming, 53% for support programming and 43% for program evaluation. Specific uses include refinement of educational messages (58.6%), preparation of educational campaigns and strategies (55.2%), and program funding applications (50.0%). ASOs value Canadian research for MSM as it confirms what was believed to exist (93.1%), gives new understandings (91.4%), raises additional questions for future research (89.7%), shows the diversity of MSM behaviour (89.7%), provides new information (88.0%), and shows the diversity of the MSM community (84.5%).A number of community and resource barriers were seen to present challenges to HIV/AIDS knowledge transfer. These included stigmatization and discrimination associated with HIV/AIDS (95.3%), lack of funding (91.5%), resistance to display/ distribution of explicit MSM related materials in public (91.3%), geographical distance (82.2%), and unwelcoming environment (80.0%).

Conclusions: While a sizable proportion of ASOs in Canada utilize research findings, a major reason for not using relates to the dearth of such research in Canada, as well as the absence of MSM specific programming in many parts of the country. There is considerable variation among areas of the country in research use and knowledge needs. Responses demonstrate the need for provincial/regional data comparisons over aggregated national data.

Contact Information: Tarik Bereket, Tel: 416-978-1830, Email: tarik.bereket@utoronto.ca

278

UNDERSTANDING THE NATURE OF MEMORY COMPLAINTS IN HIV-INFECTION: ARE PERSONALITY FACTORS IMPORTANT?

Jana H. Atkins [1]; Sarah Rubenstein [1]; Sean B. Rourke [1,2]
1-St. Michael's Hospital; 2-University of Toronto;

Plain Language Summary: Memory complaints are common in HIV and these can lead to difficulties managing everyday activities. In our recent work, we have shown that these complaints are significantly related to increases in mood disturbance (depression) but also, though more modestly, to cognitive (brain) functioning. Being able to reliably differentiate those who have cognitive impairments with and without depression is important because the treatments for each are different. In our recent subgroup (subtype) analyses, we have examined the overall cognitive profiles of four subgroups, i.e., those with low and high memory complaints with and without memory impairment on formal testing and found the following: (1) those with *low* memory complaints and *normal* memory test results (*Accurate-Normal* subgroup) were also normal in all other cognitive areas (attention, speed of processing, executive functioning); (2) those with *low* memory complaints but *impaired* memory also had impairments in attention, speed of processing and executive functioning (this latter subgroup under-reported, minimized or was not aware of the extent of their memory impairment – *Under-Reporters*); (3) those with *high* memory complaints and *impaired* memory also had impairments in attention and speed of processing but not in executive functioning (*Accurate-Impaired* subgroup); and (4) those with *high* memory complaints but with *normal* memory were also normal in the other cognitive areas (*Over-Reporters*).

In the present study, we were interested in further examining the nature and discordance between memory complaints and memory performance in the above subgroups, focusing specifically on both the presence and type of cognitive impairments and whether personality factors or style have any relationship to the reporting of memory complaints. A total of 111 adult participants completed detailed cognitive and personality testing as part of a larger longitudinal neurobehavioural study. Four subgroups were formed according to performance on the California Verbal Learning test (normal vs impaired memory performance) and level of memory complaints (high/low) on the Patient's Assessment of Own Functioning Inventory and then compared in terms of cognitive abilities, mood, and personality features and profile.

Our results showed that the *Accurate-Impaired* and *Over-Reporters* subgroups had similar elevations in depression (on the Beck Depression Inventory) and on the neuroticism scale of the NEO-FFI (a 60-item personality scale) although there were no significant distinguishing features on the NEO that could differentiate these two groups with *high* levels of memory complaints. Item analyses suggested that the elevations in *neuroticism* were mainly related to disturbances in depression and anxiety. There were no personality differences between the *Accurate-Normal* and *Under-Reporters* suggesting that minimization of memory complaints may be related principally to impairments in cognitive functioning and possibly to executive functioning. Similar cognitive profile results were obtained in the subgroups as previously demonstrated. Our results suggest that the short NEO-FFI instrument may have limited clinical utility in helping to elucidate personality features that may underlie the reporting of memory and other cognitive complaints. This study was supported by a research operating grant from the Ontario HIV Treatment Network.

Contact Information: Jana H. Atkins; Tel: 416-864-6060 x6491; Email: jhatkins@yorku.ca

279

PERCEIVED IMPACT OF HIV AND ITS ASSOCIATED TREATMENT ON ACTIVITY LIMITATIONS: ROLE OF SYMPTOM BURDEN

Michael G. Wilson [1,2]; Sean B. Rourke [1,3,4,5]; Sergio Rueda [3,6]; Sarah L. Rubenstein [3,7]; Winston Husbands [8]; Gerald Devins [5,9]
1 -Ontario HIV Treatment Network; 2 –Department of Clinical Epidemiology and Biostatistics, McMaster University; 3 -Mental Health Service, St. Michael's Hospital, Toronto, ON, Canada; 4 -Centre for Research on Inner City Health, St. Michael's Hospital, Toronto, ON, Canada; 5 -Department of Psychiatry, University of Toronto; 6 -Department of Clinical Epidemiology, University of Toronto; 7 -Institute of Medical Science, University of Toronto; 8 -AIDS Committee of Toronto; 9 -University Health Network

Plain Language: Cognitive symptoms, cognitive functioning, depression, health related quality of life (HRQOL), AIDS diagnosis and everyday functioning were assessed for 295 adult men with HIV. It was found that the subjective measures of health, particularly fatigue and cognitive symptoms, rather than biological markers of HIV are significant predictors of the everyday functioning for the study participants.

Objectives: With the development and availability of highly active antiretroviral therapy (HAART), there has been a dramatic reduction in morbidity and increase in survival, and increasingly a need to understand how HIV may affect everyday functioning.

Methods: Measures of cognitive functioning (Digit Symbol test), depression (Beck Depression Inventory), cognitive symptoms (Patient's Assessment of Own Functioning Inventory), HRQOL (pain and fatigue questions of the MOS-HIV) and everyday functioning (Illness Intrusiveness Rating Scale (IIRS)) were administered to 295 adult men (mean age and education of 42.1 (SD=8.3) and 13.9 (SD=2.8) respectively) as part of an OHTN-funded study examining the everyday functioning of people living with HIV/AIDS. Multiple regression was used to examine the unique contributions of symptom burden (depression, cognitive symptoms, pain and fatigue), cognitive functioning and AIDS diagnosis (CDC-93 staging) on IIRS total score and IIRS subscores: (1) Activities of daily living (work, recreation, diet, health, finances); (2) Psychosocial functioning (e.g., self-expression, community involvement); and (3) Intimacy (sex life and relationship with partner).

Results: Total IIRS score (R^2 = 0.43) was associated with fatigue (R^2= 0.32, p< 0.001), cognitive symptoms (R^2=0.085, p< 0.001), pain (R^2=0.015, p< 0.01) and AIDS diagnosis (R^2=0.014, p< 0.01). For the IIRS subscores, multiple regression results revealed that: (1) activities of daily living (R^2= 0.37) were associated with fatigue (R^2=0.25, p< 0.001), cognitive symptoms (R^2=0.067, p< 0.001), AIDS diagnosis (R^2=0.029, p< 0.001) and pain (R^2=0.02, p<0.01); (2) Psychosocial functioning (R^2= 0.37) was associated with fatigue (R^2=0.26, p< 0.001) cognitive symptoms (R^2= 0.076, p< 0.001), depression (R^2=0.009, p= 0.042) AIDS diagnosis (R^2=0.01, p= 0.036) and pain (R^2=0.009, p= 0.050); and (3) Intimacy (R^2= 0.19) was associated with fatigue (R^2=0.15, p< 0.001), cognitive symptoms (R^2=0.029, p< 0.01) and cognitive functioning (R^2=0.016, p= 0.02).

Conclusions: Subjective measures of symptom burden, especially fatigue and cognitive symptoms, appear to be more important in the disruption of everyday functioning than biological markers of HIV. More attention is needed to develop and test out interventions to reduce this symptom burden and improve HRQOL.

Contact Information: Michael Wilson; Tel: 416-642-6486; E-mail: mwilson@ohtn.on.ca