ashm2004canberra
16TH AUSTRALASIAN CONFERENCE 2–4 SEPTEMBER 2004

16TH ANNUAL CONFERENCE OF THE AUSTRALASIAN SOCIETY FOR HIV MEDICINE

Positive Partnerships – From Policy to Primary Care

2 – 4 September 2004
National Convention Centre, Canberra, Australia

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Australasian Society for HIV Medicine Inc

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WELCOME LETTER

Dear ASHM members, friends and colleagues, it is our great pleasure to welcome delegates to Canberra, Australian Capital Territory for the 16th Annual ASHM Conference. The conference theme is *Positive Partnerships: From Policy To Primary Care*.

The ASHM Conference is Australasia's premier HIV conference and brings together the range of disciplines including basic science, clinical medicine, epidemiology, nursing and allied health, public health and prevention, social research, education, policy, and community programs, involved in HIV management and the ever-evolving role of primary care in HIV.

This year the conference will focus on how Australia has responded to HIV and where we need to go in the future. While some of this focus will be on Australian policy responses, it is equally embracing of management and prevention strategies. The ASHM Conference will present state-of-the-art science and research, while maintaining interest in regional issues.

The ASHM Conference continues to offer participants access to information on viral hepatitis, as this year we are very pleased to be running the conference back to back with the 4th Australasian Hepatitis C Conference. We encourage you to take advantage of the overlap day of Thursday 2 September by attending some sessions particularly the closing session which will highlight sessions from the conference and discuss strategic directions for the future Hepatitis C response.

The Annual ASHM Conference always provides an opportunity for discussion, collaboration and networking. It is a time for our research centres, professional organizations, health care providers, consumer groups and government to meet, to learn and to plan for the future. We hope you enjoy the 16th ASHM Conference and find it a stimulating and innovative meeting.

Associate Professor Elizabeth Dax
President, Australasian Society for HIV Medicine and Director, National Serology Reference Laboratory

Professor David Cooper
National Centre for HIV Epidemiology and Clinical Research

Professor Anthony Cunningham
National Centre for HIV and Hepatitis Virology Research

Professor Susan Kippax
National Centre for HIV Social Research

Professor Marian Pitts
Australia Research Centre in Sex, Health and Society

Katie Costello
Australian and New Zealand Association of Nurses in AIDS Care (Victorian Branch)

Helen Young
Social Workers in AIDS

The Conference Organising Committee

Marcus Bogie, People Living with HIV/AIDS ACT

Frank Bowden, Canberra Sexual Health Centre

Phillip Habel, ACT Division of General Practice

Tuck Meng Soo, Interchange General Practice

Ashley Watson, Canberra Hospital

Clare Willington, Interchange General Practice

Levinia Crooks, ASHM

Nadine Giatras, ASHM

Edward Reis, ASHM

Nicole Robertson, ASHM

Rhian Jones, ASHM

REVIEWERS

John Ballard . . . . . Australian National University

Marcus Bogie. . . . . People Living with HIV/AIDS Australian Capital Territory

Frank Bowden . . . . . Canberra Sexual Health Centre

Mark Boyd . . . . . National Centre in HIV Epidemiology and Clinical Research

Marina Carman . . . . . Australasian Society for HIV Medicine

Jillian Carr. . . . . Institute of Medical and Veterinary Sciences

Kenneth Clare . . . . . Sunshine Coast Health District HIV and Sexual Health Services

Stevie Clayton . . . . . AIDS Council of New South Wales

Suzanne Crowe . . . . . Macfarlane Burnet Institute

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Martyn French . . . . . Royal Perth Hospital

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Paul Goldwater . . . . . Women and Children's Hospital Adelaide

Carla Gorton . . . . . Australasian Society for HIV Medicine

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Brenda Henry . . . . . Gold Coast Sexual Health Centre

Jenny Heslop. . . . . Mid North Coast Area Health Service

Jenny Hoy. . . . . Alfred Hospital

Brian Hughes. . . . . Sexual Health and Infectious Diseases Clinic Darwin

Anthony Jaworowski . . . MacFarlane Burnet Institute

Alison Kesson . . . . . The Children's Hospital at Westmead

Sue Kippax . . . . . National Centre in HIV Social Research

Carolyn Lang. . . . . University of Queensland

Sharon Lewin . . . . . Victorian Infectious Diseases Service

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Debbie Marriott . . . . . St Vincent's Hospital, Sydney

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Peter McDonald . . . . . Flinders Medical Centre

Rosemary McGuckin. . . . Gascoyne Public Health Unit

Dale McPhee . . . . . National Serology Reference Laboratory

Nicolas Medland . . . . . Victorian AIDS Council

Kristine Millar . . . . . Prince of Wales and Prince Henry Hospitals

Catherine O'Connor . . . Central Sydney Sexual Health Service

Elizabeth O'Neil . . . . . Wentworth Area Health Service

Cathy Pell . . . . . Sydney Sexual Health Centre

Patricia Price . . . . . University of Western Australia

John Quin. . . . . Liverpool Specialist Rooms

Vanessa Read . . . . . Prison Health Services Western Australia

Edward Reis . . . . . Australasian Society for HIV Medicine

Gary Rogers . . . . . O'Brien Street Practice

Norm Roth . . . . . Alfred Hospital

Darren Russell . . . . . Melbourne Sexual Health Centre

Joe Sasadeusz . . . . . Victorian Infectious Diseases Service

Cindy Shannon . . . . . University of Queensland

Tuck Meng Soo . . . . . Interchange General Practice

Graeme Stewart. . . . . University of Sydney

David Sutherland . . . . . Nine Ways Specialist Clinic

Geoff Symonds . . . . . Johnson & Johnson Research

Gilda Tachedjian . . . . . Macfarlane Burnet Institute

Kelly Tank . . . . . Sacred Heart Palliative Care Service

Cheryl Teng. . . . . AIDS, Hepatitis and Sexual Health Line Victoria

Mark Thompson. . . . . People Living with HIV/AIDS Victoria

Scott Thomson . . . . . John Curtin School of Medical Research

Claire Vajdic . . . . . National Centre in HIV Epidemiology and Clinical Research

Ashley Watson . . . . . Canberra Sexual Health Centre

John Wilkinson . . . . . Westmead Millennium Institute

Claire Willington . . . . . Interchange General Practice

John Willis. . . . . Australian Research Centre in Sex, Health and Society

Ian Woolley . . . . . Monash Medical Centre

Rudyard Yap . . . . . Palmerston North Hospital

PROGRAM AT A GLANCE

THURSDAY 2 SEPTEMBER 2004

7.30am	Registration			
8.30am	Opening Ceremony			
	Royal Theatre			
8.40am - 9.00am	Welcome			
9.00am - 9.20am	**Justice Michael Kirby, Sydney Chambers of Justice** The New Aids Equation			
9.20am - 9.40am	**Michael Kidd, President of the Royal Australian College of General Practitioners** The Management of HIV in Australian General Practice			
9.40am - 10.00am	**Ninkama Moiya, Director of the National AIDS Council (PNG)**			
10.00am - 10.15am	Contined Welcome			
10.15am - 10.30am	Peak Body Representatives			
10.30am - 11.00am	Morning Tea in Exhibition & Poster Area - Exhibition Hall			
11.00am - 12.30pm	Symposium - AusAID (Symposium Sponsor) - Meeting the Challenge: HIV, AIDS and Regional Security	Concurrent - Basic Science -Theraputics	Concurrent - Social Research - Risk	
	Bradman Theatrette	Menzies Theatrette	Nicholls Theatrette	
12.30pm - 1.30pm	Lunch in Exhibition & Poster Area - Exhibition Hall			
12.30pm - 1.30pm				ASHM Annual General Meeting (AGM) - Sutherland Theatrette
1.30pm - 1.50pm	Symposium - Epidemiology - PREP	Concurrent - Basic Science - Diagnostics & Prognostics	Concurrent - Trends - Change in Clinical Patterns Ian Thompson Memorial Session	Concurrent - Nursing and Allied Health
	Bradman Theatrette	Menzies Theatrette	Nicholls Theatrette	Sutherland Theatrette
3.00pm - 3.30pm	Afternoon Tea in Exhibition & Poster Area - Exhibition Hall			
3.30pm - 5.00pm	Symposium - Basic Science - Development of Vaccines	Concurrent - Clinical Medicine - Treatment	Concurrent - Community Uptake Phillip Medcalf Memorial Session	Concurrent - ART in Resource Poor Settings: Coming Ready or not
	Bradman Theatrette	Menzies Theatrette	Nicolls Theatrette	Sutherland Theatrette
5.00pm	Close			

FRIDAY 3 SEPTEMBER 2004

7.30am	Registration			
7.30am - 8.30am	Case Presentation Breakfast			
	Swan Room			
9.00am - 10.30am	Plenary Session			
	Royal Theatre			
9.00am - 9.30am	**Brian Gazzard, Chairman of the British HIV Association** Guidelines for Routine Care			
9.30am - 10.00am	**Mary Crewe, Director of the Centre for Study of AIDS at the University of Pretoria, South Africa** Understandings From The Epicentre			
10.00am - 10.30am	**Frits van Griensven, Associate Director for Science of the HIV/AIDS Program of the Thailand MOPH - U.S. CDC Collaboration (TUC)** Report from One of the Most Extensively Studied HIV Epidemics in a Non-Western Country - Thailand: Did it Help to Formulate the Response?			
10.30am - 11.00am	Morning Tea in Exhibition & Poster Area - Exhibition Hall			
11.00am - 12.30pm	Symposium - Clinical Medicine - HAART (Undectable)	Concurrent - Basic Science - HIV Pathogenesis	Concurrent - Nursing	Concurrent - Epidemiology of New infections Margaret MacDonald Memorial Session
	Royal Theatre	Bradman Theatrette	Menzies Theatrette	Nicholls Theatrette
12.30pm - 1.30pm	Lunch in Exhibition & Poster Area - Exhibition Hall			
1.30pm - 3.00pm	Concurrent - Clinical Medicine - Metabolic Syndromes	Symposium - Basic Science - New Drug Strategies	Symposium - International - Responding to HIV: Policy & Implications in PNG	Concurrent - Issues in Primary Care Peter Meese Memorial Session
	Royal Theatre	Bradman Theatrette	Menzies Theatrette	Nicholls Theatrette
3.00pm - 3.30pm	Afternoon Tea in Exhibiton & Poster Area - Exhibition Hall			
3.30pm - 5.00pm	Concurrent - Clinical Medicine - Treatment Issues	Symposium - Epidemiology - Rises in New Infections	Concurrent - Basic Science - Molecular Biology	Concurrent - Indigenous - Emerging Issues in Indigenous Sexual Health
	Royal Theatre	Bradman Theatrette	Menzies Theatrette	Nicholls Theatrette
5.15pm - 6.00pm	HIV Futures 4: State of the (Positive) Nation - Royal Theatre			Briefing on ASHM's International Policy and Programs - Nicholls Theatrette
5.00pm	Close			
7.00pm	Conference Dinner - National Museum of Australia			

SATURDAY 4 SEPTEMBER 2004

7.30am	Registration			
9.00am - 10.30am	Plenary Session			
	Royal Theatre			
9.00am - 9.30am	**Susan Kippax, Director of the National Centre in HIV Social Research** Medicalisation of Prevention			
9.30am - 10.00am	**Paul Sax, Clinical Director of the Division of Infectious Diseases and the HIV Program at Brigham and Women's Hospital, Boston** HAART: when to start and what with			
10.00am - 10.30am	**Michael Malim, Professor and Head of the Department of Infectious Diseases at King's College, London** Recent advances in HIV replication			
10.30am - 11.00am	Morning Tea in Exhibition & Poster Area - Exhibition Hall			
11.00am - 12.30pm	Concurrent - Epidemiology of STI's	Concurrent - Models of Primary Care	Symposium - International Policy Initatives	Symposium - ACON & NSW Health (Symposium Sponsor) - Gay Men & Condoms: The Relentless Pursuit of Rubberless Sex
	Royal Theatre	Bradman Theatrette	Menzies Theatrette	Nicholls Theatrette
12.30pm - 1.30pm	Lunch in Exhibition & Poster Area - Exhibition Hall			
1.30pm - 3.00pm	Symposium - Clinical Medicine - Consultant the Experts	Concurrent - Community - HIV Prevention and Peer Education	Concurrent - Social Research - Multicultural	Symposium - Basic Science - HIV Immunology
	Royal Theatre	Bradman Theatrette	Menzies Theatrette	Nicholls Theatrette
3.00pm - 3.30pm	Afternoon Tea in Exhibiton & Poster Area - Exhibition Hall			
3.30pm - 5.00pm	Closing Session			
	Royal Theatre			
3.30pm - 3.50pm	Prizes			
3.50pm - 4.50pm	**Hypothetical with Dr Norman Swan, Host The Health Report, ABC Radio National**			
4.50pm - 4.55pm	Frank Bowden - Closing remarks			
4.55pm - 5.00pm	Levinia Crooks - 2005 ASHM Conference			
5.00pm	Close			

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INVITED SPEAKERS

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Mary Crewe

Mary Crewe was born and raised in Johannesburg and studied at the Universities of Natal and The Witwatersrand. She helped to establish and then manage the Greater Johannesburg AIDS Program. This was one of the largest centres in Africa and had extensive international and national links.

Mary was a founder member and co-chair of the AIDS Consortium and NACOSA. She was the chair of the National Department of Education and Health Committee for HIV/AIDS education in schools, is the co-editor of the *AIDS Bulletin* and served on the boards of NAPWA, Friends for Life and AREPP. She was the co-chair of the Durban 2000 AIDS Conference for Track D, Social Impact and on the organising committee for the Barcelona Conference 2001 and the AIDS 2003 South African conference.

She works regularly with various UN agencies such as UNAIDS, UNICEF and UNESCO and is on the advisory board of the Ethical Globalisation Initiative. She has published a book on AIDS and authored many articles.

Mary is currently Director of The Centre for the Study of AIDS at the University of Pretoria.

Mary Crewe
University of Pretoria
Pretoria, South Africa 0002
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Brian Gazzard

Brian Gazzard received a Master of Arts and Doctor of Medicine from Cambridge University and has been a fellow of the Royal College of Physicians since 1983. Brian qualifi ed in 1970 and became a Consultant Physician and Gastroenterologist at Westminster and St Stephen's Hospitals in 1978 (now Chelsea and Westminster Hospital). He was appointed Professor of HIV Medicine (personal chair) in London University in recognition of his contribution to the treatment and care of HIV positive patients in 1997 and he continues as Brian started the British HIV Association and was its fi rst Chairman. He is on the Editorial Board of the *International Journal of STD and AIDS, Drugs*, and *British Clinical Practice and Genitourinary Medicine*. Brian is also the editor of *HIV Medicine*.

Brian Gazzard
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Michael Malim

Michael Malim is currently Professor and Head of the Department of Infectious Diseases at King's College London. His laboratory studies the regulation and control of HIV infection and replication using culture-based approaches. Most recently, their work has focused on the regulatory/accessory protein Vif, and its role as an inhibitor of the innate anti-HIV resistance protein APOBEC3G. Understanding the interplay between Vif and APOBEC3G may have important implications for AIDS pathogenesis, drug resistance, immune responses, virus evolution and, potentially, the design of novel therapeutics.

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Paul Sax

Paul Sax is Clinical Director of the Division of Infectious Diseases and the HIV Program at Brigham and Women's Hospital (BWH) in Boston, where he is an Associate Physician in Medicine. He has been on the faculty at Harvard Medical School since 1992, where he is currently an Assistant Professor of Medicine.

Paul Sax received his MD from Harvard Medical School in 1987. He served his residency in Internal Medicine at BWH, while continuing his postdoctoral education with a fellowship in the Infectious Diseases Unit of Massachusetts General Hospital. Dr Sax is board certifi ed in Internal Medicine and Infectious Disease. He is the Editorin-Chief of *AIDS Clinical Care*, where he also acts as Research Notes Editor, and *Infectious Diseases Special Edition*, where he is the HIV Disease of the American Academy of HIV Medicine.

In addition to his clinical and teaching work, Paul is also actively involved in HIV research. Ongoing areas of research interest include clinical trials of new antiretroviral therapies, cost-effectiveness of management strategies for HIV, toxicity of antiretroviral treatment, and identifi cation, treatment and outcome of primary HIV infection. He is presently the principal investigator at the Brigham and Women's Hospital AIDS Clinical Trials Unit, and is a member of the Cost Effectiveness of Preventing AIDS Complications Research Group (CEPAC).

Paul Sax
Brigham & Women's Hospital
Division of Infectious Diseases
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Frits Van Griensven

Frits van Griensven is the Associate Director for Science of the HIV/AIDS Program of the Thailand MOPH - U.S. CDC Collaboration (TUC). Van Griensven started his career in HIV/AIDS research in 1983 in Amsterdam, and was a visiting scientist at the University of California at Berkeley and at the Department of Public Health, San Francisco during 1991-1992. He has published over 150 articles on HIV/AIDS in peer-reviewed scientifi c journals. Prior to joining TUC he was an endowed professor of AIDS Epidemiology at Utrecht University, and a consultant for the AIDS Program of the European Union in South East Asia. Currently he is also an adjunct professor of Epidemiology and Biostatistics at the University of California, San Francisco. His main interest is HIV prevention research. Frits has a Masters Degree in Social Research Methods and Sociological Theory from the University of Nymegen, a PhD in Medical Sciences from the University of Amsterdam, and a Masters Degree in Public Health (Epidemiology) from the University of California, Berkeley.

Frits Van Griensven
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HIV/AIDS Program
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GENERAL INFORMATION

GENERAL INFORMATION

Disclaimer

All information disclosed in the Conference Program is correct at the time of printing. ASHM reserve the right to alter the Conference Program in the event of unforeseen circumstances. All speakers were invited to contribute abstracts for inclusion in the Conference Handbook. Unfortunately not all speakers were able to provide us with their abstracts at the time of printing. ASHM accepts no responsibility for errors, misprints or other issues with abstracts contained in this handbook.

Internet Café

Abbott Australasia is proud to be sponsoring the Internet Café located in the Exhibition Hall in their booth (number 1 - please refer to floorplan).

Mobile Phones/Beepers

As a courtesy to all delegates and speakers, please switch off, or set to silent, your mobile phones and beepers during all sessions.

Name Badges

For security purposes all attendees must wear their name badge at all times whilst in the Convention Centre. Entrance to the exhibition will be limited to badge holders only. If you misplace your name badge, please advise staff at the Registration Desk.

Personal Mail

The conference organisers do not accept responsibility for personal mail. Please have all mail sent to your accommodation address.

Poster Display

Posters will be displayed for the duration of the Conference in the Exhibition Hall, which also contains the exhibition booths and all the catering. Posters will be available for viewing on Thursday 2 September from 8.30am until Saturday 4 September at 3.30pm. Poster boards will be numbered as indicated in the Poster Program Section of this handbook. Delegates are encouraged to visit all the poster displays during coffee and lunch breaks and the welcome cocktail party.

Registration Desk

All inquiries should be directed to the registration desk in the main foyer, open at the following times:

- Wednesday 1 September: 7.30am – 5.30pm
- Thursday 2 September: 7.30am – 7.00pm
- Friday 3 September: 7.30am – 5.30pm
- Saturday 4 September: 7.30am – 5.30pm

Smoking

This conference has a no smoking policy.

Speaker Preparation Room

A speaker preparation room will be located in the Executive Room on the First Floor of the National Convention Centre. This room will be open at the following times:

- Wednesday 1 September: 7.30am – 5.30pm
- Thursday 2 September: 7.30am – 5.30pm
- Friday 3 September: 7.30am – 5.30pm
- Saturday 4 September: 7.30am – 3.30pm

All speakers must take their presentation to the speaker preparation room **a minimum of four hours** prior to their presentation or the day before if presenting at a breakfast or morning session.

Trade Exhibition

The trade exhibition is situated in The Exhibition Hall of the National Convention Centre, Canberra which also contains the posters and all the catering.

The exhibition will be open during the following hours:

- Thursday 2 September: 8.30am – 3.30pm and 5.30pm – 7.00pm
- Friday 3 September: 8.30am – 5.30pm
- Saturday 4 September: 8.30am – 3.30pm

The trade exhibition and posters for the 4th Australasian Hepatitis C Conference will also be available for viewing on Thursday 2 September from 8.30am – 3.30pm.

Venue

The National Convention Centre will host all Plenary, Symposia and Concurrent Sessions in the Ground Floor theatrettes. The Boardroom accessed from the First Floor is available as a quiet room for delegates, particularly those with medical conditions and we request that it be used only for this purpose and not for ad hoc meetings.

The National Convention Centre, Canberra
31 Constitution Avenue, Canberra ACT 2601
Phone: 02 6257 4905
Fax: 02 6257 6405
www.nationalconventioncentre.com.au

2003 Conference Scholarship Award Recipients

RECIPIENT	ORGANISATION
Dennis Altman	AIDS Society of Asia and the Pacific
Palanee Ammaranond	University of NSW
Jane Anderson	St Luke's Nursing Service
Michelle Baker	Aaron Diamond AIDS Research Centre
Sonia Fernandez	Department of Clinical Immunology and Biochemical Genetics
Trevor Fowles	St Vincent's Community Health Service
Kristy Hingston	Royal Perth Hospital
Angela Kelly	Australian Research Centre in Sex, Health and Society
Kamal Kishore	Fiji School of Medicine
Silvia Lee	Royal Perth Hospital
Jennifer McDonald	Straight Arrows – Positive Edge Program
Karalyn McDonald	Australian Research Centre in Sex, Health and Society
Srdjan Mijajlovic	University of New England
Kidest Nadew	Sydney Children's Hospital
Helen Orcher	South West Sydney Area Health Service
Jo Owens	St Luke's Nursing Service
Mark Page	Victorian Infectious Diseases Service
Vanessa Read	Prison Health Services - WA
Claire Ryan	Macfarlane Burnet Institute
Kevin Schamburg	AIDS Action Council of the ACT
Bernadette Shields	Department of Health & Community - NT
Kate Thompson	Monash University
Mohammed Ubaidullah	Sri Venkateswara University, India
Patrick Unemori	National Centre in HIV Epidemiology and Clinical Research
Giulia Zanetti	National Centre in HIV Epidemiology and Clinical Research

SOCIAL PROGRAM

Lunches and Tea Breaks

Lunches and tea breaks on each day will be served in The Exhibition Hall among the trade exhibition and poster displays.

Welcome Cocktail Party

5.30pm – 7.00pm, Thursday 2 September 2004
Exhibition Hall, National Convention Centre, Canberra

Tickets: One ticket is included for registered delegates
$44 for additional guests

Medical Case Presentation Breakfast

Proudly sponsored by Bristol-Myers Squibb

7.30am – 8.30am, Friday 3 September 2004
Swan Room, National Convention Centre, Canberra

Tickets: $16.50 per person

Case presentations supported by brief literature reviews and a Q & A session will take place at this early morning session, during which breakfast will be served. The best Medical Case Presentation will be awarded a donated cash prize during the closing session.

ASHM Conference Dinner

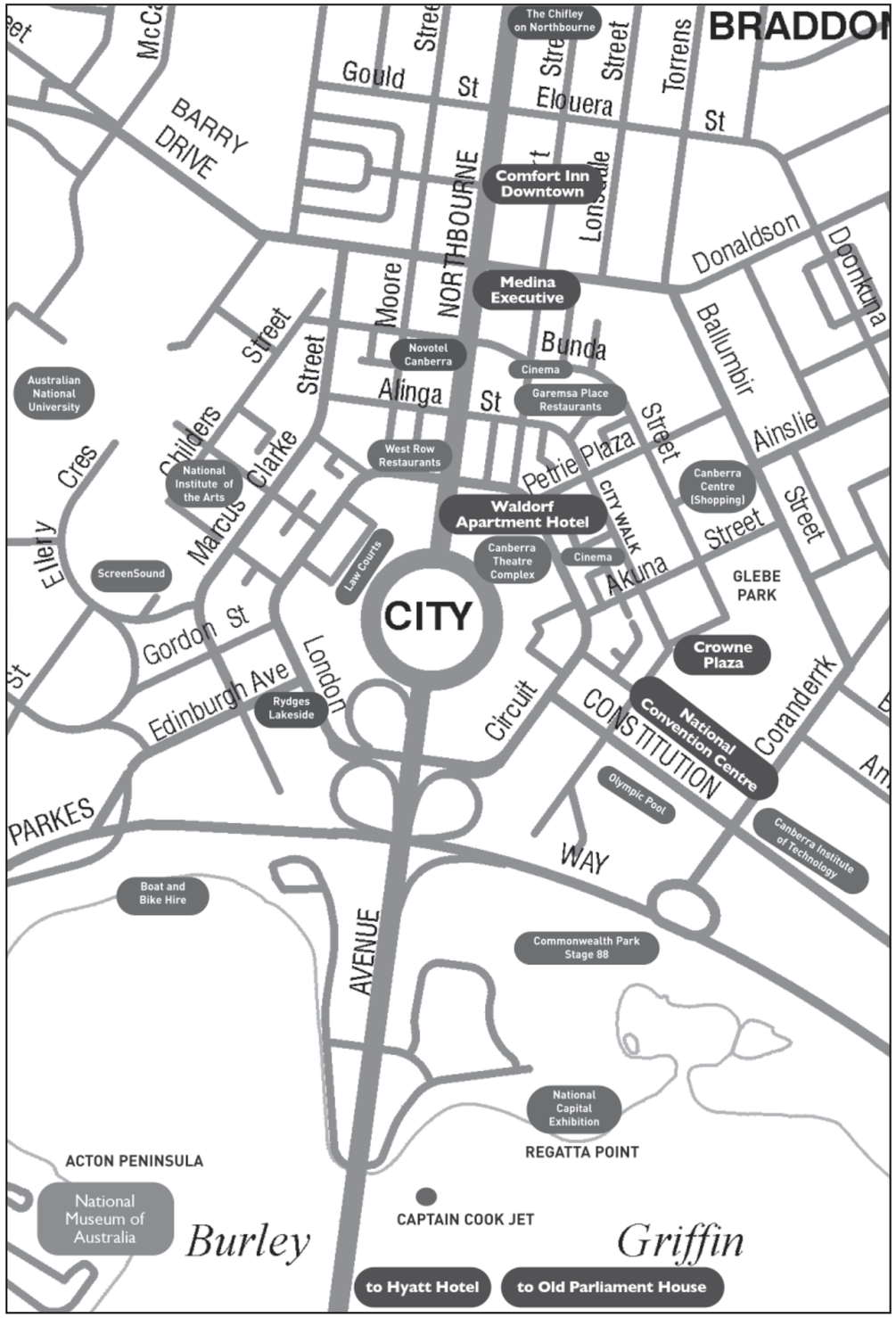
7.00pm, Friday 3 September
National Museum of Australia, Canberra.

Transfers will be provided to the Conference Dinner from the Convention Centre and returning to all Conference Hotels. Schedules will be posted on the message board at the conference.

Tickets to Social Functions

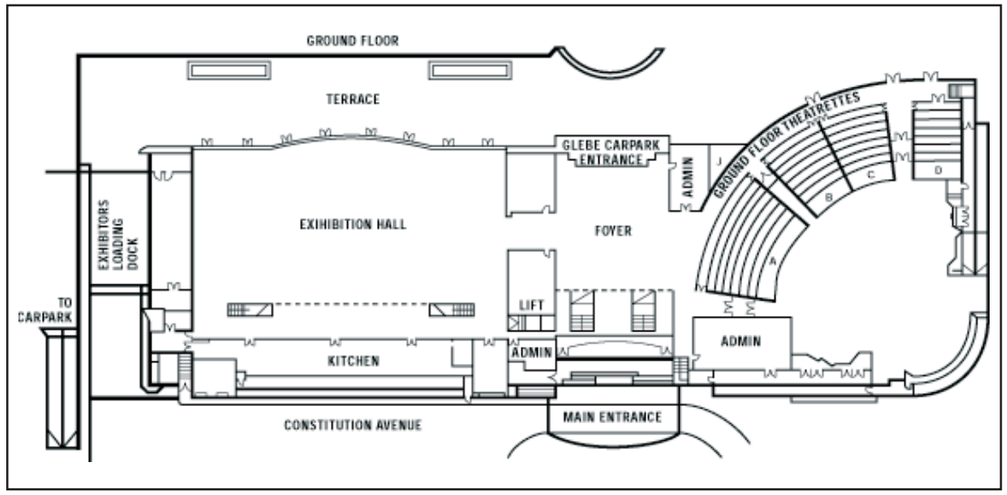
Tickets will be required for entry into the Conference Dinner and the Medical Case Presentation Breakfast. All tickets will be given out on registration. If you would like to purchase tickets to these functions you may do so up until 12 noon on Thursday 2 September at the registration desk.

LOCATION MAP – CANBERRA CITY

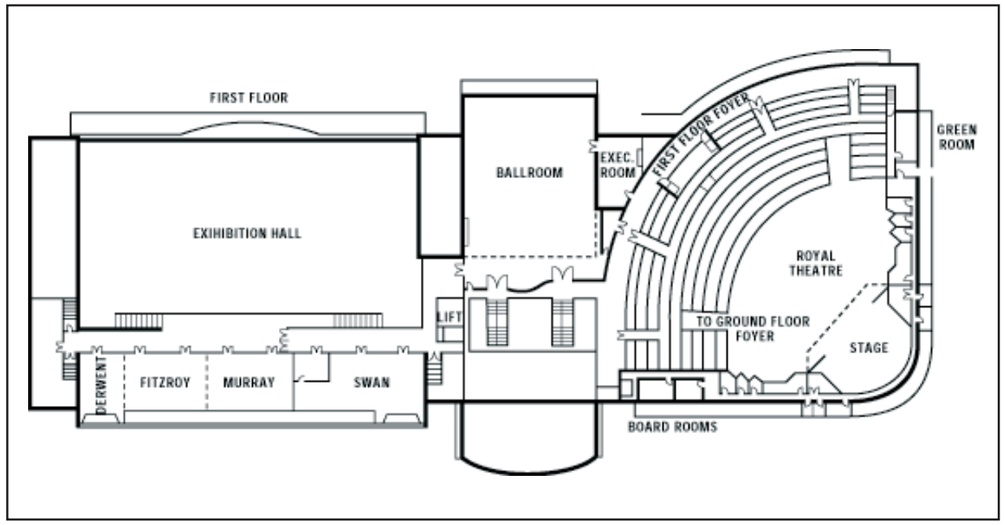


THE NATIONAL CONVENTION CENTRE, CANBERRA FLOOR PLANS

GROUND FLOOR



FIRST FLOOR



FLOOR PLAN KEY

A = Bradman Theatrette

B = Menzies Theatrette

C = Nicholls Theatrette

D = Sutherland Theatrette

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EXHIBITION DIRECTORY

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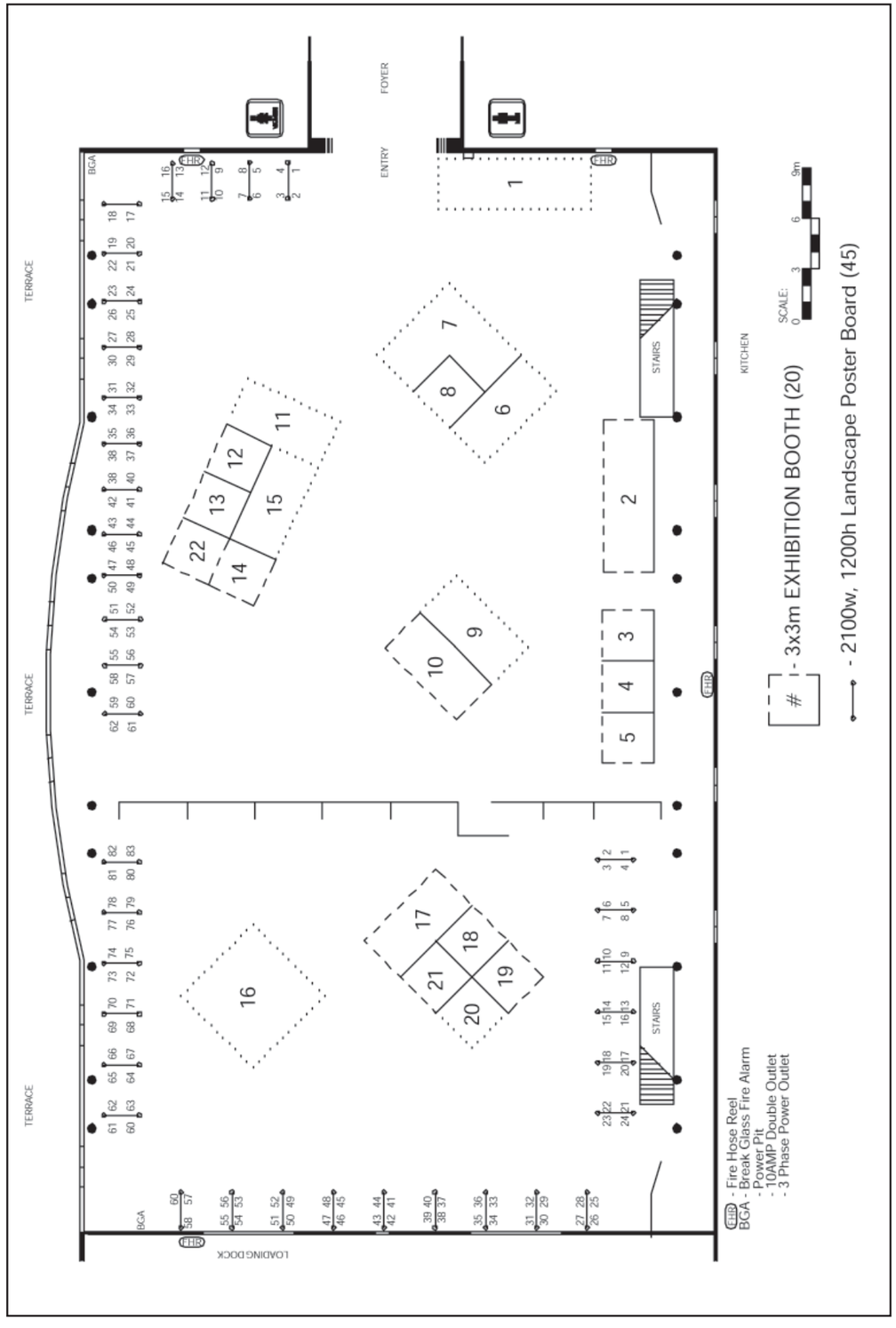
EXHIBITION HALL – FLOOR PLAN



EXHIBITOR DIRECTORY

Abbott Australasia (Booth 1)

Abbott Australasia is a world leader in HIV medicine and has been at the forefront of HIV research, treatment and diagnosis including the development of the worlds first test for HIV infection. Abbott's Protease inhibitor Norvir (ritonavir) was released in 1996 and was part of the Protease inhibitor/HAART life saving revolution. Their second Protease inhibitor Kaletra (launched 2002), has now established itself as a key component of successful HIV treatment. Abbott continues its commitment to all facets of HIV and Hepatitis both locally and globally.

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ACT Health & Community Partners - Working in Partnership in the ACT (Booth 18)

ACT Health is the ACT Government body that provides a range of coordinated health and health care services to the people of the Australian Capital Territory. Through the ACT Health Action Plan 2002 we aim to deliver the best health care and health-related services in Australia. ACT Health provides services through Calvary Public Hospital, Community Health, Health Protection Service, Mental Health ACT and The Canberra Hospital.

ACT Health has funding agreements with some community-based organisations to provide services in relation to sexual health, sexually transmissible infections and blood borne viruses. These services focus on education, prevention of transmission, care and support of affected people, delivery of sexual and reproductive health services, and training of health professionals in relation to these issues.

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AusAID (Booth 21)

The Australian Agency for International Development (AusAID), manages the Australian Government's official overseas aid program. The objective of the program is to advance Australia's national interest by helping developing countries reduce poverty and achieve sustainable development.

AusAID provides policy advice and support to the Minister and Parliamentary Secretary on development issues and develops and manages effective and innovative poverty reduction programs in partnership with developing countries, Australian businesses, non-government organisations and international agencies.

Our head office is in Canberra. We also have representatives in 25 Australian diplomatic missions overseas.

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Email: stephanie_doust@ausaid.gov.au

Australasian Society for HIV Medicine (Booth 10)

The Australasian Society for HIV Medicine is Australia's peak organisation representing medical practitioners and health care providers in the HIV and viral hepatitis and related diseases sectors. The Society conducts an annual medical/scientific conference, produces a range of educational resources and training programs, including managing continuing medical education courses, and offers information services. ASHM also participates in policy development, the setting of standards in relation to best practice care, treatment and management, and provides advice to government and non-government agencies.

Contact
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Fax: +61 2 9380 9528
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Web: www.ashm.org.au

Australian Government Department of Health and Ageing (Booth 8)

The Commonwealth Department of Health and Ageing is responsible for: implementing and monitoring the National Hepatitis C Strategy 1999 – 2004 and the National HIV/AIDS Strategy 1999 – 2004; facilitating policy formulation and secretariat support for national committees; administering funding to State and Territory governments and NGOs; developing and promoting national standards for best practice in health promotion, treatment and care for hepatitis C and HIV/AIDS; and commissioning research.

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Boehringer Ingelheim (Booth 17)

Boehringer Ingelheim is committed to providing active involvement and practical answers in HIV-infected people. Our fight against HIV/AIDS extends to resource-poor settings where Viramune® (nevirapine) has been provided to more than 290,000 mother-child pairs since the programme began. Boehringer Ingelheim is also part of the Collaboration for Health in PNG (CHPNG) and is currently working with its partners to provide education and support to health care workers in PNG.

Contact
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Bristol-Myers Squibb (Booth 6)

Bristol-Myers Squibb Pharmaceuticals is an Australian division of one of the world's leading healthcare companies, with a mission to extend and enhance human life. The company is a leading maker of innovative therapies for cardiovascular, metabolic and infectious diseases, central nervous system and dermatological disorders and cancer.

In Australia, Bristol-Myers Squibb markets VIDEX EC® (didanosine) and ZERIT® (stavudine) for the treatment of patients with HIV/AIDS. Bristol-Myers Squibb's new protease inhibitor, Reyataz® (atazanavir sulfate) is currently available through a special access program.

Contact
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Four Seasons Condoms (Booth 5)

Four Seasons Condoms are a 100% Australian owned and operated brand with a prominent range of condoms and lubrication throughout the country. With over 17 years experience, Four Seasons were the first company in Australia to introduce the Larger Fitting condom size and a number of others, including the very special Glow N Dark condoms. Four Seasons promote a strong safe sex message in particular to 14-29 year old demographic and have some interesting information on their website www.condoms.com.au, including many examples of exotic sexual positions!

Contact
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Gilead Sciences Pty Ltd (Booth 2)

Gilead is a bio-pharmaceutical company that discovers, develops and commercialises therapeutics to advance the care of patients suffering from life-threatening diseases worldwide . We focus our research and clinical programmes on anti-infectives , including anti-virals.

Our leading-edge products include Viread ® (tenofovir disoproxil fumarate) and Emtriva® (emtricitabine) for HIV/AIDS, Hepsera® (adefovir dipivoxil) for chronic hepatitis B and AmBisome® (amphotericin B) for severe fungal infections.

Our focus is on supporting the need for simplified treatment regimens. A fixed dose combination of Viread and Emtriva has been developed and Gilead recently announced a collaboration with Bristol-Myers Squibb and Merck Sharp & Dohme to create a fixed dose combination of three anti-HIV drugs - Viread, Emtriva and efavirenz-demonstrating a further commitment to helping simplify treatment.

We look forward to seeing you at the Gilead stand during the conference.

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GlaxoSmithKline (Booth 11)

GlaxoSmithKline (GSKA) Australia is one of the largest pharmaceutical and healthcare companies in the country employing more than 1500 Australians. It is Australia's largest vaccine manufacturer and a leading supplier of medicines for asthma, bacterial and viral infections, depression, migraine, gastroenterological disease, epilepsy, smoking cessation and pain relief. With a strong commitment to research GSK invests more than $25 million in R&D each year, making it one of Australia's top 20 R&D investors. Over 17 million Australians rely on at least one of GSK's medicines, vaccines or consumer healthcare products each year enabling them to do more, feel better and live longer.

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Merck Sharp & Dohme (Booth 20)

Through research and development, Merck Sharp & Dohme (MSD) has changed the course of HIV/AIDS, enabling people with HIV to live longer. Our commitment to research continues:

- Researching new targets, such as integrase
- Pursuing an effective HIV/AIDS vaccine MSD goes beyond traditional research and forges unique partnerships that address the issues of disease education, public-health infrastructure, prevention, care and treatment around the world.
- The Enhanced Care Initiative, active in Brazil, Senegal, South America, Thailand and Puerto Rico.
- The African Comprehensive HIV/AIDS Partnerships, active in Botswana.

Contact
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National Centre in HIV Social Research (Booth 3)

The National Centre in HIV Social Research (NCHSR) conducts research, which describes and analyses the social understandings, meanings and practices of peoples, institutions and communities in relation to HIV, Hepatitis C and other communicable diseases. NCHSR was established in 1990 with funding from the Commonwealth government, and is located within the Faculty of Arts and Social Sciences at The University of New South Wales, Sydney. Information about NCHSR research and publications is available at http://nchsr.arts.unsw.edu.au

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Novartis Pharmaceuticals (Booth 19)

Novartis was formed from the merger of Ciba-Geigy and Sandoz, with a major strength of Novartis being its breadth of products, which span eight major therapeutic areas including: respiratory medicine, cardiovascular medicine, diseases of the central nervous system, rheumatology, bone and HRT, oncology, dermatology and transplantation medicine.

Novartis is committed to the strengthening of its therapeutic area portfolio. A strong global Research and Development capacity is focussed on the development of products in areas of unmet medical need as well as on improving clinical outcomes where therapy already exists. These activities are complimented by ongoing programmes in the areas of health economics, quality of life and disease management.

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Roche Products (Booth 7)

Roche is one of the world's leading research-oriented healthcare groups. For more than 100 years, Roche has been active in the discovery, development, manufacture and marketing of innovative healthcare solutions. Roche's products and services address prevention, diagnosis and treatment of diseases, thus enhancing well-being and quality of life. A core therapeutic area of focus is virology and some of the innovative products developed by Roche include Fuzeon® (envurvitide) for HIV infection, Pegasys®RBV ® (peginterferon alfa-2a + ribavirin) and Pegasys® (peginterferon alfa-2a) for hepatitis C. Our mission is to create, produce and market innovative solutions of high quality for unmet medical needs. We do this in a responsible and ethical manner and with a commitment to sustainable development respecting the needs of the individual, the society and the environment.

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Schering Plough (Booth 9)

Schering-Plough is a global pharmaceutical company committed to discovering and bringing to market new therapies and treatment programs that can improve people's health and save lives. The Company's core product lines are in allergy/ respiratory, anti-infective/anticancer, dermatologicals and cardiovasculars, with a growing animal health business, complemented by leading over-the-counter and personal care brands. Schering-Plough has established itself as a leader in biotechnology, with strong research positions in genomics and gene therapy. With headquarters in Kenilworth, New Jersey USA, Schering-Plough International markets its products in more than 125 markets throughout the world, maintains subsidiaries in some 40 nations and has manufacturing facilities in over 20 of these. The Company maintains rigorous cost controls and has delivered superior financial results for more than a decade, outperforming its peers and providing attractive returns to shareholders.

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Unitract (Booth 4)

Unitract is an Australian listed company established to offer safety syringe products that can help prevent the transmission of bloodborne pathogens caused by unsafe injection practices. The Unitract Syringe technology, which this year won the prestigious Prize of the State of Geneva Award, incorporates Automatic and Controllable Needle Retraction and Independent Reuse Prevention features to help prevent the reuse of syringes and needlestick injuries. Unitract is now seeking to work with Government and Non-Government Organisations to help provide safety syringe products that can contribute towards harm minimisation efforts in Australia and around the world.

Contact
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16TH AUSTRALASIAN CONFERENCE 2–4 SEPTEMBER 2004

2004 UNDERGRADUATE AND JUNIOR RESEARCHER SUPPORT AWARDS IN HIV AND HEPATITIS AWARDEES

2004 UNDERGRADUATE AND JUNIOR RESEARCHER SUPPORT AWARDS IN HIV AND HEPATITIS AWARDEES

Juliet N. Babirye

Juliet N. Babirye is a Masters by Research student at the school of Public Health and Community Research, University of New South Wales under the supervision of Dr Andrew Grulich and Prof. John Kaldor. Her main area of interest is the prevention of mother-to-child transmission of HIV.

Juliet will be completing a comparative cross-sectional study in Bushenyi district, Uganda, East Africa. 72 HIV-positive women and 104 HIV-negative women, and 41 of their spouses have been interviewed so far using a semi-structured questionnaire. Male partners were interviewed in order to identify factors that would enhance male involvement in infant feeding.

Preliminary results reveal that there is no statistically significant difference in the choice of infant feeding mode between the HIV-positive mothers and the HIV-negative mothers (P=0.15). There is, however, a difference in actual feeding practice (P<0.05). 21% of the HIV-positive mothers practiced exclusive breastfeeding (EBF) and 25.8% mix feed compared to 11.5% and 61.5% respectively among the HIV-negative mothers.

This is not surprising since 66% of the HIV-positive mothers have heard of and only 55% have received, infant feeding counselling (IFC). Ideally, all HIV-positive mothers should receive IFC.

These results have important infant feeding policy implications for Uganda and other low-resource settings since exclusive breastfeeding has been associated with almost half the risk of HIV transmission compared with mixed breastfeeding.

Poster Presentation – Board number 24

Kerrie Dunstan

Kerrie is in her second year of a PhD (through the University of New South Wales) at the Westmead Millennium Institute. Her Honours project involved testing a candidate HIV vaccine in vitro and she has maintained an interest in the vaccine field. Her current project looks at the binding, entry and processing of candidate viral vaccine vectors, by human dendritic cells (DCs). DCs are professional antigen presenting cells which play a key role in controlling the magnitude, quality and memory of an immune response. The mechanism of entry and processing of vaccinia virus and adenovirus, two potential HIV vaccine vectors, in DCs is unclear. She hypothesises that C-type lectin receptors may play a role in initial virus binding to DCs and she has been using viral binding assays with flow cytometry, confocal microscopy and real-time PCR to assess this. In future, she will look at co-localisation between virus and endolysomal pathway compartments to determine the mechanism of processing of these vectors. Further understanding of these factors may enhance the uptake, processing and presentation of such vaccines in these key antigen-presenting cells, currently recognised as a major hurdle to improving their efficacy. She is supported by an NHMRC Dora Lush scholarship

Poster Presentation – Board number 67

Hien Ho Thi

Hien Ho Thi is working on her PhD at the School of Public Health and Community Medicine in the University of New South Wales. Her supervisor is Associate Professor Lisa Maher.

The potential for a sudden and significant increase in HIV among ethnic Vietnamese injecting drug users (VIDUs) in Australia is a growing cause for concern. Her research aims to explore cultural influence on risk behaviours and prevalence of HIV and HCV among VIDUs. In-depth qualitative interviews (n=42) were used to identify underlying explanatory models of health and illness, and cultural beliefs and practices and their influence on risk behaviours. These data were used to develop a questionnaire designed to measure knowledge, risk behaviours and barriers to health and protective behaviours, and a linked serosurvey to assess antibody HIV and HCV prevalence (n=109). Results indicate that factors influencing vulnerability to blood-borne viruses (BBVs) include: cultural characteristics such as trust, obligation and stoicism; reluctance to discuss problems with outsiders; and a belief in fate. Limited knowledge of BBVs, low perceived risk and dislike of condoms may increase vulnerability. Beliefs in natural processes, traditional remedies and self-medication influence presentation, and barriers to service access include the stigma of injecting drug use, perceived lack of confidentiality, language and cost. The data indicate a need for interventions designed to reduce the risk of BBV transmission based on culturally specific meanings and contexts of health, illness and risk.

Oral Presentation – Saturday 4 September, Social Research Multicultural & IDUs Session 1.30pm – 3.00pm

Rachel Koldej

Based at the Women's and Children's Hospital, Rachel is currently studying for her PhD through the University of Adelaide. Her supervisors are Associate Professor Donald S. Anson and Associate Professor Keryn Williams.

Gene therapy has great potential for the treatment of a range of inherited and acquired diseases. However, its development has been hindered by a lack of efficient and effective gene-delivery systems. As the target cells are often non-dividing, the system must have the ability to infect non-cycling cells, preferably resulting in long-term stable genetic modification. HIV-1 naturally possesses these characteristics and therefore we have used it to develop a gene-transfer system. The system comprises a number of plasmids that separate the *cis* and *trans* functions of the virus. The *cis* functions are incorporated into a vector construct, while the *trans* (protein-coding) functions are distributed over a number of 'helper' or packaging plasmids preventing their transfer to target cells. Modifications have included the codon-optimisation of protein-coding sequences, and the use of alternate polyadenylation signals and the removal of splice donor sites within the vector construct. Future investigations will include a detailed analysis of the viral genome packaging signal, and the requirement for the Rev Response Element and various *cis* acting signals in the 3' and 5' Long Terminal Repeats.

Poster Presentation – Board number 71

Edwin Leeansyah

Edwin is a PhD student in the Department of Medicine, Monash University, conducting his research at the Macfarlane Burnet Institute for Medical Research and Public Health under the supervision of Dr Anthony Jaworowski and Prof. Suzanne Crowe. Born in Jakarta, Indonesia, he recently obtained his Bachelor of Biomedical Science with first class Honours from Monash University and is a recipient of an Australian Post-graduate Award.

Edwin is studying the effect of HIV-1 infection on phagocytosis of IgG-opsonised pathogens, specifically how HIV-1 impairs Fcγ receptor-mediated phagocytosis and how this contributes to AIDS-related opportunistic infections. In previous work, he has shown that HIV-1 infection of human monocyte-derived macrophages inhibits signal transduction of the Fcγ receptor (CD64) which signals via a protein called FcRγ or "γ-subunit" but does not inhibit signal transduction via CD32A, an Fcγ receptor which does not require the γ-subunit for signalling. This supports the hypothesis that HIV-1-related inhibition of Fc-phagocytosis is caused by a decreased expression of the γ-subunit.

In his study, Edwin aims to determine the mechanism by which HIV infection decreases expression of the γ-subunit and whether impaired signalling via this protein extends to other cells of the immune system which normally express this protein, such as NK cells and effector T-cells.

Poster Presentation – Board number 74

Josephine McGuiness

Josephine is studying for her Masters in Clinical Pharmacy at the Victorian College of Pharmacy, Monash University in Melbourne. She is employed as a clinical pharmacist in the Specialist Medicine team at the Alfred Hospital, Melbourne.

Her primary area of research interest is the integration of acute and community service providers for HIV-positive patients, to improve patient follow-up and continuity of care within this patient population. She is currently conducting a research project based at the Alfred Hospital called the Patient Information Exchange (PIE) study.

This aims to improve and formalise the process of information exchange between all the health care providers involved in the care of an HIV-positive patient and evaluate the benefits of implementing a new service utilising a case-management model of pharmaceutical care. The study measures the impact of assigning patients a 'primary' pharmacist (one pharmacist dedicated to an individual patient's care), allowing the provision of individualised care and improving follow-up of patients by acting as the key contact regarding all medication-related issues.

Oral Presentation – Friday 3 September, Issues in Primary Care Session 1.30pm – 3.00pm

Dimitra Zotos

Dimitra completed a Bachelor of Biomedical Science at Deakin University, Melbourne in 2003. She is currently in her Honours year. For her Honours project she is examining the immune isotype responses of long-term non-progressors (LTNP) and survivors (LTS) of HIV-1 infection. These individuals represent approximately 5% of the HIV-1 infected population, who don't progress to AIDS within eight to ten years. The cohorts with whom she will work are the Sydney Blood Bank Cohort (SBBC), the Sexually Acquired (SA) Cohort and the National Centre in HIV Epidemiology and Clinical Research Cohort (NCHECR). She is doing her research at the National Serology Reference Laboratory, St Vincent's Institute, under the supervision of Associate Professor Dale McPhee.

Oral Presentation – Friday 3 September, Basic Science HIV Pathogenesis Session 11.00am – 12.30pm

UNDERGRADUATE AND JUNIOR RESEARCH IN HIV & VIRAL HEPATITIS AWARDS PROGRAM

ASHM is making up to 6 support awards available in 2005. The awards are available to promote research interest in HIV and viral hepatitis.

Applications should be made in writing via the application form on the reverse side of this flyer, and must be received in the ASHM Office, Locked Mail Bag 5057, DARLINGHURST NSW 1300 by COB **31 March 2005**. Please attach a photocopy of your most recent academic transcript.

The grant will comprise:

- Annual ASHM associate membership for 2005, valued at $66
- Linkages between the student and ASHM members in the designated area of research interest
- Access to the ASHM website to allow students to place information about their research project
- Participation in relevant ASHM Standing Committees
- Access to ASHM library and resources
- First option to take on part-time research assistant positions offered by the Society
- Registration at the 2005 ASHM Annual Conference, valued at over $500
- A scholarship for recipients requiring travel and/or accommodation to assist with attendance at the Conference, to a value of $400
- An opportunity to present work in progress at the ASHM Conference in 2005
- Publication of a short report on the research initiative in an edition of ASHMNews.

Award categories and applications:

Applications are invited from all relevant disciplines, with priority given to medicine, nursing, dentistry and allied health. Applications must relate to a degree, diploma or award program but are not available for post-doctoral programs. Applications can be received for new work or work in progress. Applications that reflect national research priorities as outlined in the National HIV and Hepatitis C Strategies will be given priority. These can be found on the Commonwealth Health Website at www.health.gov.au or via the ASHM Website at www.ashm.org.au.

Adjudication:

The Committee will review the applications and successful applicants will be notified of the outcome of their application by 23 April 2005. Your supervisor may be contacted to attest to your suitability. You may also be required to provide more information but in the first instance please only complete the application following. If you have not yet determined a supervisor you may use an academic mentor on this application. Further information about ASHM can be obtained from our website http://www.ashm.org.au.

ashm
Australasian Society for HIV Medicine Inc

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AUSTRALASIAN SOCIETY FOR HIV MEDICINE INC. UNDERGRADUATE AND JUNIOR RESEARCHER SUPPORT AWARDS IN HIV AND HEPATITIS APPLICATION FORM

Please attach a photocopy of your most recent academic transcript. Feel free to attach any extra notes or supporting documentation.

Name: _____

Postal address: _____

_____

Phone number: _____

Email: _____

Course in which you are enrolled: _____

Department/faculty: _____

Institution: _____

Supervisor: _____

Supervisor contact details: _____

Please describe your area of research interest: _____

_____

_____

What do you hope to achieve? _____

_____

What is your interest in HIV or viral hepatitis? _____

_____

How could ASHM assist you? _____

_____

Supervisor's signature: _____

Date: _____

Applicant's Signature: _____

Date: _____

Form deadline: COB 31 March 2005
Send to: ASHM Office, Locked Mail Bag 5057, DARLINGHURST NSW 1300

ashm2004canberra
16TH AUSTRALASIAN CONFERENCE 2–4 SEPTEMBER 2004

FULL CONFERENCE PROGRAM

THURSDAY 2 SEPTEMBER 2004

7.30am	Registration
8.30am	**Opening Ceremony** **Royal Theatre** **Chairs: Frank Bowden & Clare Willington**
8.40am - 8.50am	Welcome to the Land
8.50am - 8.55am	Liz Dax, ASHM President
8.55am - 9.00am	**The Hon. Tony Abbott MP, Federal Health Minister**
9.00am - 9.20am	**Justice Michael Kirby, Sydney Chambers of Justice** The New AIDS Equation
9.20am - 9.40am	**Michael Kidd, President of the Royal Australian College of General Practitioners** The Management of HIV in Australian General Practice
9.40am - 10.00am	**Ninkama Moiya, Director of the National AIDS Council (PNG)** HIV/AIDS Epidemic in a Culturally Diverse Setting
10.00am - 10.10am	Frank Bowden, Conference Representative & Chair of the HIV/AIDS & STI Subcommittee
10.10am - 10.15am	**The Hon. Alexander Downer MP, Minister for Foreign Affairs**
10.15am - 10.20am	Darren Russell, Australian Federation of AIDS Organisations (AFAO)
10.20am - 10.25am	David Menadue, National Association of People Living with HIV/AIDS (NAPWA)
10.30am - 11.00am	Morning Tea in Exhibition & Poster Area - Exhibition Hall

11.00am - 12.30pm	**Symposium - AusAID (Symposium Sponsor) - Meeting the Challenge: HIV, AIDS & Regional Security**		**Concurrent - Basic Science -Therapeutics**		**Concurrent - Social Research - Risk**	
	Bradman Theatrette Chairs: Annmaree O'Keeffe		**Menzies Theatrette Chairs: Patricia Price & Sabine Piller**		**Nicholls Theatrette Chairs: Marian Pitts & John Ballard**	
11.00am - 12.30pm	A panel of speakers will be exploring this issue. There will be an opportunity for questions from the floor.	11.00am - 11.25am	Landay A - The Role of Innate Immunity in HIV Infection	11.00am - 11.15am	Mao L - Patterns of Sexual Risk Taking Over Time In the Health in Men (HIM) Cohort	
	The panel will include: A representative from the Population Health Branch of the Commmonwealth Department of Health and Ageing	11.25am - 11.38am	Arnott A- Early Antiretroviral Therapy (ART) and Treatment Interruption in HIV-1 Infection: The Impact on the Neutralising Antibody Response, Virus Evolution and Virus Control	11.15am - 11.30am	Malpas G - Summer Survival Sexual Health Survey of Young People's Sexual Behaviours, Attitudes and Risks	
	Professor Dennis Altman, President of the AIDS Society of Asia and the Pacific	11.38am - 11.51am	Nicolle MZ - Inhibition of HIV-1 Infection of Immature Monoctyte-Derived Dendritic Cells and CD4+ T Cells by Cyanovirin-N	11.30am - 11.45am	Egan C - International Backpackers Visiting Australia: Sexual Risk in Focus	
	Dr Mak Kham, Director of the Pacific Regional HIV/AIDS Project, International Development Support Services	11.51am - 12.04pm	Van Bockel D - Analysis of Peripheral and Lymph Node Effector Lymphocyte Activity Against Mycobacterium Antigens in HIV-Infected Individuals with Unresolved Non-Tuberculous Mycobacteria (NTM) Disease	11.45am - 12.00pm	Worth H - A Dance of Death? Gay Men, Crystal Meth and Unsafe Sex	
		12.04pm - 12.17pm	Dable J - Generation of Monocyte Derived Langerhands-Like Cells with Transforming Growth Factor-b, Interleukin-4, Granulocyte Macrophage-Colony Stimulating Factor and Tumour Necrosis Factor - a	12.00pm - 12.15pm	Willis JM - The Impact of Industry Structure and Social Organisation on Male Sex Worker Work Practice	
		12.17pm - 12.30pm	Mallon PWG - Nucleoside Reverse Transcriptase Inhibitors Decrease Monocyte Mitochondrial Gene Transcription, An Effect that Persists 6 weeks After Discontinuation of the Drugs	12.15pm - 12.30pm	Questions and Discussion	

12.30pm - 1.30pm	**Lunch in Exhibition & Poster Area - Exhibition Hall**					
12.30pm - 1.30pm					12.30pm - 1.30pm	**ASHM Annual General Meeting (AGM) - Sutherland Theatrette**
1.30pm - 1.50pm	**Symposium - Epidemiology - PREP**		**Concurrent - Basic Science - Diagnostics and Prognostics**		**Concurrent - Trends - Change in Clinical Patterns Ian Thompson Memorial Session**	**Concurrent - Nursing and Allied Health**
	Bradman Theatrette Chairs; Andrew Grulich & Stevie Clayton		**Menzies Theatrette Chairs: Patrica Price & Suzanne Crowe**		**Nicholls Theatrette Chairs: Ashley Watson & Paul Goldwater**	**Sutherland Theatrette Chairs: Kelly Tank & Ruth Primrose**
1.30pm - 1.45pm	Worth H - Prevention and Power: A Comparison of Four Prevention Technologies	1.30pm - 1.55pm	Price P - Alleles of the Gene Encoding Interleukin 1-a May Predict Control of Plasma Viremia in HIV-1 Patients on HAART	1.30pm - 1.43pm	Post J - Immune Restoration Disease: Time for Review	Riley RG - Refresh 2003: An Evaluation of Mainstream Support for a Retreat for Carers and People Living with HIV/AIDS
1.45pm - 2.00pm	Kaldor J - HIV Prevention Using Antiretroviral Agents: Current Status of Clinical Research	1.55pm - 2.08pm	Almeida C - Increase in Inflammatory Cytokine Levels in Abacavir Stimulated Mono-Nuclear Cells from HIV Infected Patients with Abacavir Hypersensitivity	1.43pm - 1.56pm	Ammaranond P - An Update on the Prevalence of Transmitted Drug Resistance Mutations in Inner Sydney: No Increase in Protease Resistance Mutations and a Decrease in RT Resistance Mutations During Period 2002-3	Cummins D - Smoking Cessation Program and HIV Positive Clients

2.00pm - 2.15pm	Duffin R - PREP and Biological Prevention - Consumer Perspectives	2.08pm - 2.21pm	Keane NM - HIV-1 Viral Load Not CXCR4 or CCR5 Viral Tropism may determine the Immune Response in HIV-1 Infected Patients During HAART	1.56pm - 2.09pm	Middleton T - Transmission of Antiretroviral Drug Resistant HIV Strains Between 1996 and 2003 in Victoria, Australia, and their Subsequent Evolution in Untreated Individuals	2.00pm - 2.15pm	Gibbie T - Depression and Neurocognitive Performance in Individuals with HIV/AIDS - 2 Year Follow-Up
2.15pm - 2.30pm	Fawkes J - PREP in Cambodia	2.21pm - 2.34pm	French MA - Low CD4 T-Cells on Effective Antiretroviral Therapy is Associated with Immune Activation and CD4 T-Cells Expressing Markers of Replicative Senescence	2.09pm - 2.22pm	Cysique LA - Neuropsychological Profile of AIDS Dementia Complex Across Pre and Post Highly Active Antiretoviral Therapy (HAART) Eras	2.15pm - 2.30pm	Hood C - Evaluation of a Primary Care Based Nutrition Service for People Living with, or at Increased Risk of, HIV Infection
2.30pm - 2.45pm	Van Griensven F - Tenofovir as a Pre-Exposure Prophylactic Drug for the Prevention of HIV Transmission among Injecting Drug Users	2.34pm - 2.47pm	Cheney - HIV-1 Persistence in Double Negative T Cells From Patients not Responding to Antiretroviral Therapy	2.22pm - 2.35pm	Watson KM - An Examination of Trends and Risk Factors for Hospitalisation of HIV/AIDS Patients Post the Introduction of Highly Active Antiretroviral Therapy (HAART)	2.30pm - 2.45pm	Hutchison C - A Novel Measure of Cognitive Function that is Sensitive to CD4 T-Cell Count in HIV-1
				2.35pm - 2.48pm	Marriott D - HIV-Infected Patients Admitted to the Intensive Care Unit; Outcomes in the Era of HAART		
2.45pm - 3.00pm	Questions and Discussion	2.47pm - 3.00pm	Wilson KM - Incidence Immunoassay for Distinguishing Recent from Established HIV-1 Infection in Therapy Naïve Populations	2.48pm - 3.00pm	Post J - To Routinely Offer Testing for HIV Infection in all Cases of Tuberculosis: A Rational Policy or a Waste of Resources?	2.45pm - 3.00pm	Thompson J - The Villa
3.00pm - 3.30pm	Afternoon Tea in Exhibition & Poster Area - Exhibition Hall						

3.30pm - 5.00pm	Symposium - Basic Science - Development of Vaccines Bradman Theatrette Chairs: Sharon Lewin & Steve Wesselingh		Concurrent - Clinical Medicine - Treatment Menzies Theatrette Chairs: Ashley Watson & Tuck Meng Soo		Concurrent - Community Uptake Phillip Medcalf Memorial Session Nicolls Theatrette Chairs: Bill Whittaker & Kirsty Machon		Concurrent - ART in Resource Poor Settings: Coming Ready or not Sutherland Theatrette Chairs: Edward Reis & Andrew Grulich
3.30pm - 4.00pm	Thomson S - New HIV and HCV Vaccine Candidates and Delivery Strategies	3.30pm - 4.00pm	Gazzard B - Salvage Therapy	3.30pm - 3.45pm	Menadue D - Mapping HIV Care and Support	3.30pm - 3.45pm	Dax EM - Simplifying Testing Strategies for the Diagnosis of HIV: Towards a Re-Evaluation
		4.00pm - 4.13pm	Carey C - ESPRIT (Evaluation of Subcutaneous Proleukin ® in a Randomised International Trial): CD4 +T-Cell Responses to Subcutaneous (SC) Recombinant Interleukin-2 (RIL-2)	3.45pm - 4.00pm	Velecky M - Aligning Funding with Changing Service Needs	3.45pm - 4.00pm	Zhou J - Rates of Short-Term Clinical Progression in the Treat Asia HIV Observational Database
4.00pm - 4.30pm	Purcell D - HIV Vaccines: Safety Considerations and Neutralising Antibody Responses	4.13pm - 4.26pm	Cordwell B - Silcaat: CD4+ T-Cell Responses to Subcutaneous (SC) Recombinant Interleukin-2 (rIL-2) After One Year	4.00pm - 4.15pm	Ritt I - Discerning HIV Related Disadvantage 20 years on: Improving Community Care to Meet the Changing Needs of People Living with HIV	4.00pm - 4.15pm	Kelly A - Increasing Awareness of Cognitive Impairments in Emerging Epidemics
		4.26pm - 4.39pm	Workman C - An Open Label Study to Determine the Efficacy and Safety of Enfurvirtide in Patients Changing Therapy to an NRTI-Sparing Regimen (ML16992)	4.15pm - 4.30pm	Rawstorne P - Trends in the Uptake and Use of Combination Antiretroviral Therapy in Australia since 1998	4.15pm - 4.30pm	Burke M - Foundational Issues in VCT in a PMTCT Setting in Tanzania
4.30pm - 5.00pm	Emery S - Safety and Preliminary Immunogenicity of a B-Subtype DNA Prime/Recombinant Fowlpox Virus Boost Prophylactic HIV Vaccine Candidate: Results of a Phase I/IIA Trial	4.39pm - 4.52pm	Chen L - Tenofovir-Related Nephrotoxicity (TRN) - Prevalence and Risk Factors	4.30pm - 4.45pm	Daye J - Challenges for Delivering Community Based HIV Treatments Programs	4.30pm - 4.45pm	Aye T-T - External Quality Assessment Schemes for Anti-HIV and Anti-HCV Testing
		4.52pm - 5.05pm	Winston A - The Normalised Inhibitory Quotient (NIQ) of Boosted Protease Inhibitors is Predictive of Viral Load Response Over 48 Weeks in a Cohort of Highly Treatment Experienced HIV-1 Infected Individuals	4.45pm - 5.00pm	Duffin R - HIV Drug Side Effects - One Positive Voice	4.45pm - 5.00pm	Zhou J - The Treat Asia HIV Observational Database: Baseline Data and Response to Triple Combination Antiretroviral Treatment from Retrospective Data
	Close						

FRIDAY 3 SEPTEMBER 2004

7.30am	**Registration**
7.30am - 8.30am	**Case Presentation Breakfast** **Swan Room** **Chair: Jenny Hoy & Clare Willington**
7.30am - 7.45am	Hamlyn E - Secondary Syphilis Presenting as Tonsilitis in Three Individuals
7.45am - 8.00am	Conway D - Finding the Index Case - The Challenges of HIV Risk Management in Clinical Practice
8.00am - 8.15am	Campbell A - Posterior Reversible Encephalopathy Syndrome (PRES) In an HIV Infected Patient
8.15am - 8.30am	Singh K - An Unusual Case of Cryoglobulin-Negative Vasculitis in a Man Co-Infected with HIV and Hepatitis C (HCV)
9.00am - 10.30am	**Plenary Session** **Royal Theatre** **Chairs: Liz Dax & David Cooper**
9.00am - 9.30am	**Brian Gazzard, Chairman of the British HIV Association** Guidelines for Routine Care
9.30am - 10.00am	**Mary Crewe, Director of the Centre for Study of AIDS at the University of Pretoria, South Africa** Understandings From The Epicentre
10.00am - 10.30am	**Frits van Griensven, Associate Director for Science of the HIV/AIDS Program of the Thailand MOPH - US CDC Collaboration (TUC)** Report from One of the Most Extensively Studied HIV Epidemics in a Non-Western Country - Thailand: Did it Help to Formulate the Response?
10.30am - 11.00am	**Morning Tea in Exhibition & Poster Area - Exhibition Hall**

11.00am - 12.30pm	**Symposium - Clinical Medicine - HAART (Undetectable)** **Royal Theatre Chairs: Ashley Watson & Ian Woolley**		**Concurrent - Basic Science - HIV Pathogenesis** **Bradman Theatrette Chairs: Steve Wesselingh, Anthony Cunningham**		**Concurrent - Nursing** **Menzies Theatrette Chairs: Philip Habel & Denise Cummins**		**Concurrent - Epidemiology of New infections Margaret MacDonald Memorial Session** **Nicholls Theatrette Chairs: Frits Van Griensven & Levinia Crooks**
11.00am - 11.20am	Sax P - Undetectable - But How Long Will It Last?	11.00am - 11.25am	Cunningham A - HIV Capture and Transmission by Dendritic Cells	11.00am - 11.15am	Lambert S - The Queensland HIV Nursing Practice Course: Responding to HIV Nursing Education in 2004	11.00am - 11.13am	McDonald A - Trends in Newly Acquired and Newly Diagnosed HIV Infection in Australia, 1994 - 2003
		11.25am - 11.38am	Verity E - Neutralising Antibody Responses in Long Term Survivors Infected with Attenuated HIV-1: Correlates to Replication Competent Virus	11.15am - 11.30am	Hennessy R - Clients' Satisfaction with HIV Pre-Test Counselling Appears Related to Previous Experiences of Testing and Risk Level	11.13am - 11.26am	Hellard M - HIV Sentinel Surveillance in Victoria - A Pilot Study
11.20am - 11.40am	Riminton S - Undetectable - But What About My Immune System?	11.38am - 11.51am	Davenport MP - Viral and Immune Dynamics Following Vaccination and SHIV Challenge in Macaques	11.30am - 11.45am	Akhurst D - The Domino Effect: The Complexities of Caring for Patients with HIV/AIDS in 2004	11.26am - 11.39am	Du Cros - Investigation of HIV Infection in Victorian Women, 1999 to 2003
		11.51am - 12.04am	Sasson SC - Progressive Dysregulation of the IL-7/R System in HIV-1 Infection	11.45am - 12.00pm	Gloede D - The Experience of Fatigue and Strategies for Self-Management among Community-Dwelling Persons Living with HIV	11.39am - 11.52am	McDonald A - Evaluation of a Detuned Antibody Testing Strategy for Detecting Incident HIV Infection
11.40am - 12.00pm	Russell D - Undetectable - But What Are the Pills Doing to My Body?	12.04pm - 12.17pm	Clarke JN - A New Concept of Restricted HIV-1 Infection of Astrocytes	12.00pm - 12.15pm	Tank K - A Room with a View: The Pitfalls of Long Term Admission in a Palliative Care Unit	11.52am - 12.05pm	Hellard M - Improving HIV Surveillance in Victoria, The Role of the "Detuned" EIA
						12.05pm - 12.18pm	Poynten M - Final Results from the Australian Non-Occupational Post Exposure Prophylaxis (NPEP) Observational Study
12.00pm - 12.30pm	Panel discussion	12.17pm - 12.30pm	Zotos D - Antibody Responses in HIV-1 LTNP/LTS: Unexpected Responses to Viral Antigens by IgG3	12.15pm - 12.30pm	Herrmann SE - Combining Adherence Monitoring with Patient Education in the Royal Perth Hospital Immunology Outpatient Clinic	12.18pm - 12.30pm	Ramacciotti T - A Comparison of the Western Blot Versus Detuned EIA Methods for Detection of Incident HIV Infection
12.30pm - 1.30pm	**Lunch in Exhibition & Poster Area - Exhibition Hall**						

1.30pm - 3.00pm	**Concurrent - Clinical Medicine - Metabolic Syndromes**		**Symposium - Basic Science - New Drug Strategies**		**Symposium - International - Responding to HIV: Policy and Implications in PNG**		**Concurrent - Issues in Primary Care Peter Meese Memorial Session**
	Royal Theatre Chairs: Andrew Carr & Debbie Marriott		**Bradman Theatrette Chairs: Anthony Cunningham & Scott Thomson**		**Menzies Theatrette Chairs: John Milan & Sean Riminton**		**Nicholls Theatrette Chairs: Tuck Meng Soo & Clare Willington**
1.30pm - 1.45pm	Mijch A - Subcutaneous Injection of Polylactic Acide (PLA) in Individuals with HIV-1 Infection Associated Facial Lipoatrophy: Six-Month Outcome and Predictors of Response	1.30pm - 2.00pm	Mak J - The Virion - Associated Cholesterol of HIV-1: A Potential Target for Topical Microbicide Development	1.30pm - 1.50pm	McBride WJH & Daoni E - Introduction of Antiretroviral Drugs in Papua New Guinea: The Pilot Program	1.30pm - 1.45pm	McGuiness JVG - The Findings of the Patient Information Exchange (PIE) Study: Improving the Transition of HIV Positive Patients from Hospital to Community Management
1.45pm - 2.00pm	Cummings R & Price B - New Fill: Facing the Challenges of Lipoatrophy			1.50pm - 2.05pm	Fletcher K - Implementing the Papua New Guinea HIV/AIDS Management and Prevention Act 2003	1.45pm - 2.00pm	Price B - Complex Patients: Evaluation of Care Manager Model (CCM)
2.00pm - 2.15pm	Rogers G - Rosiglitazone in Adults with HIV Lipoatrophy: 84 Week Follow-Up (Rosey Extension)	2.00pm - 2.30pm	Wilkinson J - Inhibition of HIV Entry into DCs: A New Strategy for Microbicide Development	2.05pm - 2.20pm	Rock J - Working with Collaborating Partners - NAPWA in PNG	2.00pm - 2.15pm	Ryan L - Strengthening the Relationship Between Health Promotion and General Practice
2.15pm - 2.30pm	Law M - Observed and Predicted Rates of Myocardial Infarction in the D:A:D Study			2.20pm - 2.35pm	Muke J - Making Social Messages Content Relevant to the Wahgi Society, Western Highlands Province, PNG	2.15pm - 2.30pm	Lambert SM - HIV Management and Treatment: Where Are We At & Where Are We Going? An Update of the Queensland Experience
2.30pm - 2.45pm	Rose H - Impairment of Reverse Cholesterol Transport in HIV Infected Subjects	2.30pm - 3.00pm	Tachedjian - Efavirenz, A Potent Enhancer of HIV-1 Reverse Transcriptase Dimerization, Affects the Late Stages of HIV-1 Replication	2.35pm - 2.55pm	Bun B - PNG Government Response to HIV	2.30pm - 2.45pm	Phillips ES - Mental Health in Primary Care
2.45pm - 3.00pm	Carter V - Effectiveness of a Dedicated Lipodystrophy Clinic in Reducing Hyperlipidaemia in HIV-Infected Individuals			2.55pm - 3.00pm	Questions and Discussion	2.45pm - 3.00pm	Curran G - Therapeutic Conversations in HIV/ AIDS Care
3.00pm - 3.30pm	**Afternoon Tea in Exhibition & Poster Area - Exhibition Hall**						

3.30pm - 5.00pm	**Concurrent - Clinical Medicine - Treatment Issues**		**Symposium - Epidemiology - Rises in New Infections**		**Concurrent - Basic Science - Molecular Biology**		**Concurrent - Indigenous - Emerging Issues in Indigenous Sexual Health**
	Royal Theatre Chairs: Mark Kelly & Jenny Hoy		**Bradman Theatrette Chairs: Don Baxter & Edwina Wright**		**Menzies Theatrette Chairs: Michael Malim & Andy Poumbourios**		**Nicholls Theatrette Chairs: Edward Reis & Rosemary McGuckin**
3.30pm - 3.45pm	Drummond F - The Smart (Strategies for Management of Anti-Retroviral Therapy) Study - Adherence to Strategy	3.30pm - 3.45pm	Rawstorne P - Rises in New Infections: Social Research Findings	3.30pm - 3.55pm	Malim M - The HIV Accessory Protein Vif and the Suppression of an Innate Anti-Viral Defence Mechanism	3.30pm - 3.50pm	Shannon C - Policy Implications of Emerging Priorities in Relation to Aboriginal and Torres Strait Islander Sexual Health Issues
3.45pm - 4.05pm	Debate: Continuous Therapy is Definitely the Only Way to Treat HIV – Isn't It?	3.45pm - 4.00pm	Wentzlaff-Eggebert M- Rises in HIV Infections: Gay Men's Education Responds	3.55pm - 4.08pm	Poumbourios A - The Engagement of Alternative Chemokine Receptors by R5X4 Env of HIV-1 Evokes Distinct Conformational Signals to the gp120-gp41 Association Site	3.50pm - 4.05pm	Saunders M - Investigating the Social World of Aboriginal People Living with HIV: Aboriginal and Torres Strait Islander Cohorts in the Australian "Futures" Studies
4.05pm - 5.00pm	Panel Discussion with Debbie Marriott moderating	4.00pm - 4.15pm	Ryan L - Beyond the action plan: Building the Long Term Response to Increases in HIV Infections in NSW	4.08pm - 4.21pm	Hill MK - Investigating the Role of the Spacer Peptide P1 in HIV-1 Replication	4.05pm - 4.20pm	Sailor R - Living and Loving Across the Serodivide
		4.15pm - 4.30pm	Grulich A - Resurgent Syphilis in Gay Men: Where To From Here?	4.21pm - 4.34pm	Bodetti T - Acetylation and Methylation Pathways are Required for Processing of HIV-1 Tat Protein by the Viral Protease	4.20pm- 4.35pm	Thompson SC - Just Gettin' On with My Life Without Thinkin' About It: Aboriginal Experiences of Living with HIV in Western Australia
		4.30pm - 4.45pm	Duffin R - The Impact of the Treatments Prevention Nexus on People with HIV	4.34pm - 4.47pm	Carr J - HIV Vif in Reverse Transcription Complexes	4.35pm - 4.50pm	Knibbs PG - The Territory Two Step - Enhancing Detection of Latent MTB in HIV Clients
		4.45pm - 5.00pm	Questions and Discussion	4.47pm - 5.00pm	Ranasinghe C - HIV Recombinant Fowl Pox Virus/Vaccinia Virus Mucosal and Systemic Prime Boost Vaccine Trial in MIC	4.50pm - 5.00pm	Questions and Discussion
5.15pm - 6.00pm	**HIV Futures 4: State of the (Positive) Nation - Royal Theatre**					**5.15pm - 6.15pm**	**Briefing on ASHM's International Policy and Programs - Nicholls Theatrette**
7.00pm	**Close Conference Dinner - National Museum of Australia**						

SATURDAY 4 SEPTEMBER 2004

7.30am	**Registration**
9.00am	**Plenary Session** **Royal Theatre** **Chairs: John Kaldor & Sharon Lewin**
9.00am - 9.30am	**Susan Kippax, Director of the National Centre in HIV Social Research** Medicalisation of Prevention
9.30am - 10.00am	Paul Sax, Clinical Director of the Division of Infectious Diseases and the HIV Program at Brigham and Women's Hospital, Boston HAART: when to start and what with
10.00am - 10.30am	Michael Malim, Professor and Head of the Department of Infectious Diseases at King's College, London Recent advances in HIV replication
10.30am - 11.00am	**Morning Tea in Exhibition & Poster Area - Exhibition Hall**

11.00am - 12.30pm	**Concurrent - Epidemiology of STIs**		**Concurrent - Models of Primary Care**		**Symposium - International Policy Initiatives**		**Symposium - ACON & NSW Health (Symposium Sponsor) - Gay Men & Condoms: Exploring the Rise in Unprotected Sex**
	Royal Theatre Chairs: Frank Bowden & Anna McNulty		**Bradman Theatrette Chairs: Clare Willington & Marilyn McMurchie**		**Menzies Theatrette Chairs: Marina Carman & Liz Dax**		**Nicholls Theatrette Chairs: Adrian Lovney & Lisa Ryan**
11.00am - 11.15am	Jin F - Prevalence and Risk Factors for Gonorrhoea and Chlamydia in the Health in Men (HIM) Cohort	11.00am - 11.15am	Rogers G - The South Australian Primary Care Health Care Programme for People with HIV and People Who May Be At Risk	11.00am - 11.30am	Crewe M - Best Policies Worst Epidemic	11.00am - 12.30pm	Presenters will include:
11.15am - 11.30am	Lim M - Epidemiology of HIV and Gonorrhoea in Victoria, 1993 - 2003	11.15am - 11.30am	Quan D - Holdworth House Medical Practice, A Sydney Model for HIV Patient Care				Stevie Clayton and Alan Brotherton from ACON
11.30am - 11.45am	Russell D - HIV/HSV Nexus	11.30am - 11.45am	Soo TM - The HIV/AIDS Program in Canberra	11.30am - 11.45am	Dinh K - Impacts of Regional and Bilateral Trade Agreements on Access to Medicines		Jeanne Ellard and Garrett Prestage from the National Centre in HIV, Epidemiology and Clinical Research
11.45am - 12.00pm	McGuigan D - Managing Sexually Transmissible Infections in Gay Men	11.45am - 12.00pm	Rogers G - A Primary Health Care Programme Provides Long-Term Benefits for Homosexually Active Men: Six-Year Outcomes of the Care and Prevention Programme	11.45am - 12.00pm	Reis E - Are Donor Dollars Really Helping National HIV Programs		Derek Chan from the Albion Street Centre
12.00pm - 12.15pm	Hamlyn E - Screening for Sexually Transmitted Infections in Individuals Receiving Non Occupational Post Exposure Prophylaxis	12.00pm - 12.40pm	Keany J - HIV Hypochondria: A Workshop Towards a Compassionate Approach	12.00pm - 12.15pm	Baxter D - The Treatments/Prevention Nexus - Where are we after Bangkok?		To be followed by a Panel discussion
12.15pm - 12.30pm	Pitts M - Secondary Students and Sexual Health			12.15pm - 12.30pm	Questions and Discussion		
12.30pm - 1.30pm	**Lunch in Exhibition & Poster Area - Exhibition Hall**						

1.30pm - 3.00pm	**Symposium - Clinical Medicine - Consult the Experts** **Royal Theatre** **Chairs: Ashley Watson & Joe Sasadeusz** **Panel: Paul Sax, Jonathon Anderson & Robert Finlayson**		**Concurrent - Community - HIV Prevention and Peer Education** **Bradman Theatrette** **Chairs: David Menadue & Geoff Honnor**		**Concurrent - Social Research - Multicultural** **Menzies Theatrette** **Chairs: John Ballard & Susan Kippax**		**Symposium - Basic Science - HIV Immunology** **Nicholls Theatrette** **Chairs: Scott Thomson & Miles Davenport**
	An interactive panel discussion will complement 3 case presentations by:	1.30pm - 1.45pm	Batrouney C - Social Capital and the Phenomenology of Barebacking	1.30pm - 1.45pm	Ho HT - Cultural Characteristics and Vulnerability to Blood Borne Viruses of Ethnic Vietnamese Injecting Drug Users	1.30pm - 2.00pm	Mallal S - HIV and HCV Adaptation to HLA Restricted Immune Responses
	Richard Moore from the Carlton Clinic, Melbourne, VIC	1.45pm - 2.00pm	Madeddu D - The Geography of the Gay Community 'Ghetto' in Sydney	1.45pm - 2.00pm	Nguyen O - What Role Do Key Informants Play in Helping Us to Understand and Address Blood Borne Virus Prevalence and Risk Behaviours Among Ethnic-Vietnamese Injecting Drug Users in Melbourne?		
	David Baker from 407 Doctors, Sydney, NSW	2.00pm - 2.15pm	Prestage G - Gay Community: Subcultures, Risks and 'Comfortableness'	2.00pm - 2.15pm	Korner H - Culture and Interdependence: Negotiating HIV Diagnosis and Disclosure Among People from Culturally and Linguistically Diverse Backgrounds	2.00pm - 2.30pm	Zaunders J - Proliferating Antigen-Specific CD4+ with a CCR5, Cytotoxic T Lymphocyte Phenotype During Primary HIV-1 Infection
	Vanita Parekh from the Canberra Sexual Health Centre, Canberra, ACT	2.15pm - 2.30pm	McGuigan D - Working with Gay Men whose Sexuality and Drug Use is Culturally Specific	2.15pm - 2.30pm	Higgs P - HIV and Injection Drug Use: Is HAART a Reality?		
		2.30pm - 2.45pm	Scott S - New Applications of Peer Education in Young Gay Men's Sexual Health Promotion	2.30pm - 2.45pm	Petrohilos M - Adherence and Diversity	2.30pm - 3.00pm	Lewin S - T-cell Decline and Immune Restoration in HIV
		2.45pm - 3.00pm	Canavan P - Positive in Prevention	2.45pm - 3.00pm	Keynan M - HIV/AIDS Multilingual Recorded Lines for People from Culturally Diverse Backgrounds		
3.00pm - 3.30pm	**Afternoon Tea in Exhibition & Poster Area - Exhibition Hall**						

3.30pm - 5.00pm	**Closing Session** **Royal Theatre** **Chairs: Frank Bowden & Liz Dax**
3.30pm - 3.50pm	Prizes
3.50pm - 4.50pm	Hypothetical with Dr Norman Swan, Host "The Health Report", ABC Radio National
4.50pm - 4.55pm	Frank Bowden - Closing remarks
4.55pm - 5.00pm	Levinia Crooks - 2005 ASHM Conference
	Close

ashm2004canberra
16TH AUSTRALASIAN CONFERENCE 2–4 SEPTEMBER 2004

ORAL PRESENTATION ABSTRACTS

THURSDAY 2 SEPTEMBER 2004

THURSDAY 2 SEPTEMBER 2004

Symposium - AusAID

MEETING THE CHALLENGE

O'Keeffe A[1]
[1]AusAID, Canberra, ACT, Australia

Australia's International HIV/AIDS Response will explore the regional impact of HIV/AIDS and serve to demonstrate that HIV/AIDS is much more than a 'health issue'. This will incorporate a focus on the issue of human security, as the virus cuts across boundaries and borders, potentially devastating populations and threatening sovereignty

and security. It will explore the importance of internationally relevant policy in strengthening nations' abilities and commitment to plan and implement regional and national HIV/AIDS strategies. The symposium will explore the Australian Government's role in preventing the spread of HIV/AIDS through a multifaceted approach of high-level political advocacy, partnerships that extend across regional bodies, governments and the private sector, and will also consider the role that civil society and community-based organisations play in ensuring an effective response to the disease and its impact.

Concurrent Session – Basic Science – Therapeutics

THE INNATE IMMUNE SYSTEM: PERSPECTIVE FOR NEW HIV IMMUNE THERAPY

Landay A[1]
[1]Rush University Medical Center, Chicago, Illinois, USA

The innate immune system provides the first line of defense against pathogens by recognition via germline encoded receptors: pathogen recognition receptors. The most well known of these receptors are the Toll like receptors. There have been at least 10 TLR identified in humans that mediate their action by NFK b activity and produce rapid inflammatory responses. We have begun to characterize the cellular elements of the innate immune system including plasmacytoid dendritic cells (PDC), myeloid dendritic cells (MDC) and iNKT cells. We have found a significant reduction in PDC, MDC and iNKT cell percentage in chronic HIV infection. These cell populations are not significantly restored in subjects on HAART. We have now begun studies to determine if we can stimulate innate immune effector cells by utilizing TLR agonists. Our efforts so far have focused on the use of immunostimulatory DNA sequences that mimic bacterial DNA known as CpG ODN. We have begun to evaluate the potential mechanisms by which CpG ODN can induce PDC, MDC and iNKT effector activity in vitro focusing on the critical role of iNKT cells in producing TH1 (IFN) or TH2 IL4) cytokines. These studies are now being extended to in vivo evaluation of CpG ODN as HIV and HBV vaccine adjuvants in primate and human studies. The results of these approaches provide basic mechanistic information on ways we might be able to utilize the innate immune response as a novel immune based therapy in HIV disease.

EARLY ANTIRETROVIRAL THERAPY (ART) AND TREATMENT INTERRUPTION IN HIV-1 INFECTION: THE IMPACT ON THE NEUTRALISING ANTIBODY RESPONSE, VIRUS EVOLUTION AND VIRUS CONTROL

Arnott A[1,2,3,5], Verity E[1,2,3,5], Wilson K[2,5], Ho J[2,3,5,6], Jardine D[2], Gorry P[3], Merlin K[4], Grey P[4], Kelleher A[4], Smith D[4], McPhee D[1,2,5,6], and the Pulse Study Team
[1]Monash University, Clayton, VIC, Australia; [2]National Serology Reference Laboratory, Fitzroy, VIC, Australia; [3]Burnet Institute for Medical Research and Public Health, Melbourne, VIC, Australia; [4]National Centre for HIV Epidemiology and Clinical Research, Sydney, NSW, Australia; [5]National Centre in Hepatitis and HIV Virology Research, Australia; [6]Melbourne University, Melbourne, VIC, Australia

In a cohort of 20 acutely HIV-1 infected subjects on ART in the PULSE study, the impact of treatment interruptions and the effect of viral phenotype were investigated. Subjects were fully adherent to HAART for up to one year prior to interruption, with undetectable viral loads (VL) for at least three months prior to STIs. Two ART resumptions were undertaken, should VL exceed 5 000 copies off ART. Plasma and serum samples were taken at Baseline (BL), during HAART and upon interruption.

Sixteen subjects demonstrated neutralising ability at BL with titres between 1:42 to 1:157 against the CCR5-using Clade B reference isolate HIV-1_{MBC925}. Thirteen of these had high coincident BL viral loads (>200 000 copies/ml). Based on our observation of early neutralising antibody responses, we are currently investigating the role of complement. Autologous virus was successfully isolated from BL serum in 15 of the 20 subjects by pelleting virus to remove excess antibodies and soluble factors. Seven subjects showed a highly significant increase in neutralisation against the reference isolate and five against autologous virus. However, there was no clear correlation between neutralisation and virus control. We were unable to isolate virus from BL samples for five subjects and viral replication was attenuated for a further six subjects. Of these eleven subjects, eight contained virus replication upon interruption. There was an observed correlation between viral replication phenotype and control of virus replication upon interruption.

Based on these findings, we are currently investigating viral fitness by real time PCR analyses and viral evolution using the V1V2 Genescan assay. Very little is currently known about the impact of ART interruptions on virus evolution. Based on our observed correlation between viral replication phenotype and virus control, the results of these studies will provide an important insight into the impact of early HAART and ART interruptions on viral evolution and fitness, and indeed the importance of initial viral phenotype as a clinical marker for future virus control.

INHIBITION OF HIV-1 INFECTION OF IMMATURE MONOCYTE-DERIVED DENDRITIC CELLS AND CD4+ T CELLS BY CYANOVIRIN-N

Nicolle M Z[1], Wilkinson J[1], Boyd M R[2], Cunningham A L[1]
[1]Centre for Virus Research, Westmead Millennium Institute, Sydney, NSW, Australia; [2]Cancer Research Institute, University of South Alabama, USA

Mucosal transmission of HIV-1 initially involves binding and uptake of the virus by dendritic cells (DCs) via interactions between the viral envelope protein gp120 and DC receptors, namely C-type lectin receptors (CLRs) and CD4. Upon uptake, DCs mature and migrate from the site of infection to the lymph nodes where they present HIV-1 to CD4+ T cells, resulting in explosive infection in these cells. One potential strategy designed to prevent mucosal transmission of HIV-1 involves the use of topical microbicides targeting the virus or DC receptors. This study is designed to assess the inhibitory activities of multiple microbicidal agents targeting either gp120 or CLRs that are potentially capable of preventing HIV-1 infection of DCs and thus preventing the subsequent transfer of the virus to CD4+ T cells.

Cyanovirin-N (CV-N), a cyanobacterial protein, binds to viral gp120. Currently we are testing the potential of this protein to block HIV-1 infection of DCs. HIV-1_{BAL} was pretreated with various concentrations of CV-N and subsequently used to infect immature monocyte-derived DCs for up to 120hr. At specific time points (0-96hr) CD4+ T cells were added to the DC culture. Using real time PCR, HIV-1 was quantified in the DC cultures and DC-CD4+ T cell co-cultures. The difference between these two results provided a measure of HIV-1 transfer from DCs to CD4+ T cells. 100% inhibition of HIV-1 infection in DCs was observed when HIV-1 was pretreated with CV-N at concentrations between 100 nM - 1 μM. The subsequent transfer of HIV-1 to CD4+ T cells was also inhibited. The toxicity of CV-N on DCs and CD4+ T cells was also assessed using real time PCR. In this assay CV-N demonstrated minimal cellular toxicity at all concentrations used. These findings suggest that complete inhibition of HIV-1 infection of monocyte-derived DCs can be achieved using a compound that specifically interferes with gp120 binding to CLRs and CD4, thus ultimately preventing the transfer of HIV-1 to CD4+ T cells. Further studies are designed to test the inhibitory activity of other microbicidal agents against various HIV-1 subtypes.

ANALYSIS OF PERIPHERAL AND LYMPH NODE EFFECTOR LYMPHOCYTE ACTIVITY AGAINST MYCOBACTERIUM ANTIGENS IN HIV- INFECTED INDIVIDUALS WITH UNRESOLVED NON-TUBERCULOUS MYCOBACTERIA (NTM) DISEASE

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Up to 25% of HIV-infected individuals with late stage disease may experience immune restoration disease (IRD) related to opportunistic infections including NTM within 8 weeks of commencing HAART. NTM-IRD manifests with localised inflammation +/- colliquative necrosis of superficial/deep lymph nodes (LN). Moreover, while the pathogen is visualised in affected LN tissue it often fails to grow in culture.

Samples were analysed from three HIV-infected individuals with chronic (>12 months) NTM-IRD. Systemic and localised immune responses to the purified protein derivatives of *Mycobacterium tuberculosis* (MTB) and *Mycobacterium avium-intracellulare* (MAI) were assessed using IFN-γ ELISpot, IL-2 and IFN-γ intracellular cytokine (ICC), and lympho-proliferative (LPA) assays.

PBMCs were isolated from all three individuals and cervical LN cells from two. ELISpot and LPA were used to determine a dose-response curve to MTB and MAI using fresh PBMC (n=4) and LN cells (n=1). ICC was performed using 5μg/mL of MTB and MAI on fresh whole blood (n=4) and LN cells (n=1).

Optimal concentrations of MTB and MAI antigens for ELISpot and LPA varied between individual's PBMCs but were in the range of 1-10μg/ml. Furthermore, while LPA and ELISpot responses correlated qualitatively, there was no direct relationship between the magnitude of these responses.

The ICC assay of PBMC revealed that the mean antigen-specific IFN-γ response to MTB and MAI was 0.8% (range 0.31-1.71%) and 1.71% (range 0.73-4.02%) of CD4+ T cells, respectively. Mean IL-2 production to MTB and MAI was 0.56% (range 0.13-1.33%) and 1.32% (range 0.39-0.54%) of CD4+ T cells respectively. Correlations between IL-2 production and proliferative responses are being explored.

In the one subject with LN tissue available for comparison, the LN responses as measured by ICC to mycobacterial antigens were 2.5 to 5-fold greater than PBMC responses: 1.76% and 2.63% against 0.31% and 0.99% of CD4+ T cells to MTB and MAI respectively.

PBMC responses to MTB and MAI antigens were readily detected in individuals with NTM-IRD, with responses to MAI generally higher. These persistently exuberant immune responses to low antigen loads of mycobacteria may be contributing to the pathogenesis of NTM-IRD and may have implications for therapeutic strategies.

GENERATION OF MONOCYTE DERIVED LANGERHANS-LIKE CELLS WITH TRANSFORMING GROWTH FACTOR-B, INTERLEUKIN-4, GRANULOCYTE MACROPHAGE-COLONY STIMULATING FACTOR AND TUMOUR NECROSIS FACTOR-A.

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Langerhans cells (LC) are immature dendritic cells (DC) which are generally believed to play an important role in the mucosal transmission of HIV-1 infection and virus dissemination. Present within in the epidermis, genital tracts, bronchi and mucosae, LC are characterised by the expression of Langerin, E-cadherin, the chemokine receptor CCR6 and by the presence of Birbeck granules (BG). The monocyte derived DC (MDDC), is a unique in vitro cell type expressing CD1a and both the C-type lectin receptors (CLR) DC-SIGN and mannose receptor (MR) but not Langerin. Recent studies by our group have demonstrated the importance of both CLRs in DC-HIV interactions. To further study HIV-1 interactions with the Langerin receptor, a suitable in vitro model is required. Our aim was to produce a monocyte derived Langerhans-like cell (MDLC), using the cytokines IL-4, GM-CSF, TGF-β and TNF-α. TGF-β has been shown to induce BGs which associates with internalised Langerin and therefore may increase the overall amount of Langerin expressed. IL-4 and GM-CSF have been shown to upregulate CD1a and downregulate CD14. TNF-α was used because of its ability to induce some langerin expression when applied to CD34+ progenitor cells. High purity CD14+ monocytes were isolated using elutriation, cultured for three days with cytokine combinations of GM-CSF, IL-4 and TGF-β□□ and then cultured for a further three days in the presence of TNF-α. Cell surface phenotype was determined by flow cytometry, using a panel of monoclonal antibodies; CD1a, CD14, Langerin, E-cadherin, CCR6, DC-SIGN, MR and CD83. Early results demonstrated the importance of TGF-β and TNF-α for the upregulation of Langerin on the surface of the cells. Titration of these four cytokines in combination resulted in a cell with a mean langerin and CD1a surface expression of 26% (ranging from 14-50%). These preliminary results suggest that CD14+ monocytes may be manipulated into expressing CD1a and Langerin, a more representative model of in vivo tissue DCs.

NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS DECREASE MONOCYTE MITOCHONDRIAL GENE TRANSCRIPTION, AN EFFECT THAT PERSISTS 6 WEEKS AFTER DISCONTINUATION OF THE DRUGS

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NRTI side effects include bone marrow suppression (anaemia, increased mean corpuscular volume (MCV)) and lipoatrophy. Although NRTIs may inhibit adipocyte DNA polymerase γ, affecting mitochondrial (mt) replication, it is unclear if mtDNA depletion is the primary defect in NRTI induced toxicity in these tissues.

We examined monocyte and adipose tissue mtRNA expression from 20 HIV-negative volunteers randomised to 6 weeks d4T/3TC or AZT/3TC, followed by 6-weeks washout. Assessments included clinical history, fasting lipids and glucose, and measurement of body composition. Adipose tissue biopsies were performed at weeks 0 and 2 and whole blood monocyte extracts prepared at weeks 0, 6 and 12. RNA was extracted and mtRNA expression measured by real-time RT-PCR. Results are expressed relative to β-actin expression.

	Week 0	Week 2	Week 6	Week 12
Haemoglobin (g/L)	150 [6.5]	146 [6] **	143 [8] *	147 [9]
MCV (fL)	88.5 [4]	89 [3] **	92 [3] ***	92 [4] ***
Adipose COX1	1.64 [1.2]	0.58 [1.7]		
Monocyte COX1 (COX1/b-actin)	1.16 [0.4]		0.59 [0.2] *	0.57 [0.3] **

Table 1. Values are median [IQR]. 'p' values: *<0.05 **<0.01 ***<0.0001

Median age was 41 yrs (IQR 14.5) and 90% were male. Both groups were matched for baseline parameters with no change in body composition or serum lipids by week 6. Haemoglobin concentrations dropped by week 6, more in the AZT/3TC group, returning to baseline by week 12. MCV rose to week 6 in both groups, a feature which persisted to week 12. Adipose tissue mtRNA expression, as judged by COX1 expression, was significantly decreased at week 2 in fat and at week 6 in monocytes (table 1). Like the changes in MCV, decreased monocyte mtRNA expression persisted to week 12, six weeks after stopping drug.

In HIV-negative volunteers, exposure to AZT/3TC or d4T/3TC decreases mtRNA expression in both monocytes and adipose tissue, with the effect in monocytes persisting six weeks after discontinuing the drugs.

Concurrent Session – Social Research – Risk

PATTERNS OF SEXUAL RISK TAKING OVER TIME IN THE HEALTH IN MEN (HIM) COHORT

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Health in Men (HIM) is an open cohort of HIV-negative gay men in Sydney. Every twelve months, participants undergo a face-to-face interview and an HIV test. From July 2001 to December 2003, 346 men completed three annual face-to-face interviews. These men were the basis of the analyses herein.

Sexual risk taking was defined as *any* unprotected anal intercourse with casual (UAI-C) or with HIV-positive/unknown-status regular partners (non-concordant UAI-R). Patterns of sexual risk taking were examined in each of the six-month periods prior to respective interviews. Frequencies of sexual risk taking were also investigated.
Based on the three annual interviews, 143 men (41.3%) consistently reported no sexual risk; 154 men (44.5%) reported sometimes engaging in sexual risk taking but not in all three rounds; and 49 men (14.2%) reported engaging in sexual risk taking in each of the three rounds. For these 49 men, four men consistently engaged in non-concordant UAI-R *only* (an average of 25 non-discordant UAI-R episodes per person per six months); 17 men consistently engaged in UAI-C *only* (an average of 10 UAI-C episodes per person per six months); and 28 men engaged in a mix of non-concordant UAI-R and UAI-C (an average of 45 non-concordant UAI-R and/or 10 UAI-C episodes per person per six months).

Consistent engagement in sexual risk taking is not most commonly reported among HIV-negative gay men in Sydney. However, a considerable proportion of HIV-negative gay men sporadically engage in non-concordant UAI-R and/or UAI-C over time. Such practice places HIV-negative men at a heightened risk for HIV infection.

SUMMER SURVIVAL SEXUAL HEALTH SURVEY OF YOUNG PEOPLE'S SEXUAL BEHAVIOURS, ATTITUDES AND RISKS

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The key aim of the research was to identify sexually transmitted infection risk factors among the general youth population to help inform and plan sexual health promotion initiatives targeting young people. During the summer of 2003/2004 a convenience sample of 455 people aged 16-25 years were surveyed throughout south east Sydney. The research was an innovative partnership between sexual health services, youth services, local councils and young peer-educators. Data collection using a self-administered survey was integrated in to the annual sexual health peer outreach projects called "Summer Survival". The survey collected information about the social, behavioural and attitudinal aspects of young people's lives in relation to sexual health.

Survey respondents included over 50 different cultural backgrounds, at least 18% had sexual feelings that were non-heterosexual, and 81% had experienced sexual intercourse. Key results identified: low levels of respondents reporting they "always" use condoms during sexual intercourse; the concerning interplay between sex, not using condoms, alcohol/drugs and unwanted sex; the general willingness to access GPs for sexual health issues; the high significance of peers as a source of sexual health information; the importance of school sexuality education; the lack of access to parental support; and that half of the young people did not have a Medicare card.

The research has implications for planning responsive sexual health education, treatment and support interventions. Many varied factors make young people highly vulnerable to sexually transmitted infections. Health promotion initiatives need to: harness the dynamics of youth peer relationships; utilise peer-education models; incorporate alcohol and other drugs in to all sexual health education; develop the capacity of school communities and parents to address sexual health; improve access to general practitioners and sexual health services.

INTERNATIONAL BACKPACKERS VISITING AUSTRALIA: SEXUAL RISK IN FOCUS

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This study explored the sexual risk behaviours of international backpackers visiting Australia to determine whether this risk taking increased or was restricted to the backpacking context. Patterns of casual sex and condom non-use behaviour before and during their backpacking trip were compared. Self-administered questionnaires were completed by 563 backpackers deriving from 23 countries aged 18-39 years staying in backpacking hostels in Sydney and Cairns, Australia. In addition, 14 semi-structured interviews were conducted with Doctors, Nurses and Counsellors employed at 8 travel and sexual health clinics in Sydney. Almost half (47%) of the sample reported sex with one or more casual partners during their trip, i.e. sex with someone met within the same day or evening. More than half of those with no casual sex experience before the trip did engage in casual sex with someone they met during the trip. 37% of backpackers did not use a condom during their last encounter of sex with someone new. While most backpackers carry condoms and appear to intend to use them with new partners, unprotected sex remains common. 24% of those who reported "negotiating" condom use did not use a condom on the last occasion of sex with someone new. Perception of risk was low. While over half of the sample who did not use a condom with their last new partner regarded their risk of acquiring HIV as very low to nil. 3 participants had acquired HIV on this backpacking trip. Drinking alcohol, often to excess, is central to the backpacking setting and is both a reason for and a post-facto justification of unprotected sex. Youth embarking on a backpacking trip overseas should be made aware of the risk of sexually transmitted infections (STI). Recommendations by clinic staff with experience of treating and counselling backpacking populations will be discussed. These findings highlight the need for more broad-based dissemination of information on STIs to youth, particularly those who endeavor to backpack overseas and for those who are visiting Australia. This population needs to be informed on cost-effective sexual health services available to them while traveling in Australia in order to control the dissemination of STIs and HIV.

A DANCE OF DEATH? GAY MEN, CRYSTAL METH AND UNSAFE SEX

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Crystal meth use amongst gay men has been linked to unsafe sex and specifically to sexually adventurous gay men. Crystal and its relationship with unsafe sex has variously been called, by the media (including the gay media), 'a cascade of disasters', 'a serious health risk predisposing a young section of [gay men] to high-risk sexual behaviour', and 'a dance of death'.

Using data from Gary Smith's study of sexually adventurous men, we will examine the ways in which gay men, while using drugs for sexual pleasure, develop strategies to minimise potential harms. In general, most interviewees recognised the tension between the pleasures and dangers of drug use for sex, and employed a range of self-regulating strategies to ensure drug use remained controlled and pleasurable, and that sexual safety was paramount.

THE IMPACT OF INDUSTRY STRUCTURE AND SOCIAL ORGANISATION ON MALE SEX WORKER WORK PRACTICE

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We report on changing patterns of social organisation and emerging cultural meanings of male sex work by examining the occupational structure and work practices of a sample drawn from each sector of the male sex work industry in Melbourne (street-based, agency/brothel, and private work). We examine these as occupationally distinctive, structurally differentiated work sectors.

We used post-modern ethnography, including non-participant observation, media and policy analysis, key informant interviews and sexual life history interviews and focus groups with 54 Melbourne workers for a rich account of their social world.

We documented trajectories into and out of sex work, features of each industry sector, and recruitment and training processes as workers move between sectors. Different relationships between industry sectors and Government affect individual work practices, including the ways in which "safety" and "risk" are operationalised.

Structurally informed analysis, treating the nature and effects of work as functions of social organisation, differentiated between social characteristics and consequences of different types of sex work. Findings suggest there are distinctive features of the workers involved in these different types of sex work, and that there are patterned structural features of the work itself that facilitate or inhibit HIV transmission.

Symposium – Epidemiology – PREP

PREVENTION AND POWER: A COMPARISON OF FOUR PREVENTION TECHNOLOGIES

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There has been much discussion of late about the success or otherwise of prevention in the context of sexual transmission of HIV, where 'prevention' is usually taken to mean condom use. Monogamy and abstinence, as strategies for HIV prevention, are also under debate. While condoms are the most widely used prevention tool, other forms of prevention technologies include: microbicides, vaccines, post exposure prophylaxis (PEP) and pre exposure prophylaxis (PREP).

This paper briefly describes these six prevention strategies and evaluates each of them with reference to a number of criteria: safety, efficacy, accessibility and affordability, acceptability to the user and user's sexual partner, and social and public health impact.

The HIV epidemic is driven by social, cultural and economic inequalities. While prevention of HIV is to a large degree within the control of individuals, unlike diseases such as polio and malaria, power imbalance of any sort limits people's ability to protect themselves from HIV infection. Each of the six prevention strategies is evaluated in terms of the above criteria and with particular reference to power imbalances, such as those produced and shaped by gender and wealth.

Abstinence and monogamy are ineffective as public health prevention strategies. Condoms currently afford the best prevention: they are safe, effective, accessible and affordable, acceptable to most users and their partners, and are socially painless. The other three forms of prevention technologies are currently comparatively less successful than condoms. Although they may provide a source of prevention, their introduction needs to be monitored carefully so that they do not undermine the success of condom use. The more technological forms of prevention need to be incorporated with behavioural prevention.

HIV PREVENTION USING ANTIRETROVIRAL AGENTS: CURRENT STATUS OF CLINICAL RESEARCH

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As the new millenium began, there was a growing realisation that an effective HIV vaccine or vaginal microbicide was still years, maybe many years from reality. Faced with intractably high HIV transmission rates in many parts of the world, attention turned to the possibility of an alternative biomedical prevention strategy, based on chemoprophylaxis. Among the antiretroviral drugs with proven effectiveness against active infection, tenofovir rapidly emerged as a favourite candidate, being well tolerated with a good resistance profile, and supported by animal data that were strongly suggestive that the drug could abort infection if present at the time of exposure.

Several groups began planning safety and efficacy studies in people at higher risk of infection. Such populations were likely to be the immediate beneficiaries of an effective biomedical prevention measure. In any case it would never be possible to prove efficacy in populations at lower risk, because of the prohibitive sample size requirements.

HIV prevention trials involving chemoprophylaxis raise a number of ethical issues, most of which they share with vaccine and microbicide trials. Any prevention study needs to contemplate its impact on current safe sex practice, availability of HIV care for those found to be infected during the trial, and medical care of participants who experience adverse events in the trial.

After several years of preparatory work, randomised double blind controlled trials are now at various stages of development and implementation in eight countries. Populations being recruited in these trials include women involved in sex work, people who inject drugs, gay and bisexual men, and adults aged under 30. It is likely that the first results will be available by early 2007.

PREP AND BIOLOGICAL PREVENTION – CONSUMER PERSPECTIVES

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A number of different biological prevention technologies are under development. The development time frame for vaccines and microbicides allows appropriate debate about policy and implementation. However consensus opinion is that these technologies will not be available for many years.

Pre-exposure prophylaxis, however, is available now and trial results on its effectiveness are likely in a relatively short time frame. In Australia, relatively little attention has so far been given to the policy debate about the best and most appropriate ways to use this technology.

The Australian Federation of AIDS Organisations has prepared a detailed discussion document on Pre-exposure Prophylaxis. Responses to this document will be discussed and proposals for further processes to develop an appropriate policy response put forward.

PREP IN CAMBODIA

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Sex workers are consistently targeted as participants for research and most recently for the trial of new treatments and vaccines in Africa, Cambodia etc. As such the Australian HIV/AIDS sector and Organisations like Scarlet Alliance, AFAO, NAPWA and the National Research Centres have a clear role in advocating to ensure such trials do not jeopardize the health and safety of the sex workers who participate in research.

Following an Associated press article in March, 2004 reporting 'Health authorities were recruiting 960 sex workers in Cambodia to participate in a one-year study of the drug, tenofovir DF' and the complaints from local sex workers regarding particular elements of the research, Scarlet Alliance met with, and documented, the concerns of Women's Network for Unity, a Cambodian sex worker group.

The concerns raised are directly related to the support participants are entitled to during and after the Pre-exposure chemoprophylaxis (PREP) trial aimed at measuring the effectiveness of tenofovir. However, the group also raised ethical concerns about wealthier countries conducting trials on participants in less developed countries along with the effectiveness of such trials and the choice of a double blind placebo based trial. There are also concerns about the level of information provided on the existing questions around longer term side effects ie kidney toxicity.

Whilst Scarlet Alliance has long argued the necessity for development of best practice Ethical Guidelines for research conducted with sex workers. The events in Cambodia also raise the need for greater debate on the responsibility of this sector to ensure involvement in new technologies and treatments research is equally balanced between vested interest in the outcomes and our ethical responsibility to critique the impact on communities who participate in research, in this case sex workers.

Concurrent Session– Basic Science – Diagnostics & Prognostics

ALLELES OF THE GENE ENCODING INTERLEUKIN-1A MAY PREDICT CONTROL OF PLASMA VIREMIA IN HIV-1 PATIENTS ON HAART

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Some HIV patients treated with HAART do not resolve their plasma viraemia and/or HIV RNA may reappear after a period of virological control. We investigated whether polymorphisms in cytokine genes affect control of plasma HIV over five years on HAART.

The study utilised 81 adult HIV-infected patients treated in Western Australia. All patients had a CD4 T-cell count <100/µl before HAART and achieved immune reconstitution assessed by CD4 T-cell counts. Plasma HIV RNA levels were followed from commencement of HAART.

Control of plasma viraemia could be predicted from carriage of allele 2 at position -889 in the *IL1A* gene (IL1A-889*2). This was significant when assessed by the proportion of patients with a plasma HIV RNA level ≤400 copies/ml (p=0.002). At 48 months post-HAART proportions were approximately 0.76, 0.51 and 0.32 for IL1A(1,1), (1,2) and (2,2) patients, respectively. The outcome was independent of the patients' CD4 T-cell counts before or on therapy, drug regimen or age. Polymorphisms in *IL6, TNFA, IL1B* or *IL12B* had less significant effects, which became marginal when *IL1A* was included in the statistical model.

IL1A-889 was in linkage disequilibrium with a non-synonymous polymorphism at IL1A+4845. *IL1A+4845* may be the active polymorphism because IL1A-889 does not affect known transcription factor binding sites in the *IL1A* promoter and has no clear effect on transcription. IL-1α is translated as a 31kd precursor protein and cleaved by m-calpain to form a C-terminal fragment (able to interact with the IL-1 membrane receptors) and a N-terminal domain. The cleavage site lies close to the residue affected by *IL1A+4845.* Allele 2 encodes serine and allele 1 encodes alanine at this position. Calpain digestion is promoted by phosphorylation of residues near the cleavage site, so the additional serine residue could promote digestion, enhancing release of the C-terminal fragment from the cell. Cells homozygous for IL1A-889*2 (and hence IL1A+4845*2) release more IL-1α protein. The N-terminal domain of IL-1α contains nuclear localisation signals and can promote oncogenesis or interact with RNA processing pathways and promote apoptosis. Thus N-terminal IL-1α (generated in larger quantities by cells with IL1+4845*2) may promote HIV disease, via enhanced survival of infected T-cells and rapid apoptosis of infected antigen-presenting cells.

The results suggest that alleles carried at IL1A-889 or IL1A+4845 predict control of HIV replication in previously immunodeficient patients responding to HAART. An additional patient cohort is sought to verify these findings.

INCREASE IN INFLAMMATORY CYTOKINE LEVELS IN ABACAVIR STIMULATED MONO-NUCLEAR CELLS FROM HIV INFECTED PATIENTS WITH ABACAVIR HYPERSENSITIVITY

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Genetic factors including MHC alleles, *HLA-B*5701* and *Hsp70 Hom M493T* highly predispose Caucasoid abacavir-recipients to hypersensitivity. Depletion of immunological $CD8^+$ T cells abrogate an abacavir specific TNF production in cultured mono-nuclear cells suggesting a MHC class I restricted immune response to abacavir and or its haptenated derivative.

In this study, we sought to examine abacavir specific inflammatory cytokine response in cultured PBMCs from HIV infected abacavir hypersensitive (ABC HSR) (n=10), abacavir tolerant (n=8), abacavir unexposed (n=7) individuals. PBMCs were separated from heparinised whole blood by Ficoll density gradients and cryo-preserved. Abacavir was used at a final concentration of 4µg/mL. Production of INF gamma, IL-2, IL-4 was measured by ELISA (Pharmingen) and TNF by flow cytometry. Abacavir stimulated inflammatory cytokine expression was also examined by microarray analysis (GEArray™Q series kit for chemiluminescent detection, SupperArray Bioscience Corp).

Abacavir stimulated INF gamma production was significantly higher in ABC HSR individuals (median 42.5 pg/µL, IQR: 1.7 to 82.95) compared to abacavir tolerant (median –9.6 pg/µL, IQR –18.1 to –1.4) or unexposed individuals (median –20.6 pg/µL, IQR –24.4 to –10.7) (P = 0.01). Intracellular TNF levels were also substantially higher in ABC HSR compared with tolerant individuals (P= 0.008). Increased mRNA expression of pro-inflammatory cytokines and chemokines occurred in response to a 24 hr abacavir stimulated mono-nuclear cells of abacavir hypersensitive individuals as determined by microarray analysis.

Inflammatory cytokine levels are significantly elevated in patients with abacavir hypersensitivity thereby influencing the pathophysiology of this reaction. These data suggest that an abacavir specific immunological response *in vitro* may be useful as clinical diagnostic marker and may help to clarify the immunological mechanisms involved in the development of abacavir HSR.

HIV-1 VIRAL LOAD NOT CXCR4 OR CCR5 VIRAL TROPISM MAY DETERMINE THE IMMUNE RESPONSE IN HIV-1 INFECTED PATIENTS DURING HAART

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Highly Active antiretroviral therapy (HAART) increases CD4 T-cell counts, decreases HIV-1 viral load and increases responses to antigens in HIV patients who were extremely immunodeficient before treatment. However antigen specific responses do not improve in all patients. This may be affected by both viral and host factors. HAART decreases viral co-receptor usage and can change the cytokine environment. Here, we determined the viral tropism of seven HIV-1 infected patients and evaluated their immuno competence over five years using ELISA to measure soluble (s) CD30, lymphocyte activation gene-3 (LAG 3) and CD26 DPPIV enzyme activity and interferon gamma (IFN-γ) and interleukin-5 (IL-5) ELISpot assays to assess antigen and mitogen induced responses.

X4 virus was isolated from two drug naive patients when they had <50 CD4 cells /ul and high plasma viral loads. These patients had a sustained virological response to HAART. R5 viruses were isolated from two patients failing treatment. Two X4 viruses and one R5 virus were isolated from three patients whose control of viral replication was delayed during HAART.

We found increased sCD30 levels in all seven patients when they had detectable plasma HIV-RNA. sCD30 levels decreased with control of viral load and correlated inversely with CD4 T-cell numbers. LAG 3 levels were usually low (1.1 pg/ml) but were increased in 6/7 patients when they had detectable viral loads. High numbers of IL-5 producing cells were found in 6/7 patients during HAART. Numbers of IL-5 producing cells increased during HAART in the two treatment naïve patients who cleared X4 viraemia and remained higher than controls thereafter. PHA-induced IFN-γ responses increased in all patients with control of viral load. CMV antigen-induced IFN-γ responses increased in the two treatment naïve X4 patients during HAART, and in the two X4 patients who controlled their viral load, but responses were also seen in the two R5 patients failing treatment.

In conclusion, we found increased sCD30 and LAG3 levels in patients with replicating X4 or R5 virus, but no association between viral tropism and CMV IFN-γ responses within this small group of patients.

LOW CD4 T-CELLS ON EFFECTIVE ANTIRETROVIRAL THERAPY IS ASSOCIATED WITH IMMUNE ACTIVATION AND CD4 T-CELLS EXPRESSING MARKERS OF REPLICATIVE SENESCENCE

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The magnitude of late-phase CD4 T-cell increases in HIV patients receiving effective antiretroviral therapy (ART) varies widely. This is only partly determined by production of naïve T-cells through thymic and extra-thymic pathways. We have previously shown that some patients receiving effective ART have persistent immune activation and investigated if this affects reconstitution of CD4 T-cells.

All HIV patients who had received ART for at least a year, and had a nadir CD4 T-cell count <100/µL and plasma HIV RNA level <50 copies/mL for at least 6 months, were included in the study (n=78). Patients were divided into tertiles by CD4 T-cell count and/or percentage and studies undertaken in the groups with low and high CD4 T-cells (<300/µL [n=25]) and >400/µL [n=20] respectively). Immune activation was assessed using plasma soluble TNF receptor I (sTNFRI) levels and the frequency of $CD38^+$ and $HLA\text{-}DR^+$ T-cells. The frequency of T-cells expressing CD57 (a marker of replicative senescence) and serum levels of interleukin-7 (IL-7) [a regulator of T-cell homeostasis] were also determined.

Plasma sTNFRI levels were higher in patients with low CD4 T-cells (median: 3530 pg/ml vs 1341pg/mL; p<0.001). The frequency of $HLA\text{-}DR^+$ CD4 T-cells was also higher in the low CD4 T-cell group (median: 8.8% vs 2.9%; p=0.005) but there was no difference in $HLA\text{-}DR^+$ CD8 T-cells. The frequencies of $CD38^+$ CD4 and CD8 T-cells were not significantly different in the two groups. However, the frequency of $CD57^+$ CD4 T-cells was substantially higher in the low CD4 T-cell group (median: 10.3% vs 1.7%, p<0.001). The frequency of $CD57^+$ CD4 T-cells did not correlate with plasma sTNFRI levels or the frequency of $HLA\text{-}DR^+$ CD4 T-cells. There was no difference in serum IL-7 levels between groups.

We conclude that low CD4 T-cell counts in patients receiving effective ART are associated with immune activation and an increased frequency of CD4 T-cells with a low replicative capacity. An expected increase of serum IL-7 levels in the low CD4 T-cell group was not observed. These findings have important implications for the use of ART and/or IL-2 therapy in HIV patients with low CD4 T-cell counts.

DEVELOPMENT OF AN AN INTERNATIONAL EXTERNAL QUALITY ASSESSMENT SCHEME RESULTS IN THE IMPROVEMENT OF DETECTION OF DRUG RESISTANCE MUTATIONS

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An ongoing, international quality assessment scheme (IEQAS) was established in 2000 to standardise HIV-1 genotypic antiretroviral (ARV) resistance testing to

1. Determine the level of concordance of the sequence data and the ARV report.
2. Determine the ability of each laboratory to detect drug resistance mutations (DRM)
3. Provide an on going assessment of performance.
4. Identify technical factors critical for obtaining optimal sequence results.

The IEQAS includes 12 laboratories from Australia, New Zealand, Canada and Korea. Four plasma samples are distributed to participating laboratories annually. Laboratories are requested to perform ARV and provide the DNA sequence for analysis. We determine a target genotype (TG) for each sample and compare the sequences from each laboratory with the TG.

IEQAS results from 2000 to 2003 demonstrated:

1. A reduced level of concordance at sites associated with drug resistance (DR) compared with sites NOT associated with DR.
2. A reduced level of concordance at sites that contain mixtures of nucleotides compared with sites where a single nucleotide is present.
3. A direct correlation between a laboratories ability to detect mixtures (2 or > nucleotides present at same position) and the percentage of (DRMs) they detect. >70% of mixtures detected resulted in 100% DRM reported.
4. Laboratories are improving in their ability to detect mixtures.
5. The mean % of DRM reported by laboratories has increased from 81.6% in 2000 to 98.4% in 2003

We believe that critical factors for an effective quality assessment scheme include the distribution of clinical material, the identification of factors associated with obtaining optimal results and the ability to monitor performance between sample distributions. Our IEQAS satisfies these criteria and has resulted in an overall improvement in laboratories being able to identify DRM. The ability to identify mixtures is a critical issue for improving concordance between laboratories.

INCIDENCE IMMUNOASSAY FOR DISTINGUISHING RECENT FROM ESTABLISHED HIV-1 INFECTION IN THERAPY NAÏVE POPULATIONS

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In order to characterise the maturation of the humoral immune response to human immunodeficiency virus (HIV-1) infection, and to seek a specific antigen-antibody interaction as a marker of recent infection, we have examined in detail the antibody isotype-specific responses generated to HIV-1 antigens during seroconversion. During maturation of the immune response to HIV-1 infection there is a rapid and sustained IgG response to all the major proteins transcribed by the *env, gag* and *pol* genes. The major antibody isotype contributing to this broad response is IgG_1. Data obtained from panels of specimens collected longitudinally from individuals infected with HIV-1, has indicated that isotype-specific responses to different HIV-1 antigens appear at different time points following infection and often only appear transiently. We have found an early transient peak of IgG_3 reactivity to p24 that spans approximately 1 to 4 months following HIV-1 infection. The presence of IgG_3 reactivity to p24 permits established infection to be distinguished from recently infected individuals during this time period. An assay specific for anti-p24 IgG_3 reactivity provides an estimate of the incidence of HIV infection that may be applicable for epidemiological surveys as well as monitoring new infections during vaccine trials and managing treatment programmes.

Concurrent Session – Change in Clinical Patterns

IMMUNE RESTORATION DISEASE: TIME FOR REVIEW?

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The paradoxical worsening of opportunistic infections (OIs) with antiretroviral therapy (ART), the development of inflammatory conditions of uncertain origin and the development of new OIs after treatment with ART have all complicated the introduction of ART. They have collectively been termed Immune Restoration Disease (IRD). IRD was first reported in 1992. (AIDS 1992; 6:1293) It has been recognized in association with a range of disorders including mycobacterial infections, cytomegalovirus, *Pneumocystis jiroveci*, PML, Kaposi's sarcoma and possibly with hepatotropic viruses. At our hospital services we have recognized a number of cases where a diagnosis of IRD has either not been considered, caused significant morbidity or mortality or was associated with extensive (and expensive) investigation or required Intensive Care admission. The risk factors for this condition are incompletely defined. Similarly the pathogenesis of the condition and the optimal treatment strategies are unclear.

We will report a series of cases, illustrating the difficulties in diagnosis and management. We will discuss the recently proposed diagnostic criteria for IRD and our plan for national data collection of IRD events.

AN UPDATE ON THE PREVALENCE OF TRANSMIITTED DRUG RESISTANCE MUTATIONS IN INNER SYDNEY: NO INCREASE IN PROTEASE RESISTANCE MUTATIONS AND A DECREASE IN RT RESISTANCE MUTATIONS DURING PERIOD 2002-3

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We set out to monitor the level of genotypically determined drug resistance mutations in recently transmitted virus by monitoring their prevalence in patients identified with acute HIV-1 primary infection in Sydney.

Reverse transcriptase (RT) and protease (PR) regions were sequenced from plasma virus using a standard automated DNA sequencing platform (Trugene, Visible Genetics, Ontario, Canada).

299 therapy naïve patients have had a laboratory diagnosis of acute primary HIV infection (< 4 bands on Western blot +/- p24 Ag positive) made at St Vincent's Hospital between April 1992 and December 2003 and have plasma samples suitable for determination of genotypic resistance. Mean time from laboratory diagnosis of primary infection to sampling for resistance testing was 2.1 days. Since December 2001, 114 such individuals have been identified. Previously reported data collected up till December 2001 on 185 individuals showed that primary mutations in the protease gene were rare (3/185) and levels of primary mutations in RT were relatively stable at 14.3% in 2000 and 9.7% in 2001, having peaked at > 50% in 1995.

During 2002-2003 no primary PR mutations were observed. The level of primary mutations in RT appears to have plateaued and may even be decreasing (6.0% (3/50) in 2002and 4.7%(3/64) in 2003). We have seen an increase in the revertant TAM mutation T215D/C/S occurring in 7.9% of samples compared to 3.5% in the period 1996-2001. Unlike others studies, we have not seen an increase in the K103N multidrug NNRTI resistance mutation. These results contrast markedly with recent reports from other western urban areas such as New York and San Diego.

There does not appear to be any increase in the rates of genotypic drug resistance in transmitted virus in this predominantly urban population of MSM despite high rates of uptake of antiretroviral therapy in the HIV-infected population. The differences in these results from other similar North American studies may be attributed to availability of easily affordable medications and has implications for treatment policies in this and other countries.

TRANSMISSION OF ANTIRETROVIRAL DRUG RESISTANT HIV STRAINS BETWEEN 1996 AND 2003 IN VICTORIA, AUSTRALIA, AND THEIR SUBSEQUENT EVOLUTION IN UNTREATED INDIVIDUALS

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Transmission of antiretroviral (ARV) drug resistant HIV appears to be increasing and is likely to have a major impact on subsequent therapy and clinical progression. We assessed the level of transmitted drug resistance in Victoria, Australia between 1996 and 2003.

Genotyping was performed on plasma from 300 individuals recently infected with HIV within the previous 12 months. The evolution of the predominant resistant strain in ten individuals who acquired drug resistant virus at the time of infection but were not treated with ARV drugs was followed in association with viral load and CD4 counts.

Forty individuals had evidence of transmitted drug resistance. Class-specific drug resistance was as follows: <1% for protease inhibitors, 6% for nucleoside reverse transcriptase inhibitors and 3.6% for nonnucleoside RT inhibitors. Resistance to more than one class of drug was found in 3% of individuals. The most common mutations transmitted were thymidine analogue mutations (50%), M184V (10%), K103N (30%) and mutations associated with saquinavir resistance (10%). We followed ten individuals infected with resistant virus were not treated during the follow up period compared to a control group of individuals infected with wildtype virus (n=12). In the control group the virus load decreased by 0.8 $\log_{10}$ and the CD4 count by 85 cells/µl over the next 14 months. In contrast, individuals with resistant virus who did not undergo antiretroviral therapy post infection had a stable virus load and a decrease in CD4 count of 144 cells/µl over the same period.

Over the last 8 years transmission of drug resistant virus was approximately 13% in recently infected individuals in Victoria, Australia. Individuals who had primary HIV infection with resistant virus did poorly in terms of their virological and immunological response compared to individuals infected with wildtype virus.

NEUROPSYCHOLOGICAL PROFILE OF AIDS DEMENTIA COMPLEX ACROSS PRE AND POST HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) ERAS

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There is recent evidence that the pattern of neuropsychological impairment is changing in non-demented advanced HIV-infected HAART-treated individuals with increasing deficits in learning, complex attention besides persistent psychomotor slowing. Therefore it is important to investigate whether these changes can be observed in individuals who develop AIDS Dementia Complex (ADC) on HAART or whether the deficits remain identical to pre-HAART ADC.

Twenty-nine individuals with ADC stage 1 (mild dementia) & 2 (moderate dementia) were recruited in 1993-1994 and were on dual therapy of Zidovudine and Didanosine (*dual-therapy cohort*). Twenty individuals with ADC stage 1 & 2 on HAART were recruited in 1999-2002 (*HAART cohort*). Thirty-three matched seronegative controls for age and education were recruited for the dual-therapy cohort and thirty controls for the HAART cohort. All participants were examined with a standard neuropsychological examination assessing five cognitive domains. Comparisons between the cohorts were made on standard scores derived from controls.

As expected, the severity of neuropsychological impairment was diminished in the HAART cohort compared to the dual-therapy cohort. The neuropsychological profile in the HAART cohort showed comparable frequency of deficits to the dual-therapy cohort in learning, complex attention and psychomotor speed. There was improvement in memory, motor-coordination and verbal generativity. In the dual-therapy cohort neuropsychological scores were not associated with CD4 cell counts. In the HAART cohort, the nadir CD4 cell count was significantly associated with better recall [r=.48 ; p<.03].

In conclusion, the neuropsychological pattern of impairment does not demonstrate any worsening areas in the HAART cohort. However, similar to non-demented HIV-infected individuals, learning, complex attention and psychomotor slowing are the cognitive domains that show less benefit from HAART. The unequal neurocognitive benefit of HAART may be triggering a partial change in the neuropsychological profile of ADC patients where the traditional feature of cognitive slowing is essentially associated with executive dysfunctions more specifically involving mental flexibility, organisation and strategic skills as in learning and complex attention tasks. Whether this pattern change represents partial inactivity of ADC, differential penetration of HAART into certain brain *regions* (not just penetration into the brain), or a new process will be addressed by prospective studies.

AN EXAMINATION OF TRENDS AND RISK FACTORS FOR HOSPITALISATION OF HIV/AIDS PATIENTS POST THE INTRODUCTION OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART)

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The aim of this study was to define the risk factors for prolonged hospitalisation amongst a group of HIV infected patients. It was expected that prolonged hospitalisation would principally manifest in non-AIDS related illnesses, HAART related drug toxicities and poor immune response. The International Classification of Diseases, 10th Revision (ICD-10-AM) coded discharges of all HIV inpatients between May 2001 and January 2003 were matched to the Alfred HIV observational clinical database. A prolonged hospitalisation group was defined as those patients with cumulative length of stay in excess of 37 days (90th percentile of the State Average Length of Stay) in a 21-month period. Of the 204 hospitalised patients 77.0% (n=157) comprised the non-prolonged hospitalisation group, whilst 23.0% (n=47) comprised the prolonged hospitalisation group. The prolonged hospitalisation group accounted for 4062 (66.5%) of the total bed days. In both crude and adjusted logistic regression analyses, non-AIDS related infections, serious medical conditions (non-AIDS and non-infectious), social/accommodation issues, malignancy (AIDS related), and AIDS related opportunistic infections were found to be associated with prolonged hospitalisation. Poor immune response and HAART related drug toxicities failed to remain significant in the final multi-variate logistic regression model.

HIV-INFECTED PATIENTS ADMITTED TO THE INTENSIVE CARE UNIT; OUTCOMES IN THE ERA OF HAART

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Between January 2001 and December 2003, 32 HIV-infected patients underwent 37 separate admissions to the Intensive Care Unit (ICU), St. Vincent's Hospital, Sydney. This represents 1.7% of all admissions during this period. Overall, 4 patients died in the ICU, 5 died during the hospital admission and 23 (72%) were discharged. Nineteen patients were alive 6 months after discharge, one patient had died and 3 were lost to follow-up. Thirty eight per cent of admissions were HIV-related and 95% were male with a mean age of 45 years. The mean CD4 count was 191 (survivors, 253 and non-survivors 79, $p < 0.05$) and the mean viral load 301,225 copies/ml. Forty nine per cent of patients were receiving anti-retroviral therapy. Ten patients had a previous AIDS defining illness and 23 patients had HIV infection of >5 years duration. The mean APACHE II score was 29, median 26, range 13-45. Six deaths were related to HIV, and 3 of 4 patients with *P.carinii* pneumonia who required mechanical ventilation died. HIV infection was diagnosed on admission to the ICU in 5 patients who died.

This is the first Australian study to look at the outcome of ICU admission for HIV-infected patients. Although less than half the patients were receiving HAART and the mean CD4 count and viral load suggested significant immunodeficiency, overall, 87.5% of patients were alive on discharge from ICU and 72% left hospital, representing a significantly lower mortality rate than other published studies, and a comparable survival rate to HIV non-infected patients managed in the ICU during the same period. The APACHE II score loading for HIV infection may be inappropriate in view of the similar mortality to HIV-negative patients. HIV infection, regardless of the stage of the disease, should not alter a clinical decision to admit a patient to the ICU.

TO ROUTINELY OFFER TESTING FOR HIV INFECTION IN ALL CASES OF TUBERCULOSIS: A RATIONAL POLICY OR A WASTE OF RESOURCES?

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Recent data suggests that HIV serostatus is known in only 27% of cases with *Mycobacterium tuberculosis* (MTB) disease in Australia. (CDI 2003; 27: 455) The prevalence of HIV infection was 3.9% in those tested, and at least 1% overall. The incidence of MTB infection is increasing in NSW with a younger population being diagnosed and an increasing proportion of extrapulmonary disease reported. (Int J Tuberc Lung Dis 1998; 2:647) The reason for this trend has not been defined. HIV infection is known to be associated with a higher rate of extrapulmonary MTB disease and HIV infects a young sexually active population. Tuberculosis is increasingly reported as an AIDS defining condition in Australia. (J AIDS 2002; 29: 388) In South Eastern Sydney, at least 16% of cases with MTB lymphadenitis have HIV co-infection. (Aust NZ J Med 1998; 28:453) There are Australian data confirming that the incidence of MTB infection is markedly higher in the HIV seropositive population than the overall population.

The current National Strategic Plan for TB Control in Australia (March 2002) suggests that there is little overlap between the TB infected communities and the HIV community and makes no specific recommendations except to monitor the incidence of MTB infection in the HIV seropositive population. However, when these infections overlap there are significant clinical issues including a higher risk of dissemination, MTB reactivation, re-infection with MTB and possibly accelerated HIV disease progression. The opportunity for HIV diagnosis and the attendant benefits also need consideration.

Some authorities recommend that clinicians "consider" HIV infection in every case of tuberculosis. Clinicians may interpret such advice in many ways. Should they test those with clinical clues of immunodeficiency, specific risk factors, severe MTB disease, or offer universal testing? The HIV Testing Policy (ANCHARD, IGCARD, 1998) recommends testing of those from a high prevalence country or those with signs or symptoms of HIV infection. Data from North America would suggest that clinicians are unable to accurately predict HIV infection in persons with MTB infection.

I will present an argument for a policy of universally offering testing for HIV infection in all cases of tuberculosis.

Concurrent Session– Nursing and Allied Health

'REFRESH' 2003: AN EVALUATION OF MAINSTREAM SUPPORT FOR A RETREAT FOR CARERS AND PEOPLE LIVING WITH HIV/AIDS

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This paper documents the process and outcomes of 'refresh', the first retreat for people living with HIV/AIDS (plwha) and their carers. This successful and innovative retreat was held in October 2003 for plwha and their respective carers from the Hunter and Central Coast regions.

This presentation will look at three themes: 1) utilising resources from a mainstream agency, 2) providing support to carers, and 3) positive outcomes for plwha.

This is the first time a mainstream agency, The Commonwealth Carer Respite Centre (CCRC), in partnership with an HIV/AIDS non-government agency, Karumah, has funded a retreat for plwha. This is despite the fact that retreats have been a feature for many years in the landscape of service delivery for plwha.

The motivation for approaching mainstream agencies is based on both equity principles and the fact that they are providing services that HIV services do not provide. CCRC as the funding body, and the staff of the retreat, are looked at in terms of their ability and willingness to respond to the needs and circumstances of plwha. The ability to respond is most limited by CCRC's definition of 'carer'. The willingness to respond was most enhanced by the involvement of plwha in the training prior to the retreat.

Evaluations by plwha, carers and camp staff demonstrate the benefits of effective partnerships between HIV specific and mainstream agencies. Significant outcomes are highlighted including the formation of an ongoing HIV Carers Support Group.

SMOKING CESSATION PROGRAM AND HIV POSITIVE CLIENTS

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As antiretroviral (ARV) medications have a positive affect on life expectancy other health conditions may become important to the general health of the HIV positive person. ARV's may have side effects, which may increase the risk of heart disease. Those who smoke tobacco products and are taking ARV's may be at increased risk of this. The study aimed to ascertain smoking prevalence and behaviour, clients' knowledge concerning smoking, whether smoking habits had changed in relation to HIV diagnosis and factors associated with participation in a smoking cessation program.

The program consisted of a questionnaire for current and ex smokers. Successful recruits to program had an initial counselling session with a social worker. Each was given nicotine replacement therapy (NRT) for 8-12 weeks. The participants had a diary to note daily events and collected a weekly supply where they received support and monitoring for any side effects of NRT. On completion of NRT, follow-up consisted four sessions at six weekly intervals for six months.

53% stated smoking helped them cope with HIV and 46% stated that living with HIV has made it harder to give up smoking. Ex-smokers stated health and finances as reasons for ceasing smoking. 27 enrolled in the smoking cessation program. 93% had been smoking for > 10 years. 52% had tried to cease previously. Of those 70% stated stress as the reason for relapsing. 14 clients did not complete the program, 2 for unrelated medical conditions. Of the 13 that completed the program, 7 ceased smoking and 8 had reduced their intake. By 6-month follow-up, 6 had ceased smoking, 3 had reduced intake and 4 had returned to previous levels of smoking behaviour.

Smoking behaviour is related to many issues. These issues need to be explored and support given to people with HIV/AIDS who are trying to cease smoking.

DEPRESSION AND NEUROCOGNITIVE PERFORMANCE IN INDIVIDUALS WITH HIV/AIDS – 2 YEAR FOLLOW-UP

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The aims of this study were to follow a cohort of HIV infected individuals for two years to: assess changes in neuropsychological performance, explore the relationship between depression, HIV and cognitive performance; to examine the influence of Highly Active Antiretroviral Therapy (HAART) on depression and neurocognitive performance.

HIV seropositive outpatients were assessed at baseline (2001) and at two-year follow-up (2003/2004). At each assessment patients completed the Beck Depression Inventory (BDI), Structured Clinical Interview-DSM-IV (SCID-CV), neuropsychological tests including the Hopkins HIV Dementia Scale (HDS) and Cambridge Automated Neuropsychological Test Battery (CANTAB). Details regarding illness progression, adherence and 'at-risk' behaviours were recorded.

Baseline results: 34.8% (45/129) scored ≥14 on the *BDI* (≥14 suggests depressive symptoms (DS). The *SCID-CV* revealed 27% (35/129) of participants met the criteria for current mood disorder. High levels of depressive symptoms occurred in those participants who were found to be socially isolated and in poorer general health. 7% (9/129) of the participant's scores on the *HDS* indicated HIV associated cognitive changes, a decrease in everyday thinking skills.
Follow-up results: 80 participants retested at two-year follow-up and were spilt into two groups based on *BDI* scores at baseline.

Two-Year Follow-up of Individuals with and without Depressive Symptoms at Baseline		
	Baseline BDI < 14 (2001)	Baseline BDI ≥ 14 (2001)
N	54	26
BDI score ≥ 14 (2003/04)	10 (18%)	16 (61%)
Δ CANTAB performance **– Attention & Executive function** **– Psychomotor speed** **– Spatial working memory**	 Sig. improved Sig. improved Sig. improved	 Stable Stable Stable
– Spatial planning test	Sig. improved	Sig. improved
Plasma HIV RNA < 50 copies/ml	30 (57%)	13 (50%)
AIDS	12 (23%)	10 (39%)
Mean CD_4 count cells/µl (range)	561 (13-1325)	468 (9-1119)

Approximately 1/3 of participants in phase one and follow-up scored above the cut-off for symptoms of depression. CANTAB results revealed the cohort were significantly impaired on 9/10 measures compared with age-matched normative data, however, comparing *DS* vs no *DS*, the group with *DS* performed significantly worse on 1/10 measures. Neurocognitive performance significantly improved for participants with no *DS* at baseline, whereas participants with *DS* at baseline did not show this improvement. These results suggest a relationship between HIV illness, symptoms of depression and neurocognitive performance.

EVALUATION OF A PRIMARY CARE BASED NUTRITION SERVICE FOR PEOPLE LIVING WITH, OR AT INCREASED RISK OF, HIV INFECTION

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Comprehensive nutrition services are accepted as an integral aspect of care for people living with HIV infection. A review of recent literature indicates that most published research in this area has assessed nutritional interventions using primarily clinical measurements (e.g. BMI, dietary intake, CD4 count) to evaluate their benefit and impact within a tertiary care setting. There appears to be limited published studies examining primary care-based utilisation of nutrition services for people living with HIV, or patient satisfaction with those nutrition services.

The purpose of this study was to evaluate patient utilisation and satisfaction with a primary care-based dietetic service provided as part of 'The Care & Prevention Programme' during 1998 - 2003. The programme provides a multidisciplinary, integrated primary health care service for people living with, or at increased risk of, HIV infection in South Australia and is based centrally in a metropolitan general medical practice.

Individual consultations were offered to programme participants by a dietitian experienced in HIV medicine and men's health. Case-note and database records collated the total number of participants' visits, appointment length and reasons cited by participants for attendance. At regular programme reviews, client satisfaction surveys were undertaken.

Nutrition services were utilised by a large proportion of participants. Satisfaction levels with the service provided were high and increased over time. Reasons for attendance varied between HIV positive and HIV negative people and qualitative data suggested that lifestyle factors such as income and symptoms of illness impacted significantly on participants' perceptions of their ability to improve their nutritional status.

The presentation outlines all significant results including the important role that a dietitian has when working within primary care-based services for people living with, or at increased risk of HIV infection. These results also emphasise the importance of evaluating patient satisfaction to ensure best practice care.

A NOVEL MEASURE OF COGNITIVE FUNCTION THAT IS SENSITIVE TO CD4 T-CELL COUNT IN HIV-1

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There is a need for sensitive tests that can detect early cognitive changes in medically asymptomatic HIV+ populations. More specifically, there is a need to identify subgroups within this population that may be at risk of progressing to HIV-related dementia (HIVD). The present study evaluated the efficacy of a novel, automated test (the Subtle Cognitive Impairment Test, SCIT) at differentiating HIV+ individuals at varying stages of the disease.

The first part of this study examined 53 HIV+ men with scores ranging from 16 (unimpaired) to 3 (impaired) on the HIV-Dementia Scale (HDS), and compared their performance on several measures of cognition (Grooved Pegboard, the CANTAB, and the SCIT). The second part of the study used the same tests to compare their performance as a function of disease stage and CD4+ T-cell count: asymptomatic T-Cell > 500/mL (n = 13), asymptomatic T-Cell < 500/mL (n = 14), symptomatic/AIDS T-Cell >500/mL (n = 10), symptomatic/AIDS T-Cell <500/mL (n = 16).

All measures were sensitive to HDS score (GPB dominant $r(53) = -.363$, $p < .05$; GPB nondominant $r(53) = -.468$, $p < .01$; Simple RT $r(53) = -.473$, $p < .01$. However, the SCIT showed the highest correlation with performance on the HDS ($r(53) = -.527$, $p < 01$). Further, the test was not significantly influenced by depression ($r(53) = .106$. $p > .05$). The second part of the study found that SCIT scores were highly sensitive to CD4 status ($r(53) = -.439$, $p < .01$). Performance was significantly better in the asymptomatic T-Cell > 500 group relative to those with T-Cells < 500 ($t(25) = -2.107$, $p < .05$). Similarly, participants in the symptomatic/AIDS T-Cell > 500 group performed at a significantly higher level than symptomatic/AIDS T-Cells < 500 participants ($t(24) = -2.145$, $p <. 05$).

The findings indicate that the SCIT is a sensitive measure of cognitive impairment in HIV infection. Further, it showed that the SCIT is highly sensitive to CD4 T-cell status. These data suggest that the SCIT may prove to be a useful clinical tool in discriminating HIV+ individuals who are at risk of progressing to HIVD.

'THE VILLA'

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'The Villa' represents a unique partnership between health, housing and ADAHPT, a NSW statewide service for people with HIV and Complex needs. ADAHPT has assumed responsibility for care and support whilst SWISH (South West Inner City Housing) has taken responsibility for the provision and maintenance of housing. In addition to the ADAHPT/SWISH partnership, the project is made possible by a network of partnerships, including those with a number of other specialist HIV/AIDS agencies within the Central Sydney Area, other health and support teams, government as well as private agencies.

The 'Villa' partnership is based on the principle that by providing adequate support, people living with HIV/AIDS who have cognitive impairment and complex needs are able to maintain secure accommodation. Through the range of partnerships an additional level of care in the continuum of HIV supported accommodation has been provided, as well as an increase in the overall HIV supported accommodation capacity.

This paper will describe the ADAHPT co-case management model used at 'The Villa' to provide support to HIV positive people with complex needs in order to sustain long-term tenancy. Prior to tenancy at 'The Villa' the residents have been seen as having unconventional lifestyles and have been unable to manage independently in the community. Some residents have spent considerable time living at 'The Bridge' where they received twenty-four hour care and support.

The partnerships used in this model of care aim to provide more flexible support specifically around individual need. Such partnerships working together to provide case management, brokered care, assessment of living skills and training as well as medical care have enabled the clients to maximise their independence. Assessment conducted with residents before and after involvement in this project shows that considerable improvement has occurred. Discussion of this assessment will form part of the presentation.

A case study will be used to highlight one particular client's journey from almost complete dependence in a hospital setting, through twenty four hour support at our residential facility, 'The Bridge', to his current situation of tailored support at 'The Villa' as he moves towards his ultimate goal of living independently in the community.

Symposium – Basic Science – Development of Vaccines

NEW HIV AND HCV VACCINE CANDIDATES AND DELIVERY STRATEGIES

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The Synthetic Vaccine Laboratory and Vaccine Immunology group has been developing a range of new HIV, HCV and TB vaccine candidates in collaboration with a number of researchers and institutions around Australia. Two main approaches have been used to develop the genetic sequences for the candidates; the whole gene approach that includes extensive safety modifications and a novel scrambled antigen vaccine (SAVINE) technology. Recent research has also involved the development of new delivery approaches that are variations of the prime boost approach originally developed in the group. The presentation will describe an overview of the vaccines under development by the lab, features of the candidates, summarise testing undertaken in the group and present an overview of the future direction of vaccine development.

HIV VACCINES: SAFETY CONSIDERATIONS AND NEUTRALISING ANTIBODY RESPONSES

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An optimal HIV vaccine would stimulate both high levels of HIV-specific T-cells and broadly neutralising antibody. CTL-based vaccines that express multiple HIV proteins blunt the viral load and the onset of pathogenesis but do not prevent infection. The expression of multiple HIV proteins and pseudoviral particles broadens the coverage of T-cell epitopes and efficient priming, but requires great attention to safety, because the antigens should not reconstitute an infectious virus or perform viral functions that are detrimental to the recipient. Vaccine design must include many changes that guarantee safety by inactivating key functions of the viral enzymes and sequence motifs. The approach taken and the tests performed to satisfy regulatory agencies of vaccine safety will be presented. While T-cell vaccines show great promise for reducing HIV disease after infection, antibody passive transfer experiments have shown that HIV neutralising antibodies (NAb) offer the only way to prevent infection. Despite the clear importance of NAb in protecting against HIV, progress in this area has been slow due to significant difficulties in identifying and delivering HIV Env immunogens that elicit broadly neutralising responses in small animal models, and the complex nature of the assays that measure NAb efficacy. This presentation will describe the progress made in this area with Env expression plasmids and Sindbis replicon (SIN) based vectors. Constructs containing HIV-1 Env immunogens that may improve NAb responses were prepared from primary brain-derived HIV strains (UK1br15), high affinity CCR5 binding (15888), and glycosylation site mutants (ADA(R/S)). These Env are highly susceptible to neutralisation and may intrinsically expose neutralising epitopes that are normally only exposed after CD4 binding. Ahead of mouse vaccination studies we have developed a rapid neutralising antibody assay that uses GFP expressing reporter viruses that are pseudotyped with these and other prototypic Env.

SAFETY AND PRELIMINARY IMMUNOGENICITY OF A B-SUBTYPE DNA PRIME/RECOMBINANT FOWLPOX VIRUS BOOST PROPHYLACTIC HIV VACCINE CANDIDATE: RESULTS OF A PHASE I/IIA TRIAL

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This study aimed to assess the safety and preliminary immunogenicity of a prophylactic HIV vaccine consisting of a DNA (pHIS-HIV-B) prime/recombinant fowlpox (rFPV-HIV-B) boost in healthy volunteers at "low risk" of HIV infection. This is the first report of a multigenic DNA prime/rFPV boost strategy to induce T cell immunity to HIV-1.

This placebo controlled, double blind, single centre trial is currently ongoing in Sydney. pHIS-HIV-B contains 60% of the genomic material of HIV-1 NL(AD8), a subtype B variant, and includes mutated forms of *gag*, *pol, env* and *tat* and *rev* under the control of the CMV immediate early promoter as well as humanised CpG motifs (Coley Pharmaceutical Group). rFPV-HIV-B contains identical *gag* and *pol* inserts. Healthy individuals were screened for eligibility and defined as low risk by behavioural criteria. One mg of pHIS-HIV-B was administered at weeks 0 and 4 followed by boosting with 5 $x10^7$ plaque forming units (pfu) of rFPV-HIV-B at week 8 by intramuscular injection. Primary endpoints are safety and immunogenicity determined by interferon gamma ELISpot assay at week 9 to a pool of overlapping 15mer peptides representing a prototypic subtype B Gag. Secondary endpoints include immunogenicity using lymphoproliferation, and interferon gamma and IL-2 production by intracellular cytokine assay to HIV antigens.

24 eligible individuals (15 male) were randomised to either active or matched placebo in a 3:1 ratio. Recruitment commenced in June 2003 and was successfully completed in February 2004. Final vaccinations were administered in April 2004. At the time of submission, immunogenicity and safety data were still blinded. However, the results of the immunogenicity as well as a formal analysis of the safety data to week 12 will be presented in full. Ongoing clinical review of volunteers reveals that the vaccine regimen is well tolerated; no serious adverse events were noted and local and systemic reactions were mild to moderate.

A novel DNA/rFPV prime/boost prophylactic HIV vaccine clinical trial has been successfully recruited and the vaccines appear well tolerated. A battery of immunologic assays have been performed and as the last subject reaches the primary endpoint in May 2004, results assessing immunogenicity will be available for presentation.

Concurrent Session – Clinical Medicine – Treatment

SALVAGE THERAPY

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The term salvage therapy is an unfortunate one, raising images of wrecks on the seashore but I shall assume that this term means resistance to all three of the presently available classes of drugs. The scale of this problem is presently unclear. Although marketing experience suggest that large numbers of patients have been exposed to all three classes of drugs, resistance to these agents is somewhat less common and with the correct application of modern antiretroviral therapy may become less common in the future. Most of our patients with triple class resistance have in fact been given sub-optimum therapy in the past (all that was available at the time), or were poorly adherent to a variety of previous drug regimes. Equally in a survey in our Unit, the causes of deaths of our patients are not primarily related to virological failure and lack of treatment options but more to the development of tumours and patients presenting late who died before antiretroviral therapy can become effective.

Various treatment options for these patients will be discussed. There was a vogue for structured treatment interruption and one study from France suggested that such an approach followed by multiple antiretroviral therapy may improve prognosis in terms of reductions in viral load. This study is counter-balanced by another study performed by the CPCRA in earlier disease in which the outcome was significantly worse in terms of clinical progression and CD4 count levels as a result of therapy. This latter study was at a much earlier stage of disease with higher CD4 counts than the French study and many patients had viable further options that would have made therapy successful without structured treatment interruption. The current view would be that structured treatment interruption in an attempt to cause the virus to revert to wild type is not likely to have a major impact on disease therapy. The French study also utilised large numbers of drugs in an attempt to find a combination that would work with a view that, drugs, even though there was resistance to them, might have some effect on reducing viral load. Such an approach is the subject of a randomised controlled trial (OPTIMA) and while cohort studies have shown some benefits from such an approach, this is at the expense of unexpected pharmacological interactions, a high pill burden and considerable toxicity. There is good evidence, both from randomised trials and cohorts that staying on some form of therapy is better than discontinuing. A more minimalist approach would therefore be that sufficient drugs should be retained to try and keep the CD4 count as high as possible (the most important predictor of imminent death).

The fusion inhibitor T20, which is now licensed, and Tipranavir which is shortly to be licensed have been mainly used in a salvage situation although the optimum positioning of both drugs remains to be determined., When either of these agents are used as the only active component of a combination, the viral load drops are often short lived although the CD4 count may rise for a more prolonged period.

The belief of most clinicians and a post hoc analysis of the major studies performed withT20 (TORO 1 and 2) would suggest that these drugs would be better used in combination with other active agents and, therefore, the best method of treatment in salvage is to prevent it from occurring by using agents more judiciously at an earlier stage of disease. A number of other agents including new nucleosides, new NNRTIs, Capaverine and TMC125, and novel agents attacking either integrase or the process of interaction either between the CD4 receptor and GP120 or between CCR5 and GP 41 should also be licensed in the foreseeable future which gives further hope to people in this situation.

ESPRIT (EVALUATION OF SUBCUTANEOUS PROLEUKIN® IN A RANDOMISED INTERNATIONAL TRIAL): CD4+ T-CELL RESPONSES TO SUBCUTANEOUS (SC) RECOMBINANT INTERLEUKIN-2 (RIL-2)

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ESPRIT, is a phase III study evaluating the clinical impact of intermittent SC rIL-2 plus antiretroviral therapy (ART) *vs* ART alone in HIV-1-infected individuals with baseline CD4 ≥300 cells/μL. Induction consists of three rIL-dosing cycles (7.5 MIU q12h for 5 days every eight weeks) in the first 6 months. Thereafter, additional cycles are given to achieve/sustain CD4 target i.e. doubling of baseline was 300-499 or ≥1000 cells/μL

As part of an ongoing initiative to better understand CD4 responses to rIL-2, we assessed predictive factors for months 12 and 24 counts in selected populations of rIL-2 recipients.

1,437 of 2,090 patients randomised to rIL-2 had initiated ≥3 rIL-2-dosing cycles in year 1 and had month 12 data available. Mean age was 41 years, 19% were female, 21% had a history of AIDS-defining illness and median entry and nadir CD4 counts were 463 and 207 cells/μL respectively. Median ART-duration was 48 months and 80% had HIV RNA below the level of quantification (LLQ <500 copies/mL). The median amount of rIL-2 received was 224MIU; 26% and 17% had missed a dose or dose reduced respectively.

Positive predictors of CD4 response (≥200 cell increase) at month 12 were higher CD4 nadir (p=<0.001), baseline HIV RNA <LLQ (p=0.025), larger cumulative dose of rIL-2 (p=<0.001); negative predictors were older age (p=0.047) and longer duration of ART at baseline (p=<0.001).

Further exploration of rIL-2-cycling in year 2 was undertaken in rIL-2 recipients who were at CD4 target at month 12 and for whom month 24 CD4 data were available (n=335). 186 (56%) recipients remained at target at month 24, of these, 61% required no further IL-2, 32% required 1 and 7% required 2-4 additional rIL-cycles to sustain target. 149 (44%) were no longer at target at month 24, of these, 77% did not receive further rIL-2 in year 2.

In conclusion, the amount of rIL-2 received is a significant positive predictor of CD4 response. Moreover, relatively little additional rIL-2 is required to maintain CD4 target in those achieving target following the induction phase. Continued rIL-2 cycling guided by protocol-specified CD4 target should be encouraged.

SILCAAT: CD4+ T-CELL RESPONSES TO SUBCUTANEOUS (SC) RECOMBINANT INTERLEUKIN-2 (RIL-2) AFTER ONE YEAR

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SILCAAT is an open-label, randomised study comparing the effects of SC rIL-2 *vs*. no SC rIL-2 on HIV-disease progression (ADI) and death in HIV-1-infected individuals over 5-7 years. Participants have baseline CD4+ T-cells of 50-299 cells/μL and plasma HIV-RNA (VL) ≤10,000 copies/mL on stable antiretroviral therapy (ART). Year 1 induction consists of 6 rIL-2 dosing cycles. Further rIL-2 is given to maintain/achieve the CD4+ goal i.e. an average of 150 cells/μL increase from baseline.

This analysis describes the predictors of CD4+ response after one year. Covariates including age, gender, ethnicity, nadir and baseline CD4+ count, prior ADI, VL and duration of ART at baseline, body-mass index (BMI) and rIL-2 received (number of cycles and total dose of rIL-2) were considered in a multiple regression analysis.

Baseline data for 987 subjects randomised to rIL-2 revealed the mean age was 42 years; 16% were female; 79% of white ethnicity; 34% had prior ADI and the median nadir and baseline CD4+ counts were 59 and 201 cells/μL respectively. VL was undetectable (LLQ<500copies/mL) in 80% and median duration of ART was 4.1 years (n=982).

After one year, 6% (n=56), 11% (n=109), 20% (n=195) and 63% (n=627) of participants randomised to rIL-2 completed 0, 1-2, 3-5 and ≥6 rIL-2 dosing cycles respectively. Month 12 CD4+ data were available for 838 (85%); median CD4+ change from baseline was 128 cells/μL; 44% were ≥ CD4+ goal.

Of those completing ≥6 (n=603) *vs.* <6 (n=235) rIL-2 dosing cycles in year 1, CD4+ decreased from baseline in 7% *vs.* 17% respectively and increased by 0-99, 100-199, ≥200 cells/μL in 27%, 30%, 36% *vs.* 41%, 26%, 16% respectively.

In a multiple regression analysis the positive predictors of achieving CD4+ goal at month 12 were higher baseline CD4+ (p=0.01), baseline VL <LLQ (p=<0.001) and number of rIL-2 dosing cycles received (p=<0.001).

There is a diverse exposure to rIL-2 in year 1 on study. Investigators and patients are encouraged to continue cycling with rIL-2 to induce and sustain an average CD4+ increase of 150 cells/μL for the study's duration.

AN OPEN LABEL STUDY TO DETERMNIE THE EFFICACY AND SAFETY OF ENFUVIRTIDE IN PATIENTS CHANGING THERAPY TO AN NRTI – SPARING REGIMEN (ML16992)

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Adverse effects restrict long term HIV-1 therapy. This study explored the use of enfuvirtide and NRTI-sparing regimens in heavily pre-treated patients.

59 HIV-1 infected, triple class (NRTI, NNRTI, PI) experienced individuals with current or prior NRTI treatment limiting toxicity were enrolled in an open-label, multicentre, single-arm trial to receive enfuvirtide 90mg bd, sc for 48 weeks and an optimised background regimen guided by a genotype. NRTI drugs were excluded, except for tenofovir. The primary endpoint was mean change from baseline in plasma HIV load at 48 weeks. Secondary endpoints included changes in CD4+ cell count, changes in NRTI toxicity signs and symptoms and percentage of patients on enfuvirtide at week 48. Data were analysed using intention to treat methodology.

At entry the mean age of participants was 47 years, 97% were male, 58% were classified as CDC-C, mean duration of prior antiretroviral therapy (ART) was 9 years, with a mean exposure of 12 ARTs, mean CD4+ cell count was 242 (median 164) cells/ mm^3 and mean HIV load was 4.5 log copies/mL (5/59 patients had viral < 400), lipodystrophy was reported in 66% of patients (39/59). At baseline patients were prescribed a mean of 3 ARTs in addition to enfuvirtide. 4 patients continued to take NRTIs. 19 patients recommenced NRTIs during the study. At week 48 mean change from baseline in HIV plasma viral load was a decrease of 1.49 log 10 copies/mL (p=0.0001), 49% of patients had an HIV plasma viral load < 400 copies/mL (p=0.001).The mean increase in CD4+ cell count was 45 cells mm^3 (p=0.059). During the study total body lean and fat mass increased significantly by 1.25 Kg (p=0.01) and 1.6 Kg (p=0.001) respectively. Peripheral fat increased significantly by 0.32 Kg (p=0.03). Fasting lipids and glycemics were unchanged. NRTI toxicities resolved in 12 (20%) of patients. 52 (88%) of patients were still taking enfuvirtide at week 48.

The strategy of an NRTI sparing regimen plus enfuvirtide provided significant viral suppression at week 48. A high proportion of patients were still taking enfuvirtide at week 48.Quantitative improvements in lean and fat tissue reflect an improved health status.

TENOFOVIR-RELATED NEPHROTOXICITY (TRN) - PREVALENCE AND RISK FACTORS

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Tenofovir is a novel anti-HIV nucleotide reverse transcriptase inhibitor. Closely related drugs such as adefovir and cidofovir have been associated with severe nephrotoxicity. Initial efficacy studies showed tenofovir to have a favourable safety profile. As its use became widespread, tenofovir-related renal complications have become more prevalent.

We report the prevalence of and risk factors for tenofovir-related nephrotoxicity (TRN) at Alfred Hospital Melbourne, Victoria.

From Jan 1 2001 to March 31 2004, 224 HIV-1 infected patients commenced tenofovir containing anti-retroviral therapy. Using a prospective clinical database and medical record review, we identified incident renal impairment, defined by a greater than 30% decrease in renal function (serum creatinine or measured creatinine clearance) compared with pre-treatment baseline, in the absence of intercurrent illness or other nephrotoxins and resolving with cessation of tenofovir.

Risk factors examined for TRN include demographics, HIV associated, treatment associated and intercurrent illnesses. The proportion of treatment limiting renal events, and outcome will be described.

Preliminary results revealed 14 (6.5%) patients developed TRN during tenofovir therapy. 12 of these patients have AIDS (86%). 29% of TRN events were treatment limiting. Five (2.2%) patients demonstrated renal salt loss compatible with Fanconi Syndrome.

Median time to TRN was 10 months post tenofovir commencement. Mean rise in serum creatinine was 149% (range: 39% to 450%). Mean time to recovery of renal function after cessation of tenofovir was 29 days (range: 13-52 days). Two patients never returned to baseline renal function.

This study reveals that TRN is a significant complication to tenofovir therapy. In HIV-infected patients TRN may occur with or without Fanconi Syndrome. It is usually a delayed phenomenon and causes a prominent rise in serum creatinine in the absence of other nephrotoxins or intercurrent factors. The recovery time from this complication is prolonged and some individuals demonstrate irreversible renal dysfunction.

THE NORMALISED INHIBITORY QUOTIENT (NIQ) OF BOOSTED PROTEASE INHIBITORS IS PREDICTIVE OF VIRAL LOAD RESPONSE OVER 48 WEEKS IN A COHORT OF HIGHLY TREATMENT EXPERIENCED HIV-1 INFECTED INDIVIDUALS

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HIV drug resistance testing provides information of susceptibility to antiretrovirals. However it does not incorporate a measure of drug exposure. This may be of particular importance when using pharmaco-enhanced HIV protease inhibitor (PI) regimens. We assessed associations between 48 week clinical outcome and a range of covariates including normalised inhibitory quotient (NIQ).

A cohort of 87 HIV infected individuals were assigned a new boosted PI regimen by physician choice depending on random allocation to genotypic or virtual phenotypic resistance test result (52% v 48%). PI therapy consisted of lopinavir, indinavir, saquinavir and amprenavir in 50%, 32%, 11% and 6% respectively. Fold Change (FC) in chosen PI was determined from resistance test at baseline with trough drug concentration (Cmin) determined at week 4. NIQ was derived individually by the logarithm ratio of Cmin/FC divided by the fixed ratio of population mean trough drug concentration/biological cut off. Viral load (VL) response over 48 weeks was correlated with baseline VL, FC, Cmin, NIQ, method of resistance testing and selected PI using regression modelling.

Median baseline VL was 4.3 log. Median change in VL was 0.83 log at week 48. In multivariate analysis, baseline VL and NIQ were the parameters most associated with change in VL from baseline at week 48 (p=0.042 and 0.061 respectively). FC, Cmin, selected PI and method of resistance testing were not significantly associated with VL changes. When dividing NIQ into inter-quartile groups, percentage with undetectable VL (<400 copies/ml) at week 48 were 23%, 52%, 66% and 64% respectively (p=0.013).

In this cohort of highly treatment-experienced individuals treated with boosted PI regimens, baseline VL and NIQ were significantly predictive of virological response over 48 weeks whereas FC and Cmin were not. These prospective results support the use of a NIQ at week four, as a tool in predicting response to therapy in this setting.

Concurrent Session – Community Uptake

MAPPING HIV CARE AND SUPPORT

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The reviews of the 4th National HIV/AIDS Strategy, and preliminary discussions about a 5th, have identified the care and support for positive people as a priority area. However, in a time where much attention is (understandably) turned to prevention, and in the light of recent treatment improvements, it might be tempting to justify a more limited role for a national and strategic approach to care and support.

This paper argues that the need for a co-ordinated, national approach to care and support is more urgent than ever. A national strategy can facilitate:

- adequate, nationally-endorsed models of care to ensure better co-ordination and/or co-location of health services;
- support for general practitioners and allied health care workers, so they are able to care for increasingly complex clients in a way which is financially sustainable for both clinician and patient;
- strong stakeholder community organisations, such as those representing HIV positive people, to be involved in the development of programs of care, support and prevention.

A co-ordinated national attack is also needed on poverty, access to essential services like dental care, affordable housing, and returning to work. Mental health care remains an issue for many HIV positive people, with State-based services in areas such as dementia care still at or above capacity. Finally, a national strategy should ensure that national health policy directions or changes are broadly consistent with the identified priorities and directions of the national HIV strategy.

The National Association of People Living with HIV/AIDS (NAPWA) has recently called for a 'mapping exercise' to document current services for people with HIV, identify best practice, and ensure that services are adapting to changing needs. This paper argues that leadership in care and support for people with HIV should remain a central responsibility of a national HIV strategy.

ALIGNING FUNDING WITH CHANGING SERVICE NEEDS

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With PLWHA experiencing improved outcomes from treatment, the service needs of people with HIV infection now follow patterns similar to those of a chronic rather than an acute illness. In particular service demands are longer term and more commonly in ambulatory care settings including through general practitioners and other types of community support.

In NSW the funding of many AIDS specific services has a historical basis. While the introduction of a resource distribution formula (AIDS-RDF) and minimum service levels have promoted greater funding equity and better access to local services in the 17 Area Health Services across NSW, the recent shift in patterns of service needs makes it is a challenge for a health system to deliver services that are responsive to the changes, particularly in a context of no growth in funding.

During 2003/04 NSW initiated two important steps to provide a basis for aligning the needs of PLWHA with service delivery. These involved a review of the AIDS-RDF and an assessment of the care and treatment needs of PLWHA.

Key directions identified as an outcome of the initiatives include a redistribution of funding allocated to some Areas, an increased focus by the health system on utilisation data in the ambulatory care setting and monitoring of services; support for general practitioners; strengthening of specific statewide services; articulation of models of care for delivering services; and strengthening of the care for PLWHA with complex needs including the integration and coordination of services and the development of a supported accommodation strategy.

While the findings of these projects provide guidance for the AIDS Program into the future there are various interests in the status quo being maintained. As a step towards progressing the recommended directions, NSW Health is initiating a range of strategies to strengthen key services. This paper discusses the strategies within the context of the AIDS-RDF review and the HIV/AIDS Care and Treatment Needs Assessment.

DISCERNING HIV RELATED DISADVANTAGE 20 YEARS ON: IMPROVING COMMUNITY CARE TO MEET THE CHANGING NEEDS OF PEOPLE LIVING WITH HIV

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HIV related disadvantage is experienced in a variety of ways by people with HIV and has changed over time. In particular, HARRT has increased longevity and given many people living with HIV the capacity to consider greater participation in social, employment and education arenas. The experience of Bobby Goldsmith Foundation (BGF) in providing direct financial assistance over 20 years is briefly discussed, the changing needs of our clients living with HIV and the review of BGF and its services is outlined, and its new service provision and support objectives to address HIV related disadvantage are described.

TRENDS IN THE UPTAKE AND USE OF COMBINATION ANTIRETROVIRAL THERAPY IN AUSTRALIA SINCE 1998

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To investigate the use and uptake of combination highly active antretroviral therapy (HAART) in Australia since 1998.

Data were from four Austraian studies: the cross-sectional Gay Community Periodic Surveys (GCPS) in Sydney, Melbourne, Perth, Adelaide, Canberra and Queensland; HIV Futures, a nationwide cross-sectional study of people living with HIV/AIDS (PLWHA); Positive Health (PH), a prospective longitudinal study of PLWHA living in NSW and Victoria; and the Australian HIV Observational Database (AHOD), a longitudinal study of PLWHA recruited from clinics in NSW, NT, SA, Qld, Vic, and WA. Combination HAART was defined as two or more antiretrovirals.

Trends in the use of combination HAART were analysed cross-sectionally. GCPS data showed a significant decline in the three largest cities: Sydney (72% in 1998 to 67% in 2003. Trend, $p<.005$), Melbourne (83% in 1998 to 56% in 2003. Trend, $p<.001$) and Brisbane (69% in 1998 to 55% in 2003. Trend, $p<.001$). Corroborating these findings, a significant decline in HAART was also observed amongst PH participants in NSW (78% in 1999 to 68% in 2003. Trend, $p<.005$) and in Victoria (82% in 1999 to 59% in 2003. Trend, $p<.005$) No decline in use was evidenced in Perth and Adelaide GCPS data, nor in the clinic-based AHOD sample. Longitudinal analysis, based only on the same PH participants at each data point, also provided evidence of a significant decline in HAART in NSW (83% in 1999 to 69%. Trend, $p<.01$) but not in Victoria (80% in 1999 to 74.3% in 2003).

To explore trends in uptake of combination HAART, data were analysed for participants who were newly recruited into PH at each round of data collection (largely representing newly infected/diagnosed). These results showed a significant decline in HAART in NSW (78% in 1999 to 67% in 2003. Trend, $p<.05$) and Victoria (82% in 1999 to 47% in 2003. Trend, $p<.005$).

The evidence is that in Australia there has been a significant decline in HAART use. This decline would appear to be attributable to PLWHA stopping treatment as well as to newly diagnosed PLWHA delaying the commencement of treatment.

CHALLENGES FOR DELIVERING COMMUNITY BASED HIV TREATMENTS PROGRAMS

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HIV treatments maintenance is a well documented challenge to people living with HIV/AIDS. Managing side effects, the risk and / or development of toxicities, and the emergence of resistance to classes of drugs, can impact markedly on a person's capacity to maintain these strict regimes, and potentially undermine their future personal and clinical management of HIV/AIDS. The challenges of how to also incorporate long term treatments into daily lifestyles, while avoiding disclosure of HIV status, have also been described and reported widely in plwha research.

In Australia, NAPWA has been involved in national treatments advocacy and information provision for many years, and coordinates the national community based HIV treatments networks. This presentation will describe the various mechanisms NAPWA uses to help inform the policy response to HIV health and treatments education programmes. We will also outline the various collaborations and partnerships that enable NAPWA to deliver timely and reliable HIV health and treatments information to its member organisations and constituents.

How to inform positive people about treatments options and debates in useful and engaging mediums is a challenge to the HIV sector, and complex information is absorbed in a population that has increasingly diverse and varied treatments experience and history.

Finally, this presentation will describe the various estimates of treatments uptake and extent of treatment breaks being utilised within plwha populations in Australia, and suggest some of the possible interpretations of these trends and future projections. It will also suggest possible interventions and responses to address some of these challenges for delivering HIV treatments and health maintenance programs.

HIV DRUG SIDE EFFECTS – ONE POSITIVE VOICE

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A significant amount of the morbidity and mortality experienced by people with HIV infection is due to the long term side effects of the drugs used to treat HIV infection and to diseases such as cardiovascular disease that have multiple risk factors associated with them one of which is length of time of HIV treatment.

The personal experience of the potentially life threatening but rare side effect of lactic acidosis is described. Interviews of four other people with HIV who also had lactic acidosis and survived are described. Some common themes are drawn from these interviews that have broad implications for the ways in which many side effects are managed.

The paper then describes a national workshop of people with HIV and HIV-positive educators to discuss the changed experience of living with HIV, particularly the experience of morbidity associated with drug side effects.

A number of themes that emerged during the workshop are explored including health promotion and prevention programs for preventable diseases associated with HIV treatments, the changed service needs of people with HIV and the lack of positive voices to tell the diversity of the current stories of people living with AIDS.

The lack of positive voices to balance the perception of HIV disease in Australia as 'mostly solved' is a major concern of some people with HIV and it is the intention of this paper to be one of many voices needed to be heard.

Concurrent Session – ART in Resource Poor Settings: Coming Ready or Not

SIMPLIFYING TESTING STRATEGIES FOR THE DIAGNOSIS OF HIV: TOWARDS A RE-EVALUATION

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The World Health Organisation (WHO), in an effort to decrease the use of expensive confirmatory tests such as the western blot, suggested testing strategies employing the sequential use of one to three less costly tests. The strategic use of the tests depends on the purpose of testing and the prevalence of infection. In resource-poor countries the strategies have nominally been adopted but often without understanding of the logic behind their use and never with evaluation of their efficacy.

Evidence for misuse of the WHO strategies was found on field trips to several countries in South-east Asia and the Western Pacific and through the NRL's External Quality Assessment Scheme (EQAS). Tests were employed without consistency because often the same tests are not supplied to individual laboratories or are purchased by non-technical departments on the basis of cost. Data reported in the EQAS were reviewed to determine if the incorrect assignment of sero-status was as a consequence of laboratories not following WHO testing strategies.

The results reported from six anti-HIV panels tested between 2001 and 2003 were reviewed. During this time period a total of 77 laboratories tested panels using 52 anti-HIV assays. Eighty-two percent of laboratories used between one and three assays, as recommended by WHO, to test the panels. However, 14% used four assays, 3% used five assays, 1% used six assays and 0.2% used seven assays to test the panels.

Laboratories reported 8022 test interpretations for individual assays of which 79 were incorrect (average error rate for the six panels was 0.98%). Forty-two (53%) of the 79 incorrect test interpretations resulted in an incorrect sero-status being assigned. Eighteen of the 42 incorrect sero-status were due to laboratories not following their testing strategies (11/42 due to laboratories testing samples on an immunoblot that were negative on a screening assay and 7/42 due to laboratories not testing further samples that were initially reactive).

More evidence is required to place the use of WHO strategies on an evidence base. Where strict testing strategies are not followed errors are likely. Errors in EQAS are now few so that data to support the argument are sparse and further analyses are necessary.

RATES OF SHORT-TERM CLINICAL PROGRESSION IN THE TREAT ASIA HIV OBSERVATIONAL DATABASE

Kumarasamy N[1], Zhou J[2] on behalf of the Australian HIV Observational Database
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Rates of disease progression in HIV disease in terms of overall and AIDS-free survival are well described in western populations. However, these aspects of HIV disease are less well described in Asian populations.

Data from the TREAT Asia HIV Observational Database, a prospective, mulitcentre cohort study involving 11 sites in the Asia-Pacific Region, were analysed to estimate short-term survival and rates of newly diagnosed AIDS in treated and untreated patients. Endpoints were defined as the time from study entry to diagnosis with AIDS or death. Treatment was fitted in the Cox proportional hazards model as a time-dependent variable. Two Cox models, with and without baseline CD4 count and HIV viral load measurement, were developed to assess the predictors of progression to AIDS or death.

1069 patients were included with baseline data and at least one appropriate follow-up visit. Median follow-up was 4.6 months. During a total of 426.8 person-years of follow-up, 43 patients were diagnosed with AIDS or died, giving an overall rate of 10 per 100 person years (95% confidence interval, CI, 7.5-13.6). In univariate analysis, rate of progression to AIDS and death was 8.0 per 100 person years among patients on antiretroviral treatment, compared with 18.2 per 100 person years among patients not on treatment (p=0.017). Baseline CD4 count, baseline CDC classification of HIV infection and hepatitis C status were the significant predictors of progression to AIDS and death in the full model. However, when excluding baseline CD4 and HIV viral load from the model, being on antiretroviral treatment and baseline haemoglobin level were significant predictors.

As seen in western countries, baseline CD4 was the most important factor in determining patient's short-term risk of disease progression. Data on prognostic markers will become more important for optimal treatment and care as antiretroviral treatment becomes more widespread among Asian populations.

INCREASING AWARENESS OF COGNITIVE IMPAIRMENTS IN EMERGING EPIDEMICS

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In emerging epidemics, issues of cognitive impairment have received limited attention despite estimates that at least 2.16 million PLWHA in the Asia-Pacific region live with or will live with at least one neurological complication. Health care workers (HCWs) in these settings report being unable to identify HIV-associated cognitive impairment due to widespread lack of recognition of central nervous system involvement and that symptoms are often wrongly ascribed to, or masked by, other health issues.

This paper will detail how a workshop currently being piloted in PNG is, amongst other things, seeking to increase HCWs understanding of HIV-associated cognitive impairments. Awareness is being addressed in two distinct but related ways: clinical care and care & support.

The clinical care component of the workshop focuses on the identification of a range of symptoms associated with cerebral involvement. Participants develop familiarity and competence in using an international diagnostic tool for HIV dementia. Care and support aspects of the workshop involve participants considering the impacts of cognitive impairments on a range of people. Drawing on a model of habilitation for the PLWHA, once these impacts are identified, participants are assisted by workshop facilitators to develop care and support plans appropriate to the range of people involved.

The methodology of the workshop is interactive, working on a capacity building approach, requires participants to engage simultaneously with their affective and cognitive knowledges. Participants rated these sessions highly. The secondary effect being, the dispelling of cultural myths and a reduction in stigma and fear.

In developing an approach to cognitive impairment that focuses on increasing awareness and habilitation, than on the inability to treat such conditions in these settings, this type of innovative workshop will continue to be important. The reason being that while the introduction of ART may benefit many PLWHA, it will not reduce the impacts of or prevalence of some of the cognitive impairments. As emerging epidemics continue to grow, so too will the impacts of HIV-associated cognitive impairments.

FOUNDATIONAL ISSUES IN VCT IN A PMTCT SETTING IN TANZANIA

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The data presented here identify key factors influencing male support of and participation in VCT in the context of PMTCT in Tanzania. Male support of voluntary counselling and testing (VCT) is central to the uptake and success of VCT in the prevention of mother-to-child transmission (PMTCT) of HIV. Such support and participation is essential to garnering community support for VCT and for undermining the stigma and discrimination associated with HIV testing.

Interviews were conducted with key informants (n=7) and male community members (n=23) to explore the men's understandings of and attitudes towards VCT and PMTCT. Both single and married men were interviewed in a face-to-face setting, the interviews taped and transcribed and the qualitative narrative data analysed using Grounded Theory methodology.

The data indicate that VCT has positive as well as negative outcomes. Male attitudes towards their female partners, who test positive, ranged from compassionate to hostile. For many of the male participants, women were positioned as the carriers of disease. Masculine strength was associated with being negative, however many men actively avoid testing. Stigma and discrimination, and associated issues of visibility and confidentiality, are key to the success of VCT.

Unless public health practitioners engage with the cultural and social worlds which their potential patient populations inhabit, VCT will continue to have an uneven impact on PMTCT.

EXTERNAL QUALITY ASSESSMENT SCHEMES FOR ANTI-HIV AND ANTI-HCV TESTING

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Since 1989, the National Serology Reference Laboratory, Australia (NRL), in collaboration with the World Health Organization, has provided an External Quality Assessment Scheme (EQAS) to laboratories that test for anti-HIV in the Asia and Pacific regions. An anti-HCV EQAS has been provided since 2000. The EQAS aim to assess the quality of assays used in the regions, monitor the performance of laboratories and educate participants in quality assurance issues.

Panels consisting of ten coded samples that were characterised by the NRL were distributed to laboratories twice a year. Laboratories were requested to process these samples using their routine testing procedures. Results were reported to the NRL.

The NRL has provided feedback to laboratories on their performance. When errors were identified, the NRL advised the laboratories of the probable cause of the error and suggested ways in which their testing process could be improved

The results reported from six anti-HIV panels tested between 2001 and 2003 were analysed to calculate error rates. An error rate was defined as the number of incorrect test interpretations reported expressed as a ratio of the total interpretations reported. Possible causes of errors were investigated.

Between 2001 and 2003, 8022 test interpretations were reported by a total of 77 laboratories using 52 anti-HIV assays. The average error rate for the six panels was 0.98% (range 0.68-1.61%). Seventy-three percent of the errors appeared to be due to technical difficulties that occurred during the testing process. Twenty percent of errors were due to laboratories not following their testing strategies. Six percent of errors were transcription errors. Error rates were comparable for HCV testing. Error rates between 2001 and 2003 were less than for panels distributed previously.

Errors in HIV and HCV testing still occur for both negative and positive samples. Technical errors are most common.

THE TREAT ASIA HIV OBSERVATIONAL DATABASE: BASELINE DATA AND RESPONSE TO TRIPLE COMBINATION ANTIRETROVIRAL TREATMENT FROM RETROSPECTIVE DATA

Kumarasamy N[1], Zhou J[2] on behalf of the Australian HIV Observational Database
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Relatively little is known regarding HIV disease natural history and response to antiretroviral treatments among Asian HIV patients. The TREAT Asia HIV Observational Database (TAHOD) is a recently established collaborative observational cohort study, and aims to assess HIV disease natural history in treated and untreated patients in the Asia-Pacific region.

Observational data are collected on HIV patients at 11 sites in Asian countries. Data are centrally aggregated for analyses, with the first baseline and retrospective data transferred in November 2003. Retrospective data were analysed to assess the response to highly active antiretroviral treatment (HAART) over a six-month period in terms of changes in CD4 count and proportions of patients achieving undetectable HIV viral load (<400 copies/ml).

By the end of April 2004, 1869 patients had been recruited to TAHOD. 72% of patients were male, with median age 36 years. The majority of patients (78%) reported HIV infection through heterosexual contact. Over 40% of patients had a previous AIDS diagnosis, of whom, 59% had tuberculosis, and 34% Pneumocystis carinii pneumonia. Nearly 70% of the patients were having antiretroviral treatment at time of entry to TAHOD, of whom, the majority (67%) were treated with HAART. 713 patients had started triple combination therapy and had a baseline and six-month CD4 count measurement reported. The mean CD4 count increase was 115 (standard deviation 115) cells/µl. Smaller CD4 count increases were associated with higher CD4 count before starting treatment, prior treatment with mono/double therapy and treatment with a HAART regimen containing Nucleoside Reverse Transcriptase Inhibitor (NRTI) and/or Protease Inhibitor (PI) but without Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI). 598 patients had started HAART and had a viral load assessment after six months, with 69% reaching undetectable viral load. Older patients, patients not exposed to HIV through heterosexual contact, and patients treated with HAART containing NRTI and NNRTI but without PI, were found to be more likely to achieve undetectable level.

Analyses of retrospective data in TAHOD suggest that the overall response to HAART in Asian populations is similar to that seen in developed countries.

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ORAL PRESENTATION ABSTRACTS

FRIDAY 3 SEPTEMBER 2004

FRIDAY 3 SEPTEMBER 2004

Medical Case Presentation Breakfast

SECONDARY SYPHILIS PRESENTING AS TONSILLITIS IN THREE INDIVIDUALS

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Recent increases in syphilis notifications have been observed in men who have sex with men (MSM) in several Western countries including Australia.

We describe three MSM presenting with severe tonsillitis. One patient had bilateral irregular ulcerated tonsils and regional lymphadenopathy. The second patient, who presented with unilateral tonsillar enlargement and an enlarged cervical lymph node, had findings suggestive of lymphoma and underwent tonsillectomy. The third patient presented with sore throat and bilateral tonsillar hypertrophy. The first two men were HIV infected (CD4 cell count 414 and 390 mm^3 respectively). All three patients had high Rapid Plasma Reagin (RPR) titres and positive syphilis EIA antibodies consistent with secondary syphilis. Spirochaetes resembling Treponema Pallidum were visualised by dark ground microscopy of a throat swab from one individual.

Secondary syphilis of the tonsils is a rare manifestation of syphilis, particularly in the absence of other typical features. These cases illustrate the importance of considering the diagnosis of syphilis in high risk individuals presenting with refractory tonsillitis or tonsillar enlargement.

FINDING THE INDEX CASE – THE CHALLENGES OF HIV RISK MANAGEMENT IN CLINICAL PRACTICE

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The latest Human Immunodeficiency Virus (HIV) antibody and antigen screening tests that are widely used in clinical practice today have improved our ability to detect early HIV infection.

When a new diagnosis of HIV infection is made our duty of care towards, and the rights and responsibilities of, the client concerned may in some cases come into conflict with our duty of care towards, and the rights and responsibilities of, another client or involved person or society at large.

In this case presentation, the challenges and complexities of HIV index case tracing and risk management will be described with emphasis on the ethical, legal and public health issues involved.

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES) IN AN HIV INFECTED PATIENT

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A 40-year-old male with known HIV/AIDS infection for nineteen years was admitted to hospital for management of chronic pain. His CD4 count was 212/uL and viral load 300 copies/mL. He had ceased all medications including highly active anti-retroviral therapy several days prior to admission. His past medical history includes oesophageal candidiasis, cryptococcal meningitis, HIV wasting syndrome, mycobacteriosis, Kaposi's sarcoma, pancreatitis secondary to didanosine, depression, borderline personality disorder traits, chronic pain and associated opioid dependency. He had no history of hypertension and was not hypertensive on presentation. Five days after admission he experienced a generalised tonic-clonic seizure with post ictal cortical blindness and vomiting, lasting less than 24 hours. There were no other focal neurological findings.

A noncontrast CT scan demonstrated multifocal low attenuation in a subcortical distribution bilaterally. An MRI performed one day after the seizure revealed bilateral occipital and cerebellar white matter T2 hyperintensity. These appearances were consistent with PRES. The patient's neurological symptoms resolved spontaneously and the MRI lesions on a follow up study performed two weeks following the seizure demonstrated total resolution.

PRES is a cliniconeuroradiologic entity most commonly described in association with hypertensive encephalopathy, eclampsia, uraemic encephalopathies and immunosuppressive agents. Patients have an acute or subacute presentation typically characterised by headache, nausea, vomiting, decreased consciousness, altered mental status, seizures or visual loss, including cortical blindness. Imaging is an essential component of the diagnosis. CT and MRI demonstrate a relatively symmetrical pattern of oedema, typically in the parietooccipital subcortical white matter. These findings usually resolve on follow up studies after appropriate therapy. The pathophysiology is controversial and poorly understood. Two diametrically opposed theories exist, one pertaining to brain hyperperfusion and the other to reversible vasospasm and associated cytotoxic oedema.

Only one other case of PRES has been described in an HIV-infected patient and was thought to be secondary to indinavir-induced hypertension. This report is the first description of PRES in an HIV infected patient with no clear aetiology.

AN UNUSUAL CASE OF CRYOGLOBULIN-NEGATIVE VASCULITIS IN A MAN CO-INFECTED WITH HIV AND HEPATITIS C (HCV)

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A 37 year old man with HIV (CD4 count 331 cells/ul, HIV viral load 8,600 copies/ml) and HCV presented with a 24-hour history of diffuse arthralgia and rash over his limbs and trunk. His stable antiretroviral regimen included zidovudine, tenofovir, didanosine and abacavir. Relevant history included depression, alcohol and intravenous drug use and epilepsy. Examination demonstrated palpable purpura. Skin biopsy revealed leucocytoclastic vasculitis. Serum cryoglobulins, cryofibrinogen and autoantibodies were negative. Blood, urine cultures and sexually transmitted infection screens were negative.

Subsequently the patient developed testicular pain, synovitis, myalgias and abdominal pain. Mesenteric angiogram revealed changes consistent with vasculitis. High-dose steroids were given with minimal benefit and caused diabetes and delirium. Antiretroviral therapy was ceased. A new regimen was later instituted, achieving undetectable HIV viral load. The patient developed significant proteinuria and plasma exchange was commenced with rapid improvement in rash and abdominal pain. Repeat skin biopsy showed small and medium vessel vasculitis with IgA deposition consistent with polyarteritis nodosa (PAN). A renal biopsy demonstrated diffuse crescentic glomerulonephritis with features of IgA nephropathy. The patient improved and was discharged on a weaning course of prednisolone.

Four months later the patient represented with rash and arthralgia. Plasma exchange was instituted immediately and the rash improved rapidly. The patient was discharged well after 6 exchanges, however he promptly relapsed and was treated with high-dose steroids with incomplete response. Pegylated interferon and ribavirin therapy was commenced to effect control of HCV and probable HCV immune-complex related PAN. This therapy was well tolerated and achieved full HCV virological response. The patient has not had further episodes of vasculitis despite cessation of plasma exchange and steroids.

This is an unusual case of cryoglobulin-negative, small and medium vessel vasculitis likely related to HCV liver disease and immune complex deposition. This case highlights the complexity of diagnosis and management of HIV/HCV co-infected individuals.

Plenary 2

GUIDELINES FOR ROUTINE CLINICAL CARE

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Over the last few years guidelines for clinical care have come closer together across most of the developed world in terms of both when to start treatment and the optimum agents to use for therapy. I will explore some of the research in this area and give personal views about optimum treatment. The when to start question appear to me to be relatively settled. The advantages of starting treatment relatively late with a CD4 count of around 250 include reduction in toxicity, a longer period when the patient is likely to be highly adherent and major reductions in cost. The disadvantages include an increased incidence of tumours with later treatment and an increased incidence of virulent infections such as chest disease including tuberculosis.

With regard to lymphoma and Kaposi's sarcoma it appears that these become commoner when the nadir CD4 count has fallen below 250 and, therefore, earlier treatment is unlikely to have a major impact on these diseases. Virulent chest infections are largely treatable and are unlikely to be a major reason to shift to earlier treatment in the developed world. Clearly the view about earlier versus later treatment may shift as drugs which are easier to adhere to and with less toxicity are developed.

There is a consensus now in most guidelines that combinations of two nucleosides and a non nucleoside reverse transcriptase inhibitor are the drugs of first choice, because of increased forgiveness of these regimes, good pharmacokinetics to allow once a day dosing and more controversially that using this class of drug in second line therapy is less likely to be successful. The choice of NNRTI depends upon the interpretation of the results of the 2NN study and also a view about the feasibility of genetic testing for Nevirapine hypersensitivity. The choice of nucleoside analogue backbone is also not entirely clear although it does appear that a 3TC (or possibly FTC) combination with Efavirenz is a particularly effective one. Whether this should be combined with Tenofovir, Abacavir or ddI relates to the clinician's views about the likely toxicity of these compounds in the short and long run and the relative view about potency of such regimes.

Several trials are in progress to assess the value of a nucleoside analogue sparing regime to alleviate toxicity. Enthusiasm for this approach is tempered by the toxicities of a combination of NNRTIs and PIs and the fact that some of the newer nucleoside analogues may not have the same toxicities as more well established drugs. The two reasons for combination regimes are the additive potency and the complexity of the genetic barrier that is created for the virus to overcome. It may be that some agents are so potent and require such a complex set of mutational patterns to produce resistance that single agent therapy could be used. Exploratory studies are underway for both Kaletra monotherapy and Ritonavir/Saquinavir monotherapy. Such regimes may have a class sparing effect and would certainly be associated with considerable cost savings.

Another further controversial issue is whether or not individuals failing initial therapy should be immediately switched to a different regime to ensure virological non-detectability or whether more attention should be paid to keeping the CD4 count elevated. This question may be partly answered by the SMART study which is recruiting in both Australia and the UK in which a policy of CD4 count driven structured treatment interruptions is being compared with continuing virological control.

UNDERSTANDINGS FROM THE EPICENTRE OF THE PANDEMIC

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What can the rest of the world learn from the African epidemic? What is the leadership role that the African experience can offer for the unfolding epidemics in SE Asia, China and India? What is the likely scenario for African countries as they understand and manage maturing epidemics?

This paper will address the complexities of the HIV and AIDS epidemics in sub Saharan Africa in general and South Africa in particular. It will investigate how the international and regional responses have shaped the epidemic and the responses to it. It will critique the current perceptions that the epidemic will cause the destruction of the continent and look at what the forces are that are shaping this perception Through new categories of explanation, such as taking 'hopelessness' seriously and looking at the 'optimism of the will', the paper will present a new way of looking at the epidemic, what we have learned from this experience and how a transformed response could be developed.

A great deal has been learned about the epidemic and about living in high prevalence countries – these lessons are ones that need to be taken seriously for the next wave of HIV, as well as for the development of strategic responses for countries that have been so dramatically affected.

Symposium – Clinical Medicine – HAART (Undectable)

UNDETECTABLE – BUT HOW LONG WILL IT LAST?

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While an undetectable HIV RNA level is one important goal of antiretroviral therapy, several questions remain even after achieving this goal.

These include:

1. How long will the undetectable viral load last?
2. What are the best predictors of a sustained response?
3. Is there evolution of resistance even with apparently "suppressed" viral replication?
4. What significance, if any, is there to low-level intermittent viremia ("blips")?
5. Should we be using assays that measure virus below 50 copies/mL?
6. Given a long-term undetectable viral load, what is the expected CD4 response?

The purpose of this review is to try and answer these commonly asked questions based on the latest clinical studies.

UNDETECTABLE: BUT WHAT ABOUT MY IMMUNE SYSTEM?

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Achievement of undetectable HIV replication following the introduction of combination antiretroviral therapy is most often but not invariably associated with reconstitution of immune competence, most reliably measured by the recovery in $CD4^+$ T cell numbers and reductions in the risk opportunistic infections. This is one of the great therapeutic achievements in modern medicine. Reversal of the pathogenic HIV-induced chronic immune activation, particularly involving effector-memory $CD4^+$ T cells is essential to immune recovery. Immune reconstitution illness and immune-mediated inflammatory pathologies are potential dangers of this process, including the potentially fatal unmasking of opportunistic infections such as herpesviruses and mycobacteria. Although measurement of $CD4^+$ T cell numbers correlates well with immune status, the $CD4^+$ T cell is not a single functional entity. Complete healing of the immune system would require sustainable reconstitution of a diverse repertoire of antigenic specificities; functional lymphoid microarchitecture; balanced naïve, effector and memory populations; balanced Th1, Th2 and regulatory populations; restored cell traffic and activation synapses. Surprisingly little is known about many of these aspects of immune function in the age of ARV therapy, although returning prognosis towards that of the uninfected population is likely to depend on them. Unfortunately, persistent markers of immune dysfunction are demonstrable even in patients with $CD4^+$ T cell numbers that have been restored to normal levels. Furthermore, 61% of ARV-treated subjects fail to reach a normal $CD4^+$ T cell count at 4 years (the Swiss Co-hort). Age, residual thymic function, replicative senescence, ongoing immune activation, and failure to modulate rates of lymphocyte apoptosis all appear to be factors. Strategies to manage immunological non-responders who experience poor $CD4^+$ T cell recoveries despite virological control will need to be enhanced – options might include cytokine therapies such as interleukin (IL) -2 and IL-7. Despite the impressive recent advances in HIV management, immune deficiency and immune dysfunction will continue to concern clinical practitioners and their patients for some time to come.

Russell #451 – may come after 26 July

Concurrent Session– Basic Science – HIV Pathogenesis

HIV CAPTURE AND TRANSMISSION BY DENDRITIC CELLS

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Dendritic cells (DCs) have a number of roles in HIV pathogenesis, including HIV uptake, infection and transport to lymphoid tissue where they stimulate explosive HIV replication in CD4+ T cells. R5 strains of HIV-1 virus predominate in the early period of infection and there are many theories why. One is that R5 viruses are preferentially transmitted as a result of the repertoire of HIV coreceptor expression at mucosal sites, where the majority of new infections occur. The high number of CCR5+ target cells at these sites act as 'gatekeepers' selectively transmitting R5 virus strains. Here we add to this model by demonstrating that the type of transfer is involved in HIV-1 strain selection. We have recently shown that following binding to C type lectin receptors, HIV_{Baj} is internalised into the endolysosomal pathway where it can be transferred to CD4+ T cells in two phases of transfer, *trans* and *cis* (the latter requiring infection of the DCs and *de novo* virus production*)*.

Pre-treatment of the DCs with lysosomotropic drugs, those that neutralise the endosome, greatly enhances DC infectivity and HIV transfer. Viral escape from this compartment and the subsequent infection of DCs requires viral binding to CD4 and a coreceptor. Immature monocyte derived DCs (MDDCs) were pre-treated +/- Bafilomycin A, pulsed with high titre $HIV\text{-}1_{Bal}$ or $HIV\text{-}1_{NL4\text{-}3}$ and activated CD4+ T cells added at specific time points. HIV-1 was quantitated in the DC and DC-T cell co-cultures, using real time PCR. Here we use our HIV-1 viral transfer assay to show that whilst both R5 and X4 strains are internalised by the MDDC and presented to CD4+ T cells in *trans*, only the R5 virus is able to exit the compartment and infect the MDDC. We conclude that this is a result of CXCR4 availability and not a difference in viral processing, as pre-treatment of the MDDC with bafilomycin A prior to infection with X4 did not result in MDDC infection. The X4 virus remains trapped within the endosome and is degraded not transferred. We aim to follow this up with a wider range of virus strains, including clinical isolates and visualise the process using confocal microscopy.

NEUTRALISING ANTIBODY RESPONSES IN LONG TERM SURVIVORS INFECTED WITH ATTENUATED HIV-1: CORRELATES TO REPLICATION COMPETENT VIRUS

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Attenuation of HIV-1 replication due to deletions in the *nef* gene often results in long-term non-progression in infected individuals. Although the long-term survival of such patients is likely to be dependent upon reduced viral fitness, it is unclear what role neutralising antibodies play. Here we have studied neutralising antibody responses in members of the Sydney Blood Bank Cohort (SBBC). This cohort consists of a blood donor and eight transfusion recipients who were infected before 1985 with HIV-1 containing a deletion in the region in which *nef* and the long terminal repeat overlap. This resulted in long term infection characterised by extremely low to undetectable viral loads, and no signs of progression except for slowly declining $CD4^+$ lymphocyte numbers in some individuals. The blood donor was the single exception to this, when he presented an unusual case of AIDS dementia associated with a high viral load and declining $CD4^+$ cell counts. This was effectively treated with antiretroviral therapy.

This study demonstrates a strong correlation between enhanced antibody response and a low but detectable viral load. One individual with a consistently undetectable viral load has not yet fully seroconverted, whereas those members with detectable viral loads (<10,000 RNA copies/ml) displayed unusually strong IgG responses to all HIV-1 proteins, comparable to the strong response observed after primary HIV-1 infection. Both early and late sera from these patients potently inhibited the replication of heterologous and contemporaneous cohort viruses, compared with control HIV-1 positive sera. Additionally, we are examining the full spectra of HIV-1 neutralisation by SBBC sera by investigating cross-clade neutralisation and the role of complement. These results indicate that infection with *nef*-attenuated HIV-1 can potentiate a strong neutralising antibody response, dependent upon the presence of detectable HIV-1 antigen to drive antibody production.

VIRAL AND IMMUNE DYNAMICS FOLLOWING VACCINATION AND SHIV CHALLENGE IN MACAQUES

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Many vaccines for HIV are currently being tested in primate models of infection. These are aimed at inducing T cell and / or antibody responses to the virus. Trials using DNA and viral vectors to induce potent CD8 T cell responses have shown significant success in controlling long term viral loads and preventing disease progression. However, CD8 T cells do not appear to mediate sterilizing immunity to infection. We have analysed the results of a DNA vaccine trial in macaques in order to investigate the viral-immune dynamics underlying this failure to prevent acute infection. We find that viral kinetics do not differ between control and vaccinated monkeys prior to day 10 after challenge. The number of virus specific CD8 T cells also does not appear to increase significantly prior to day 10, and at this time is only increased 1.5 fold compared with the level prior to vaccination. From day 10 onwards, virus-specific CD8 T cells increase in number, and viral growth is significantly slowed in vaccinated animals. However, the initial 10 day delay in immune control allows time for the establishment of viral latency and persistent infection prior to immune activation.

By contrast, passive antibody administration is capable of mediating sterilizing immunity in many animals. In addition, antibody treated animals that become infected show improved outcomes compared with control animals. Analysis of viral kinetics demonstrates that antibody treated animals exhibit lower viral loads from the earliest timepoint after infection (day 7).

Thus, whereas CD8 T cells appear to act too late to control the establishment of chronic infection, antibody acts early. An understanding of the kinetics of immune control by CD8 T cells and antibodies has important implications for the rational design of vaccines for HIV.

PROGRESSIVE DYSREGULATION OF THE IL-7/R SYSTEM IN HIV-1 INFECTION

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Interleukin-7 (IL-7) is essential for T-cell homeostasis. Plasma IL-7 levels are elevated in HIV-1 infection, inversely correlate to total and naïve CD4+ T-cell counts, and predict immune reconstitution. The IL-7 receptor (IL-7R) consists of CD127 dimerised to the common γ-chain (CD132). The effect of IL-7 on cellular expression of IL-7R components remains unknown. We hypothesise that expression of IL-7R components is dysregulated secondarily to elevated IL-7.

Healthy volunteers (n=8) and patients with primary (PHI; n=9) and chronic (CHI; n=9) HIV-1 infection were studied at baseline and following 10 months of ART. PBMC isolated from healthy volunteers were cultured with rhIL-7 (0-10ng/ml) for 7 days. Protein synthesis was inhibited using cycloheximide (50μM). Plasma IL-7 levels were determined by ELISA. Cell-surface CD127, CD132, and intracellular Ki-67 expression were determined by flow-cytometry. Differences between groups were analysed using the Mann-Whitney test.

PHI patients displayed a trend towards elevated baseline IL-7 levels that normalised following ART. Plasma IL-7 levels were significantly elevated in CHI and remained elevated following ART. There was decreased CD127 expression on naïve and memory CD4+ T-cells during CHI but not PHI. Plasma IL-7 levels inversely correlated with CD4+127+ populations and positively correlated to CD4+127- populations in both PHI and CHI. CD4+127+ and CD4+127- populations over-expressed cell-cycle protein Ki-67 in PHI and CHI. Ki-67 over-expression was restricted to memory CD4+ T-cells except in CHI following ART, where both CD4+127+ and CD4+127- populations proliferated.

Exogenous IL-7 down-regulated surface CD127 but not CD132 in a dose-dependent manner *in vitro*. CD127 down-regulation was reversible after removal of IL-7 and relied on *de novo* protein synthesis. CD127 turned-over on the quiescent cell-surface.

HIV-1 infection induces progressive elevation of plasma IL-7 and reduction of CD127 expression. CD4+ T-cell subsets undergo both antigen and homeostatic driven proliferation. *In vitro*, IL-7 down-regulates CD127 in a dose-dependent, post-transcriptional mechanism. Dysregulation of the IL-7/R system may impact on the quality of immune reconstitution.

A NEW CONCEPT OF RESTRICTED HIV-1 INFECTION OF ASTROCYTES

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HIV-1 infection astrocytes *in vivo* and *in vitro* is restricted. Despite this, astrocyte infection is involved in neurological disease and is a possible source of viral persistence. Hence, characterisation of HIV-1 infection of astrocytes at the molecular level is essential. Several stages of HIV-1 replication restriction have been identified, including HIV-1 strain dependent properties, inefficient viral entry, and intrinsic intracellular blocks at transcriptional and translational levels. Co-culture with permissive cells 'rescues' infectious HIV-1 from restricted astrocyte infection. Knowledge on the mode of HIV-1 entry into astrocytes is just beginning to emerge, and the early viral replication events of reverse transcription and integration have not been described previously. The present study demonstrates vesicular uptake of HIV-1 by astrocytes. Cell associated proviral DNA, attributed to input virus inoculum, was detected, however *de novo* reverse transcription and integration was not. Surprisingly very low amounts of infectious virus were sporadically released into the cell culture medium over a 13 day period. This data, taken together with previous models of astrocyte infection, supports the notion that multiple pathways of HIV-1 infection occur in the brain microenvironment. One pathway in astrocytes gives rise to low, sporadic/inducible virus production. An additional pathway which may exist in some types of astrocytes, as supported by this data, involves viral uptake and transmission without the virus actually replicating. It will be important to understand the relative impact of each of these infection modes to HIV-1 neurological disease and viral persistence.

ANTIBODY RESPONSES IN HIV-1 LTNP/LTS: UNEXPECTED RESPONSES TO VIRAL ANTIGENS BY IGG_3

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For HIV-1 infected individuals there is an initial acute infection followed by a chronic long-term infection, leading to AIDS. There are some individuals that do not progress to AIDS, maintaining low viral loads. This group are considered long term non-progressors or survivors (LTNP/LTS). Lack of disease progression can be due to mutations in genes encoded by the virus or the host, primarily *nef* gene deletions and CCR5 co-receptor mutations (CCR5-Δ32), respectively.

We have developed an EIA to determine accurately the presence of reactivity to p24 by IgG_3, permitting an established infection to be readily distinguished from acute infection. Preliminary data suggest that some LTNP antibody responses mimic profiles normally seen during seroconversion and this may be a contributing factor to or surrogate marker for lack of disease progression.

We have now assembled a diverse selection of LTNP/LTS from multiple cohorts, many with known viral or host defects associated with delayed progression. The aim of this study was to determine the antibody response to viral antigens focusing on total IgG and IgG_3 antibodies and comparing this with samples from progressors and AIDS patients. Detection of antibody responses was by western blot to all HIV-1 antigens and EIA to specific viral proteins p24, gp41 and gp120.

Overall immune responses to the viral antigens were broader and consistently stronger with LTNP/LTS, in comparison to progressor and AIDS patients. Responses were much more varied in individuals with a known viral attenuation, ranging from an intense broad- based response through to detection of only two viral proteins. More specific analysis of IgG_3 responses revealed a lack of consistent detection of p24 antibodies. Despite this there was an unexpected IgG_3 response to gp41 in several subjects. These unusual responses may reflect the possible presence of protective antibodies. Previously published data has indicated superior neutralization by IgG_3 antibodies compared to other IgG isotypes. This unusual finding parallels that seen for seroconverters possibly because of the retention of functional helper T cells in LTNP/LTS enabling the prolonged IgG_3, resulting in intense total IgG response and IgG_3 responses to multiple HIV-1 antigens, including gp41 and gp120.

Concurrent Session– Nursing

THE QUEENSLAND HIV NURSING PRACTICE COURSE: RESPONDING TO HIV NURSING EDUCATION IN 2004

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The Education offered to nurses in Queensland by the HIV & HCV Education Projects covers three courses. Firstly, the 'Education Course in HIV Medicine' is offered twice a year across the state; secondly the advanced course titled "The HIV Nursing Practice Course" is offered once a year and is open to those nurses who have completed initial training. Finally, the third component comprises yearly updates for nurses who are working in the field.

The HIV Nursing Practice Course has now been conducted in Queensland 9 times since August 1998 with a total attendance of 164. In both 2003 and 2004 the program of this two day weekend course was updated substantially and reflects the changing education needs of nurses working in HIV medicine. This presentation explores those changes and opens a discussion of the emerging education needs of nurses working in this area.

Areas of emerging need that have been added to the HIV Nursing Practice Course include: issues for women; paediatric HIV management; pregnancy; sex and sexuality; and motivational interviewing. Additionally, each time the course has been redrafted more time has been allocated to discussion of the role of the nurse in assistance with management of drug regimens. This has included discussion of adherence; Post Exposure Prophylaxis (occupational and non occupational); management of side effects; information on current trials; and management of use of complementary therapies.

Finally, an examination of the topics utilised in case discussions over time reflect the continuing and emerging difficult and complex scenarios presented by a subset of the population with HIV.

This presentation will begin with a summary of the history of the HIV Nursing Practice Course, move through the content presented in the course over time and emerge into a reflection of these changes as identifiers for trends in nurse management issues in HIV medicine.

CLIENTS' SATISFACTION WITH HIV PRE-TEST COUNSELLING APPEARS RELATED TO PREVIOUS EXPERIENCES OF TESTING AND RISK LEVEL

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This study investigated client satisfaction with HIV pre-test counselling in clients attending a HIV specialist clinic, the Albion Street Centre (ASC) for HIV testing. 49 (44 male and 5 female) clients rated their experience of pre-test counselling using a validated satisfaction scale relating to HIV counselling issues (the Albion Centre Scale, ACS) and a specifically developed satisfaction scale relating to pre-test counselling issues (PCS). Psychologists performed all pre-test counselling and rated the level of HIV risk taken by clients.

65% of the clients had received pre-test counselling before and 71% of those had tested previously at ASC. 90% were booked appointments, with 10% presenting for intake and/or Post Exposure Prophylaxis (PEP).

Overall clients rated their experience of the pre-test counselling service as highly satisfactory (84% ACS, 98% PCS). Clients who had not previously experienced HIV pre-test counselling found pre-test counselling more satisfying overall than those who had previous experience of pre-test counselling and this was significant on the PCS ($p<0.01$).

Of the 49 participants 36.7% were rated as having had a high to very high risk, 18.4% a medium risk, and 34% a low risk to very low risk. Interestingly, clients presenting with risks rated as medium to high indicated that they found the information pertaining to pre-test counselling, as measured by the PCS, significantly more satisfactory than those who attended with risks rated as low ($p<0.01$).

Findings suggest that HIV pre-test counselling is viewed as informative, helpful to mood and behaviour change, and generally a positive experience for clients who continue to test at services which they are aware provide formal pre-test counselling. The experience was rated as even more satisfactory by those who have not previously experienced pre-test counselling. This may be associated with these clients not having been tested before but this information was not collected. The recent debate regarding the usefulness of pre-test counselling appears to ignore the client's perspective. In considering the process and benefits of pre-test counselling the client's perspective should be taken into account. This study suggests that the majority of client's surveyed for this study experience pre-test counselling as beneficial and satisfying.

THE DOMINO EFFECT: THE COMPLEXITIES OF CARING FOR PATIENTS WITH HIV/AIDS IN 2004

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While the management of advanced HIV disease has never been "simple", anecdotal reports of increasingly complex clinical and nursing management scenarios appear to be becoming more frequent. A person presents with a seemingly straightforward diagnosis and commences on a course of treatment, however, somewhere along the line, the dominos start to fall, the client is barely recovering from one issue when another one appears and compounds their already impaired health state.

Our presentation includes just such a case. We follow their trajectory of ill health and interventions including acute admission, palliative respite, ICU admission and ultimately their death, which occurred in a somewhat unexpected sequence.

This case study is an initial step in a process of further investigating and understanding the complexities of care in advanced HIV disease, and how best to provide nursing support to clients in this phase of their illness.

THE EXPERIENCE OF FATIGUE AND STRATEGIES FOR SELF-MANAGEMENT AMONG COMMUNITY-DWELLING PERSONS LIVING WITH HIV

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Royal District Nursing Service of SA Inc (RDNS) Clinical Nurse Consultants (CNCs) drew attention to the problem of fatigue experienced by their clients living with HIV. These CNCs, supported by the literature, suggested that fatigue was one of the most prevalent, yet under-reported, under-recognised and under-treated aspects of living with HIV. This research project responded to the questions raised by clinicians. The objectives for this project were to understand the experience of HIV-associated fatigue and to describe the strategies for self-management of fatigue that HIV-positive people use in the context of daily life. Recruitment was conducted for adults who had been diagnosed with HIV for at least twelve months and who perceived that fatigue was a problem in their lives.

This inquiry was conducted by the RDNS Research Unit in 2003/2004. Data were generated from three sources: 1) In-depth interviews with 15 participants and observational notes; 2)Two Participatory Action Research (PAR) mixed gender groups (contact time 5 hours); and 3)A single page self-report questionnaire.

In collaboration with participants, we explored self-management strategies and identified the catalysts and constraints to self-management of their condition. The project was funded by a grant from the AIDS Trust of Australia and the South Australian Department of Human Services. The research report can be located on www.rdns.net.au (under research reports).

A ROOM WITH A VIEW: THE PITFALLS OF LONG TERM ADMISSION IN A PALLIATIVE CARE UNIT

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The provision of palliative care for PLWHA has undergone many changes since the beginning of the epidemic. While the overall number of clients has decreased dramatically over the years, the care needs of those still requiring support have remained complex.

One such complexity is the provision of extended care for clients too frail for independent living. While community services can provide intensive support for short to medium term situations, these clients sometimes require 24-hour care and supervision for many months or even years.

There are a number of supported housing options available to PLWHA however, there are clients whose needs do not correlate with what is available. These clients are often admitted to palliative care units. While these are excellent for supportive and comprehensive care, they are not without their limitations. The psychological impact of spending and extended period of time in a unit whose core business is caring for the dying can not be underestimated.

On a background of an ever tightening HIV funding belt, the aim of this case presentation is to highlight the complexities of meeting holistic care needs in a sometimes less than appropriate environment and to generate discussion on possible solutions.

COMBINING ADHERENCE MONITORING WITH PATIENT EDUCATION IN THE ROYAL PERTH HOSPITAL IMMUNOLOGY OUTPATIENT CLINIC

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At Royal Perth Hospital we conceptualise a model of adherence support that considers the adaptive and dynamic nature of adherence behaviour in the current clinical context. Our 2002-2003 survey of adherence showed that `25% of patients reported never missing medication. We wished to feedback results of the survey to the patients and reinforce good adherence behaviours whilst continuing to monitor missed doses.

The monitoring 'tool', is an A4 sheet. On one side is information regarding issues related to HIV treatment, this changes ~3 monthly. On the other is a table that does not alter, which allows the patient to identify the number of doses they have missed in the last month. The physician asks the patient for an estimate of tablets missed. This allows for a discussion of how the patient is managing with their medication. The doctor records a percent score of medication taken in the last month. To determine the usefulness of this practice we correlated the scores with viral load, CD4 count, and mean cell volume (MCV).

Medication scores were obtained from 381 individuals (mean number per person = 2.5), over a one year period. A total of 180 patients (47%) achieved scores of 100% for all visits. Scores were highly correlated with viral load ($p < 0.0001$) and, amongst those on at least 6 months of therapy, 76% of individuals with a score reflecting 100% adherence maintained plasma HIV RNA levels below 50 copies/ml. The proportion with undetectable viral load levels was reduced to 25% amongst those with average scores below 85%. Higher medication scores were associated with improved immunologic response as measured by the rate of increase in CD4 + T cell count ($p = 0.003$) and %CD4 + T cells ($p = 0.03$). To assess the correlation of these scores with an independent measure of adherence, values of MCV were obtained from those individuals on at least 6 months of AZT or d4T therapy. MCV was found to be consistently higher in those with higher scores ($p = 0.01$).

This simple monitoring tool appears to provide a useful measure of adherence that is associated with both virological and immunological response to therapy.

Concurrent Session – Epidemiology of New Infections

TRENDS IN NEWLY ACQUIRED AND NEWLY DIAGNOSED HIV INFECTION IN AUSTRALIA, 1994 – 2003

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The potential for an increase in HIV transmission in Australia has recently been suggested following reports of increases in unsafe sexual contact, new diagnoses of sexually transmissible infections other than HIV and the annual number of new HIV diagnoses. We report the pattern of HIV transmission in Australia, based on the results of national surveillance for newly diagnosed HIV infection.

Cases of newly diagnosed HIV infection were notified through State/Territory health authorities to the National HIV Database. Information sought on each case included the State/Territory of first HIV diagnosis in Australia, the date of HIV diagnosis, exposure to HIV and evidence of the recency of infection. Cases with a negative test or a diagnosis of HIV seroconversion illness within the 12 months prior to HIV diagnosis were defined as cases of newly acquired HIV infection. Trends over time were tested by negative binomial regression.

In 1994 – 1998 and 1999 – 2003, a total of 4,442 and 3,914 cases of newly diagnosed HIV infection, respectively, were notified to the National HIV Database. The annual number of new HIV diagnoses declined significantly from 1,023 in 1994 to 757 in 1998 ($p<0.0001$) and then increased from 717 in 1999 to 848 in 2003 ($p<0.0001$). Diagnoses of newly acquired HIV infection increased from 911 in 1994 – 1998 to 1,096 in 1999 – 2003. In 1994 – 1998, the number of diagnoses of newly acquired HIV infection declined from 214 to 151 ($p<0.0001$) and then increased from 171 in 1999 to 277 in 2003 ($p<0.0001$). Median age at diagnosis of newly acquired HIV infection increased from 29 years in 1994 to 30 years in 1998 ($p=0.029$) and from 32 years in 1999 to 33 years in 2003 ($p=0.19$). Exposure to HIV for the majority of cases of newly acquired HIV infection was attributed to a history of male homosexual contact (87.3%); a history of injecting drug use, heterosexual contact or an undetermined exposure history was reported in 2.6%, 7.8% and 2.3% of cases.

National HIV surveillance suggests a recent increase in HIV transmission in Australia and indicates that efforts to minimize HIV transmission need to be strengthened.

HIV SENTINEL SURVEILLANCE IN VICTORIA – A PILOT STUDY

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New diagnoses of HIV have increased markedly in Victoria in recent years, from 140 in 1999 to 225 in 2003. The majority were among males reporting homosexual/bisexual contact. As part of the Victorian routine surveillance process, information such as demographics, clinical history and brief risk behaviour information are collected on all new diagnosis. To enhance the current surveillance we have undertaken a pilot study of "linked" HIV sentinel surveillance among aimed at men who have sex with men (MSM) in Victoria. This enables us to collect HIV testing numbers (denominator data) and detailed risk behaviour information in a timely fashion.

Five sentinel sites (1 regional, 4 metropolitan) were chosen based on individual clinics having a high case load of MSM, variation in the likely demographics of the MSM and the willingness of the clinics to participate in the pilot study. Clients receiving HIV testing as part of normal clinical management were interviewed by their doctor using a brief questionnaire added to the standard HIV laboratory request form. The information collected includes demographic data, HIV testing history, STI history and testing, number of sexual partners, occurrence of unprotected anal intercourse (UAI), HIV status of partner with whom UAI occurred and place where UAI occurred. Questionnaire data were entered into an access database and merged with HIV results obtained through the HIV notification process. HIV testing was performed by the Victorian Infectious Diseases Reference Laboratory.

The pilot commenced on 1 April 2004. Within five weeks 400 questionnaires were completed. Results as of 31 July 2004 will be presented.

This is the first extensive linked HIV sentinel surveillance system in Australia. The results from linked HIV sentinel surveillance will help inform education strategies aimed at MSM in Victoria and will aid in evaluating the "HIV/STI testing campaign" undertaken by the Victorian AIDS Council in February 2004. After the pilot is evaluated, we anticipate that "linked" HIV sentinel surveillance will be expanded to more clinics across Victoria.

INVESTIGATION OF HIV INFECTION IN VICTORIAN WOMEN, 1999 TO 2003

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Victorian surveillance data indicate an increase of 140% in the number of new human immunodeficiency virus (HIV) diagnoses amongst women between 1999 and 2002, most notably in women born in countries with high prevalence rates of HIV and women having heterosexual contact with partners from those same countries. Little is known about the access, usage and utility of health services and supports amongst this population, though a recent study showed that HIV-infected women in Australia are more sceptical than men about antiretroviral treatment. In addition, migrant women may be especially vulnerable to marginalisation and difficulty accessing health resources.

We undertook a study of HIV infected women in Victoria at four major HIV treatment centres. The three aims of the study were: 1) describe the current sociodemographic and behavioural characteristics of women recently notified with HIV infection in Victoria, 2) identify barriers to access and utilization of support and treatment services and 3) use the information gained to inform intervention strategies. The Victorian HIV registry was used to identify women who reported heterosexual contact as their only risk for HIV infection. Trained interviewers conducted face to face interviews which included questions about HIV risk factors, use of HIV services, supports, medical care, effects of HIV on life, sexual relationships, pregnancy, childbirth and breastfeeding.

Eighty nine women were notified with HIV infection between 1 January 1999 and 31 December 2003, of whom 18 were known to have died or to no longer reside in Victoria. The study will recruit 20 women; enrolment is ongoing and will be completed in August 2004. This paper will present the study findings. Conclusions from this study will be informative for the new multicultural HIV service in Victoria. Recommendations for improvements in services and supports for HIV-infected women in Victoria will be made.

EVALUATION OF A DETUNED ANTIBODY TESTING STRATEGY FOR DETECTING INCIDENT HIV INFECTION

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The pattern of HIV transmission in Australia has been monitored through reports of newly diagnosed HIV infection including diagnosed cases of newly acquired infection. However, diagnosis of newly acquired HIV infection requires repeated testing of individuals, and hence provides a lower bound for HIV transmission. We have made use of a detuned HIV antibody testing strategy to identify early HIV infection in a single specimen and have compared the detuned test result with testing and clinical history available through national HIV/AIDS surveillance.

Cases of HIV infection newly diagnosed at St Vincent´s Hospital, Sydney, were tested with a detuned assay. Cases with a detuned result were matched to cases notified to the National HIV/AIDS Registry, to retrieve the date of first HIV diagnosis and the previous testing and clinical history. The detuned test result was compared with the evidence for newly acquired HIV infection.

A total of 1,125 cases of HIV infection with a detuned test result were matched to the National HIV/AIDS Registry. A total of 442 cases had detuned evidence of early infection (39.3%) and 355 cases (31.6%) had testing or clinical evidence of HIV acquisition within 12 months of HIV diagnosis. Among 163 cases with evidence of HIV acquisition within 30 days of the detuned test, 142 (87.1%) had early infection. Of 28 cases with a prior testing history only within 30 days of the detuned test, 25 had evidence of early infection, including 22 of 23 cases with virologic evidence of newly acquired infection. Of 109 cases with an HIV seroconversion illness only, 92 had detuned evidence of early infection and 25 of 26 (96.1%) cases with an illness and a prior testing history had early infection. Of 640 cases without evidence of newly acquired HIV infection and without an AIDS diagnosis, 150 (24.1%) had detuned evidence of early infection. Detuned evidence of early infection was detected in 24 of 130 (18.5%) cases with AIDS.

The detuned testing strategy validates estimates of HIV transmission among cases with a short interval between the last negative test and the first HIV diagnosis. The detuned test also falsely identified early HIV infection among cases of established infection, indicating that further work is needed to improve the accuracy of diagnoses of early infection based on detuned assays.

IMPROVING HIV SURVEILLANCE IN VICTORIA, THE ROLE OF THE "DETUNED" EIA

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The first indication of an increasing trend in HIV notifications in Victoria was when diagnoses jumped from 140 in 1999 to 197 in 2000. Determining the proportion of recently acquired infections provides valuable demographic information to better inform prevention strategies. In Victoria incident cases are identified on the basis of a past negative or indeterminate HIV test and/or a seroconversion illness within 12 months of HIV diagnosis. This method has limitations; it is reliant on individuals serially testing for HIV and a relatively non specific definition for "seroconversion illness". We examined the correlation between incident HIV infection identified through surveillance and recent infections identified through a "detuned EIA" laboratory method.

Sera from all new HIV notifications In Victoria between 1999 and 2000 were tested using the Organon Teknika "detuned" EIA with cases classified as recent (within 170 days) or established. Incident cases were identified using the standard surveillance definition outlined previously.

Of 317 specimens, 97 (31%) incident infections were detected using surveillance and 114 (36%) identified using the "detuned" assay and 66 were classified as incident cases by both methods. Of the 97 incident cases defined by surveillance, the "detuned" assay classified 31 (32%) as established infections, with 20 of these 31 having a history of a negative/indeterminate test or seroconversion illness 170 to 365 days prior to HIV diagnosis. Of the 114 cases identified as recent infections by the "detuned" assay, 48 cases were classified as non-incident cases by surveillance and 13 of the these 48 were likely to have been erroneously classified by the "detuned" assay as 11 cases presented with AIDS and two cases with CD4 counts ≤200 at the time of HIV diagnoses. The two methods combined were able to classify an overall 42% of specimens as incident cases (37% in 1999 and 45%in 2000), 36% more than the 31% detected through surveillance alone.

As new diagnoses of HIV in Victoria have markedly since 1999, from 140 to 225 in 2003, we believe the utilization of a "detuned" assay or similar test in combination with surveillance could be a timely and important tool to guide public health action by providing more accurate information about those who have recently acquired HIV and maximize the opportunity to interrupt ongoing viral transmission through partner notifications strategies.

FINAL RESULTS FROM THE AUSTRALIAN NON-OCCUPATIONAL POST EXPOSURE PROPHYLAXIS (NPEP) OBSERVATIONAL STUDY

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NPEP against HIV remains a controversial HIV prevention strategy that has been implemented in relatively few countries worldwide. Australia is one of few nations that has adopted guidelines and implementation programs. The NPEP observational study was conducted between 1998 and 2004 to monitor the implementation of this preventive therapy.

People who presented to registered anti-retroviral prescribers, reported a recent non-occupational exposure to HIV and were eligible for PEP according to the national guidelines were recruited into the study. Data was collected at the time of prescription, at four-weeks and six months following the exposure.

By May 2004, over 1500 participants had been enrolled. Data were analysed on those enrolled by December 2003. There were 1370 participants enrolled and 96.6% (1324) received PEP. Participants were predominantly men (1289, 94.1%) with a median age of 32.7 years. The median time from exposure to receipt of PEP was 23.2 hours. As the study progressed, more recipients commenced PEP within 72 hours of exposure ($p=0.004$). The majority of prescriptions (1175, 85.8%) were after male homosexual exposure. The source person was known to be HIV positive in 32.9% (450) of cases. The proportion of study participants with a known HIV positive source significantly declined over the study period ($p= 0.004$). The majority of PEP prescriptions (58.1%) were for three or more ARV drugs. An increase in PEP prescriptions containing two drugs was observed over the study period, increasing from 23.8% in 1999 to 52.2% in 2003 ($p<0.0001$).

Six participants were found to be HIV positive at baseline. 68.5% (869) of participants returned at four weeks or more for repeat HIV testing. The majority of these (604, 69.5%) reported side effects. Most reported at least two side effects, nearly all mild or moderate. Prescription of three or more drugs was associated with a greater incidence of side effects at any severity level ($p< 0.0001$).

There was considerable loss to follow-up, with only 26.7% of participants returning at 168 days (24 weeks) or more. The median length of follow up was 88 days. No HIV seroconversions definitely related to treatment failure were observed and it is estimated that two to nine new HIV infections should have occurred based on risk behaviours reported.

This study is one of the largest in the world of its kind. Initially designed to monitor the implementation of NPEP guidelines, important data have been accumulated which have contributed to the evaluation of the role of NPEP in HIV prevention, but definitive data that prove the efficacy of NPEP are still needed.

A COMPARISON OF THE WESTERN BLOT VERSUS DETUNED EIA METHODS FOR DETECTION OF INCIDENT HIV INFECTION

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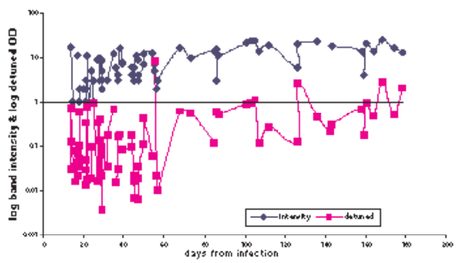
We propose a new method for classifying newly diagnosed HIV-infected persons as either incident or established infections.

Western blot (WB) results (n=745) from 330 persons (cohort A) newly diagnosed and with independent evidence of primary HIV infection were analysed to create a model. All specimens were taken prior to initiation of ARV therapy. A second set of WB results from 197 patients (cohort B), categorised as either primary HIV infection, or as late stage disease, was used for validation. A third set of ~150 patients from university clinics in the USA (Cohort C) was used to re-validate the model using external data. A fourth analysis of 58 patients having both WB and detuned EIA results assessed relative assay performance in the first 180 days of infection. Bands measured were gp160, gp120, p68, p55, p53, gp41, p34, p24, and p18 for cohorts A and B; gp160, gp120, p65, p55, p51, gp41, p31, p24, and p18 for cohort C. Individual bands were scored as negative, indeterminate, or positive (UCSF only), or as negative, trace positive, or 1+, 2+, or 3+ positive. Intensity score was defined as the sum of individual bands scores.

Two patients were excluded of Cohort A because of conflicting evidence regarding length of infection. Using a cut-off of <= 3 bands positive on WB as the predictor, and classifying specimen dates as either <=, or >180 days post-infection, logistic regression found the model to have from 50-70% sensitivity, but consistently 100% specificity in cohorts A, B, and C. Restricting analysis to patients having both WB and detuned EIA results available and fitting a linear regression model, the WB intensity score had a stronger correlation than the detuned assay in estimating time from infection within 180 days following infection (adjusted R-square 0.5372 versus 0.3478 respectively). Combining intensity score and detuned EIA SOD in the same model, the detuned variable lost significance (P=0.6478) while the intensity score remained highly significant (P<0.0001). (See graph)

Use of WB patterns and intensity score may present a fast, efficient, inexpensive method for monitoring incident HIV infection. Further comparison of the methods for use on specimens taken post- ARV therapy may reveal additional applicability of the model.



Concurrent Session– Clinical Medicine – Metabolic Syndromes

SUBCUTANEOUS INJECTION OF POLYLACTIC ACID (PLA) IN INDIVIDUALS WITH HIV-1 INFECTION ASSOCIATED FACIAL LIPOATROPHY: SIX-MONTH OUTCOME AND PREDICTORS OF RESPONSE

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Loss of facial subcutaneous fat is a distressing and durable component of the lipodystrophy syndrome for some HIV-infected individuals treated with combination antiretrovirals. There are few treatment options. We report the six-month outcome of an open label study of subcutaneous injection of PLA in 27 individuals, enrolled after assessment by a Plastic Surgeon as having moderate to severe facial thinning. Primary efficacy measure is facial atrophy assessed by independent plastic surgical review of standardised clinical photography (baseline and six months post treatment). Secondary efficacy measures include patient-scored changes in facial thinning, and changes in facial soft tissue volume on Spiral CT scan (baseline and 4 months post treatment), quality of life and HIV treatment outcome (adherence). Adverse events were assessed by patient questionnaires at end of treatment and at six months.

	Severity Lipoatrophy Mean (SD)*		Patient Distress Mean(SD)*
	Photographic Grade (MO)	Patient assessment	
Baseline	2.9 (0.9)	3.6 (1.1)	3.9 (1.2)
Month 6	2.3 (1.0)**	2.6 (1.3)**	2.9 (1.7)**
* Six point grade 0=nil, 5=severe.			
** Difference from baseline P < 0.05			

20 of 27 individuals were assessed as having improvement in facial appearance at 6 months. Age, baseline CD4 cell count, and type of antiretroviral therapy did not predict the degree of facial improvement at 6 months.

Twenty of 27 patients' self-assessment showed improvement in facial appearance at 6 months (Concordance with photography grading - 48.1%). Psychological/ emotional distress was reported as substantially reduced in those with photographically as well as patient self-assessed improved appearance.

Local pain was recorded by 63% of individuals, mean severity 3.4/10; redness by 74%, mean severity 3.7/10 and swelling by 89%, mean duration 2.4 days, severity 4.04/10. No patient withdrew due to adverse events.

Conclusion Subcutaneous injection of PLA produced durable improvement over 6 months in facial appearance in 74% of these individuals with moderate to severe facial atrophy. Few adverse events were recorded and patient distress was markedly improved.

NEW-FILL: FACING THE CHALLENGES OF LIPOATROPHY

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Many people with HIV are facing lipodystrophy related body changes, thought to be a side effect of HIV antiretroviral treatment. Facial lipoatrophy, part of the lipodystrophy complex, is wasting of adipose tissue which occurs to varying degrees in affected individuals. It often impacts negatively on the quality of lives of people living with HIV/AIDS.

This research focuses on the use of intradermal injection of Polylactic Acid (PLA) into facial areas affected by lipoatrophy. The main arm of this study was designed to quantitatively evaluate the durability and extent of changes resulting from the PLA treatment for 28 individuals. This paper presents an arm of the trial that explored the lived experience of participants, pre and post PLA treatment, through semi structured interviews and a qualitative discourse analysis

Pre treatment interviews, conducted 2 weeks prior to commencing the PLA treatment, sought to explore the personal impact of facial lipoatrophy and individual's thoughts in anticipation of the treatment. Common themes include; stigmatisation, erosion of self image and self esteem, problems with social and sexual relations, anxiety, depression, social withdrawal and perception of unintentional HIV disclosure. There was also evidence that participants were anticipating major life changes as an outcome of the PLA treatment. For some individuals, knowing that they were going to have the treatment assisted them to plan or begin to make changes in their lives.

The second interviews, conducted 6 months post treatment, explored the physical and psychosocial responses of participants to the treatment. Predictably there were a range of treatment responses. Some people described the procedure as very painful while others experienced minor discomfort. For some people the results were quite dramatic, resulting in increased confidence, social interaction and the ability to return to paid work. For others the results were not as dramatic but suggested minor improvements in quality of life. For a minority the treatment did not meet their pre-treatment expectations resulting in disappointment.

These research results will assist clinicians to more fully understand the many possible effects of facial wasting on people's lives. It will also assist them to incorporate realistic counselling regarding treatment expectations and outcomes for those contemplating PLA treatment. Furthermore, the research justifies the powerful effect treatment with PLA for facial lipoatrophy can have in terms of an individuals overall sense of wellbeing. As such it is recommended that it is considered as an essential element of quality care within existing HIV/AIDS medical services.

ROSIGLITAZONE IN ADULTS WITH HIV LIPOATROPHY: 84 WEEK FOLLOW-UP (ROSEY EXTENSION)

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The 48 week randomised, placebo-controlled, double-blinded ROSEY study found that rosiglitazone (RSG) 4mg bd did not improve lipoatrophy in HIV-infected adults receiving antiretroviral therapy, despite significantly improving insulin sensitivity and plasma adiponectin levels. We assessed whether lipoatrophy might improve over a longer follow-up period.

All 108 participants, including 55 previous placebo recipients were offered open-label RSG at week 48 up to week 96. 12 participants did not consent to open-label (5 from RSG group). During open-label 1 patient died (placebo group) and 10 ceased study drug (6 RSG group) but continued follow-up. The study was ceased early as the results for the blinded phase showed no benefit on lipoatrophy and adverse effects on lipids. Participants were called in to complete a final visit at this time. Data collected at weeks 84 and 96 were combined to one time-point (week 84).

Limb fat increased by 0.40 (SD=0.69) kg in the RSG group and 0.38 (SD=0.90) kg in the placebo group at week 84 (mean difference, 0.02 [95%CI, -0.46, 0.51] kg; p=0.93 by t-test). Independent baseline predictors of greater increases in limb fat at week 84 were higher total cholesterol (ρ=0.28, p=0.003) and greater subcutaneous thigh fat (ρ=0.04, p=0.01). There was no significant between group difference in:

1. subcutaneous mid-thigh fat (p=0.16), subcutaneous abdominal fat (p=0.52) or visceral fat (p=0.60) on computed tomography;
2. total body fat mass (p=0.80), total trunk fat (p=0.86), lean body mass (p=0.55) on DEXA or the lipodystrophy case definition score (p=0.29, week 72)
3. cholesterol (p=0.72), HDL (p=0.52), LDL (p=0.99), triglycerides (p=0.25), glucose (p=0.51), insulin (p=0.46).

As in the randomised phase, the key adverse effects of RSG were asymptomatic hypertriglyceridaemia (grade 3 or 4 in 58% and 49% of the RSG and placebo groups respectively, to week 84), hypercholesterolaemia (grade 3 or 4 in 26% and 18% of the RSG and placebo groups respectively, to week 84), and asymptomatic high creatinine kinase (grade 3 or 4 in 42% and 20% of the RSG and placebo groups respectively, to week 84).

RSG 4mg bd for 84 weeks did not improve lipoatrophy in HIV-infected adults receiving antiretroviral therapy.

OBSERVED AND PREDICTED RATES OF MYOCARDIAL INFARCTION IN THE D:A:D STUDY

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Recent results from the D:A:D Study, a prospective observational cohort of 23,468 HIV-patients, indicated that the incidence of myocardial infarction (MI) increased by 26% per year of exposure to combination antiretroviral treatment (CART). We compared the rate of MIs observed in the D:A:D Study to the expected rate based on conventional cardiovascular disease (CVD) risk equations.

The Framingham equation was applied to individual patient data in the D:A:D Study to predict MI rates by duration of CART (no CART, <1 year, 1-2 years, 2-3 years, 3-4 years and 4+ years) assuming a 5 fold increase in MI risk in those with prior CVD and adjusting for regional differences in MI risk. CVD risk factors were time-updated for patients who contributed follow-up to more than one CART category. Sensitivity analyses were performed to assess the effect of model and data assumptions.

Patients with longer CART exposure had a less favourable cardiovascular risk profile in term of prevalence of male sex (no CART: 70%; 4+ years: 81%), age (37 and 41 years), prior CVD (1% and 2%), diabetes (2% and 4%), total cholesterol (3.9 and 5.1 mmol/L) and triglycerides (1.3 and 2.2 mmol/L). Conversely, smoking prevalence decreased (63% and 55%). In patients receiving CART, the numbers of MI observed during D:A:D follow-up were of similar magnitude and possibly somewhat higher than the numbers predicted from Framingham: 9 observed vs 5.5 predicted, 14 vs 9.8, 22 vs 14.9, 31 vs 23.2 and 47 vs 37.0 in <1 year, 1-2 years, 2-3 years, 3-4 years and 4+ years CART duration, respectively. In patients not receiving CART, the observed number of MIs was fewer than predicted (3 observed vs 7.6 predicted). Predicted MI rates were within the 95% confidence interval of observed rates. Sensitivity analyses consistently showed that in patients receiving CART the observed and predicted rates of MI increased in a parallel fashion with greater CART duration.

The observed rate of MI in the D:A:D Study was of a similar magnitude to, or somewhat higher than, that predicted by the Framingham CVD risk equation. That observed and predicted rates of MI increased in a parallel fashion with increased CART duration suggests that the observed increase in risk of MI may largely be explained through CART-induced changes in conventional CVD risk factors.

IMPAIRMENT OF REVERSE CHOLESTEROL TRANSPORT IN HIV INFECTED SUBJECTS

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Clinically, HIV and protease inhibitors (PI) independently induce changes in blood lipids and subsequently the increased risk of coronary artery disease (CAD). These issues become more significant as the life expectancy of individuals is extended by treatment. As reverse cholesterol transport (RCT) is critical in protecting against atherosclerosis, it can be hypothesised that the increased risk of developing CAD may reflect an impairment of RCT.

To identify further mechanisms by which HIV and/or PI impact on lipid parameters, we assessed the levels and activity of transfer proteins and lipoproteins of RCT in 33 HIV negative, 22 untreated HIV positive subjects and 34 PI treated HIV positive subjects. The results (Table 1) show that one element of the anabolic arm of reverse cholesterol transport, namely the activity of lecithin cholesterol acyl transferase (LCAT) an enzyme responsible for the remodelling of high density lipoprotein (HDL), is increased in subjects with HIV infection irrespective of treatment. At the same time, parts of the catabolic arm of RCT, phospholipid transfer protein (PLTP) and cholesterol ester transfer protein (CETP) are reduced. Increased anabolic and decreased catabolic activity may result in accumulation of dysfunctional HDL particles and retardation of RCT. In addition the reduced cholesterol content of the HDL in both HIV positive groups suggest the particles are triglyceride rich and supports the fact that they are potentially dysfunctional. Impairment of RCT may have a substantial contribution to the observed increased risk of CAD in HIV infected subjects.

	HIV negative	HIV positive untreated	HIV positive PI treated
LCAT (nmol/µl/hr)	24.2 ± 7.9 (n=33)	50.3 ± 11.9 * (n=20)	52.1 ± 25.1 * (n=25)
PLTP (nmol/µl/hr)	3.5 ± 0.2 (n=17)	3.5 ± 1.1 (n=12)	1.5 ± 0.8 * (n=27)
CETP (µmol/µl/hr)	73.4 ± 10.2 (n=33)	46.5 ± 27.1 * (n=19)	51.5 ± 19.6 * (n=20)
HDL-C (mmol/L)	1.4 ± 0.4 (n=33)	1.0 ± 0.2 * (n=18)	0.9 ± 0.3 * (n=33)

Table 1 Mean levels of lecithin cholesterol acyl transferase (LCAT), phospholipid binding protein (PLTP), cholesterol ester transfer protein (CETP) and high density lipoprotein (HDL-C) in each subject group.

* Indicates a statistically significant difference (P<0.05) when compared with control.

EFFECTIVENESS OF A DEDICATED LIPODYSTROPHY CLINIC IN REDUCING HYPERLIPIDAEMIA IN HIV-INFECTED INDIVIDUALS

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Since March 1999 The Alfred Hospital has had a dedicated, multidisciplinary clinic to address the problems of HIV-associated lipodystrophy with a focus on control of hyperlipidaemia and management of cardiovascular risk. Included in the therapeutic team are infectious diseases physicians, a cardiologist, dietitians, occupational therapists, physiotherapists and nurses. A variety of strategies are used including dietary manipulation, lipid lowering agents and change of antiviral therapy. Clinic Guidelines for management were developed and promulgated, recommending referral of individuals with multiple risk factors for cardiovascular complications . Since December 2001 we have seen 52 patients with average maximum total cholesterol of 8.4 mmol/L (range 3.7-24.5 Standard deviation [SD] 3.4) and an average maximum triglycerides of 11.3 mmol/L (range 1.3-64.5 standard deviation 11.4). The most recent levels of all patients seen are equal or reduced for all patients but one, who has a small rise in triglycerides. Mean declines are 2.75 for cholesterol (range of reduction 0-18.3) and 6.9 for triglycerides (range of reduction -2.4 to 60) to give current mean levels of 5.6 for cholesterol (SD 1.6) and 4.4 for triglycerides (SD 4.2), P values for significance by t-test <.001 for both cholesterol and triglycerides. A dedicated multidisciplinary clinic is effective at reducing lipid levels significantly.

Symposium – Basic Science – New Drug Strategies

THE VIRION-ASSOCIATED CHOLESTEROL OF HIV-1: *A POTENTIAL TARGET FOR TOPICAL MICROBICIDE DEVELOPMENT.*

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While condom is an effective barrier to prevent HIV transmission, the economical and the cultural constrains for women in developing countries often prevent them to negotiate condom use with their partners. Consequently, a prevention strategy that can be administrated by women is vital for the prevention of HIV transmission in these settings. HIV-1 particles are enriched with cholesterol. Lipid rafts are enriched in cholesterol and sphingomyelin and are isolated on the basis of insolubility in detergents, such as Brij 98 and Triton X-100. We and others have found that Brij 98-insoluble rafts can be found in HIV-1 and virus-like particles, respectively, but the significance of this cholesterol enrichment or the presence of lipid rafts in HIV-1 is unknown. Using methyl-β-cyclodextrin (CD) to remove cholesterol from HIV-1 envelope, the infectivity of cholesterol deficient HIV-1 particles were impaired compared with the wild type untreated control. To directly assess the functional requirement of virion-associated rafts and various features of cholesterol on HIV-1 replication, we have replaced virion-cholesterol with exogenous cholesterol analogues that have demonstrated either raft-promoting or -inhibiting capacity in model membranes. We have observed that (1) CD in combination with a raft-disrupting sterol analogue further inhibits viral infectivity, (2) CD in combination with excess sterols acts to suppress HIV-1 infection and (3) sterols with high affinity for the HIV particle may lower the amount of cholesterol analogue or CD required to affect the particle, thus reducing the likelihood of cytotoxic effects. One would predict that the combination of CD with a synthetic cholesterol analogue that encompasses these features would be invaluable for the formulation of a CD-based topical microbicide against HIV-1. The development of this new topical microbicide is likely to have wider applications in preventing the transmission of other sexually acquired pathogens that rely on lipid rafts in their replication cycle, including Herpes simplex virus and *Chlamydia*.

INHIBITION OF HIV ENTRY INTO DENDRITIC CELLS: A NEW STRATEGY FOR MICROBICIDE DEVELOPMENT

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Globally, more than 40 million people are currently infected with HIV-1, with the majority of infections present or initiated at mucosal surfaces. Vaginal, intravenous, rectal, oral and mother-to-child routes of transmission all involve mucosal exposure. Post-infection, HIV quickly establishes a reservoir in the lymphatic tissue in the 2-3 weeks following mucosal transmission resulting in virus production and tissue pathology. As a result of this rapid, persistent infection the development of effective microbicides and vaccines, which will target the very early stages of the virus-host interactions are likely to be the most effective at preventing or limiting HIV infection and dissemination. The development of such microbicides for topical use may represent a more viable alternative to condom use in many HIV infected regions of the world especially by empowering women.

Many compounds are currently being tested as microbicides including topical application of standard antiviral drugs, surface blockers such as CCR5 inhibitors and novel compounds, which inactivate HIV-1. Essentially there are two approaches to microbicide development; either target the incoming virus or target the cells that the virus attaches to. Targeting the virus with small molecules that interact with the viral envelope glycoproteins (gp120/41) and are able to interfere with the HIV binding has had some success with the fusion inhibitors T-20 and T-1249. The interaction of gp120 with CD4 and a coreceptor (usually CCR5 and CXCR4) provides a target for the development of small molecule receptor-specific drugs or modified ligands to prevent infection of the cell.

Here we propose a similar strategy, that of targeting one of the first cells that HIV-1 encounters, the dendritic cell (DC) and inhibiting HIV entry into these cells via the C-type lectin receptors (CLRs) that we have shown can bind HIV, resulting in transmission and infection. DCs have a number of roles in HIV pathogenesis, including initial HIV uptake, infection, transport to lymphoid tissue where they stimulate explosive HIV replication in T cells and conversely priming CD4 and CD8 cell mediated immunity. Immature DCs, such as Langerhans cells (LCs) and interstitial DCs are among the first cells infected by HIV following mucosal exposure. DCs express CD4, CCR5 and a variety of CLRs, DC-SIGN being the most extensively studied, all of which are capable of binding HIV. We have recently shown different subsets of tissue DCs express a wide diversity of CLRs, with the virus able to use specific CLRs on each subset enabling capture and infection and/or dissemination. Therefore, strategies to block sexual transmission of HIV may require blockade of several CLRs on genital tract DCs: Langerin on LCs, mannose receptor and DC-SIGN on dermal DCs. To date there has been an excessive focus on only producing surface blockers for DC-SIGN, and these have not even been tested in an appropriate tissue DC setting.

EFAVIRENZ, A POTENT ENHANCER OF HIV-1 REVERSE TRANSCRIPTASE DIMERIZATION, AFFECTS THE LATE STAGES OF HIV-1 REPLICATION

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The human immunodeficiency virus type 1 (HIV) reverse transcriptase (RT) is an asymmetric dimer formed by the association of p66 and p51 polypeptides. Previous studies have demonstrated that nonnucleoside reverse transcriptase inhibitors (NNRTIs) can enhance RT heterodimerization and p66 and p51 homodimerization. Since p66 is part of the Gag-Pol polyprotein precursor we investigated whether NNRTIs can affect the late stages of virus replication. 293T cells were transfected with full-length clones of HIV-1 (NL4.3). Cell lysates and sucrose cushion purified virus from transfected cells were lysed and subjected to Western blot analysis. The effect of drugs on viral particle release was determined by metabolic labelling of viral proteins. Cells transfected with wild-type NL4.3 and treated with efavirenz (EFV), a potent enhancer of RT dimerization, showed more efficient cleavage of p66 to p51 and altered levels of Gag-Pol processing intermediates compared to untreated cells. In contrast, cells treated with zidovudine and NNRTIs that are either weak (nevirapine, NVP) or do not enhance RT dimerization (delavirdine) displayed Gag and Gag-Pol processing patterns similar to untreated cells. In contrast, EFV did not alter the pattern of protein expression in viral particles indicating that the effect of EFV was intracellular. Examination of viral particle release from EFV treated cells revealed a concentration dependent decrease compared to untreated and NVP treated cells. Significantly, decreases in intracellular p24 levels and cellular protein synthesis were not observed at the drug concentrations tested. EFV failed to decrease viral particle release of an HIV protease (PR) active site mutant. Furthermore, EFV treated cells transfected with NL4.3 containing the K103N mutation, which confers EFV resistance, failed to demonstrate decreased viral particle release. These data demonstrate that EFV increases intracellular Gag-Pol processing and decreases viral particle release, presumably by premature activation of the HIV PR at drug concentrations observed in patients. This effect was shown to be dependent on a functional PR and appears to be mediated by the drug binding to p66 in the context of Gag-Pol. These data demonstrate for the first time a novel mechanism of inhibition of HIV replication by EFV, in addition to its inhibitory effect on RT activity.

Symposium – International – Responding to HIV: Policy and Implications in PNG

INTRODUCTION OF ANTIRETROVIRAL DRUGS IN PAPUA NEW GUINEA: THE PILOT PROGRAM

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The HIV epidemic in Papua New Guinea (PNG) has reached alarming proportions and there may be as many as 50,000 infected individuals in the country. The response has been, until recently, directed at the prevention of infection through community awareness. Meanwhile HIV/AIDS has become the second most common cause for medical admission to the Port Moresby General Hospital and the most common cause of death.

HIV is a treatable disease, but the availability of treatment has been limited by cost. Recent price reductions brought about by generic competition has made antiretroviral drugs more affordable. A concerted international campaign to introduce treatment for HIV in resource-poor settings is now underway. The "3 x 5" program of the WHO has broad international support and is being funded by a number of international agencies, most notably the Global Fund. AUSAID has an active multisectoral HIV program in PNG. This organisation has been involved with some of the infrastructure support the program, but not the purchase of medication.

Papua New Guinea has national treatment guidelines. In February 2004, a Short Course in HIV Medicine and Antiretroviral Prescribing was held in Madang. A pilot program for the provision of antiretroviral drugs commenced in Port Moresby in February 2004 and had enrolled over 40 patients by the end of May. The provision of antiretroviral drugs occurs in an environment where laboratory support is highly constrained and even the treatment of common opportunistic infections is not always possible. Implementation and progress of the program will be described.

IMPLEMENTING THE PAPUA NEW GUINEA *HIV/AIDS MANAGEMENT AND PREVENTION ACT* 2003

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The management of HIV/AIDS presents challenges to governments worldwide. Well resourced governments in first world countries struggle with the implementation of appropriate laws for the protection of public health and of the rights of individuals affected by HIV/AIDS who may subjected to sweeping powers in health legislation.

Developing countries must face greater challenges. Lack of resources, cultural resistance to broad education programs, an overwhelmed health workforce and difficulties with legislative infrastructure are just some of the potential challenges.

The PNG Parliament passed the *HIV/AIDS Management and Prevention Act* 2003 in June 2003. The Act is progressive and contains privacy protections and protections against discrimination and stigmatization. It protects access to means of protection against HIV/AIDS. It requires consent to testing and counseling for those tested and protects the privacy of those affected by HIV/AIDS.

The PNG National AIDS Council, supported by AusAID, is currently developing a process for implementing the Act. This includes extensive consultation with stakeholders such as police, courts, prosecutors, ombudsman, correctional and health authorities, defence personnel etc. These stakeholders, together with the broader community in PNG must be informed about the Act and the rights and obligations it contains. For some, becoming accustomed to a new approach will be unwelcome and difficult. Patience and persistence will be required.

This is the story of the development and implementation of progressive public health oriented legislation in a developing country. It is both a celebration of achievement and a description of almost impossible challenges.

WORKING WITH COLLABORATING PARTNERS – NAPWA IN PNG

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The National Association Of People Living with HIV/AIDS (NAPWA) has been a partner with the Collaboration for Health in Papua New Guinea (CHPNG) group to support a specific program with HIV positive people and their carers, for the development of plwha spaces and the establishment of day care centres in PNG.

This project has been ongoing since February 2003, and has involved the support of the NAPWA International Portfolio, the AIDS Treatment Project Australia (ATPA), and the Australasian Society of HIV Medicine (ASHM). Merck, Sharpe and Dohme Australia (MSD) has been the pharmaceutical company involved directly with the funding of this initiative.

This presentation will describe the alliance structure, and partner responsibilities in this innovative pilot. The programme of training included training and briefings for NAPWA volunteer representatives and secretariat support, as well as the development of the programme of activities for the participants from PNG who were facilitated through the NAPWA Biennial Conference, and a subsequent "Reflections Workshop" over two days.

Models of peer facilitation and community development that were utilised and adapted will be described, and the contributions from both HIV peer educators and technical support workers will be discussed and critiqued. The areas of treatment advocacy and health maintenance support, notions of cultures of care, and issues of stigma and cultural difference will be described, to illustrate how the programme aimed to develop local and culturally appropriate mechanisms for reaching the objectives of the project.

The evaluations of the project from the PNG delegates will be reported, and the planning and implementation of Phase two of the project, a NAPWA follow up mission to PNG in May 2004, will also be presented.

Finally, the involvement of NAPWA in this intensive and unique program of HIV capacity building and skills and knowledge sharing will be discussed, for both consideration of lessons learned, as well as a broader discussion of the implications of this work for future involvement of NAPWA in peer support activities in PNG, and with future community development collaborations.

MAKING SOCIAL MESSAGES CONTENT RELEVANT TO THE WAHGI SOCIETY, WESTERN HIGHLANDS PROVINCE, PNG

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Sexual freedom is an aspect of the religious affairs of the Wahgi society, Western Highlands Province, Papua New Guinea. Sexual behaviour is concealed knowledge that is sanctioned through rituals. Use of sexually explicit words is culturally unacceptable and even the act of sexual intercourse is labelled as 'doing bad things', which is linked to the wider conceptions of order, balance, moral goodness and contravention of acceptable standards. If sex takes centre stage in the Wahgi social affair, should it not be that the entire culture is labelled as 'high risk'. Some cultures in PNG promote sexual freedom, multiple marriages and ritualised homosexuality. These cultures, including the Wahgi, can be categorised as HIV-AIDS high risk, just as much as epidemiologically diagnosed groups such as gays and sex workers.

Efforts to change individual sex behaviour alone without partnership between content owners (producers of social messages) and the target groups (an assumption that it is a single cultural entity) undermines the fact that there are hundreds of ways of speaking, behaving and practicing sex in PNG. For the Wahgi what is at stake is not an individual being coerced to forfeit multiple wives, adultery and promiscuous affairs, but the entire beliefs and cultural values on reproduction, growth, expansion and continuity.

This paper discusses how the Wahgi people attempt to sensitise culturally irrelevant HIV/AIDS messages and create, own and deliver these to themselves in culturally and linguistically acceptable forms. It argues that the models of social messages need to be rooted in the community and change in behaviour may be productive if the communities use their own communicative ways of initiating such changes.

Concurrent Session – Issues in Primary Care

THE FINDINGS OF THE PATIENT INFORMATION EXCHANGE (PIE) STUDY: IMPROVING THE TRANSITION OF HIV POSITIVE PATIENTS FROM HOSPITAL TO COMMUNITY MANAGEMENT

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The increasing longevity in the HIV-positive population brought about by the advent HAART (Highly Active Antiretroviral Therapy) is accompanied by a growing prevalence of co-morbidities, long-term complications of HIV, its therapy & psychosocial issues. Consequently, patients are frequently managed by several members of the multidisciplinary team & external service providers, emphasising the need for greater integration of acute & community service providers to improve patient follow-up & continuity of care. Currently, there is no formalised network for clinical communication between all of these parties.

The Patient Information Exchange (PIE) study is an innovative program developed to address these issues. The aims are to improve & formalise the process of information exchange between the healthcare providers involved in the management of HIV-positive patients & to evaluate the benefits of implementing a new service utilising a case-management model of pharmaceutical care.

This study measures the impact of assigning a "primary" pharmacist (one pharmacist dedicated to an individual patient's care), who acts as the key contact regarding all medication-related issues, to allow the provision of 'seamless' individualised patient care. The program allows patients & healthcare providers access to medication related advice outside of normal pharmacy operating hours & to communicate information via telephone & small message service (SMS).

Data will be presented from a pilot study of twenty-two HIV-positive patients aged 18-65 years conducted at the Alfred Hospital, Melbourne from April to July 2004. The study population incorporates a broad spectrum of patients, 19 males (86.4%) & 3 females (13.6%) with co-morbidities including hepatitis C co-infection, haemophilia, HIV-related dementia & schizophrenia. A selection of healthcare providers who care for HIV-positive patients were invited to complete pre-intervention questionnaires, allowing the determination of existing practices. Primary outcome measures include participant & healthcare provider satisfaction with the service, determined by survey; the number of contacts made to the primary pharmacist during the intervention period & the accuracy of participant medications lists held by healthcare providers.

The presentation will include analysis of the results obtained & highlight the key strategies required to improve healthcare provider communication, to facilitate better transition of patients from hospital to community care.

COMPLEX PATIENTS: EVALUATION OF CARE MANAGER MODEL(CCM)

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The introduction of highly active anti-retroviral therapy for people living with HIV has resulted in an increased life expectancy, yet subgroups of individuals have difficulty accessing these improved outcomes. A number of co-morbidities, (mental illness; cognitive impairment; behavioural and personality disorders; drug and alcohol issues; intellectual disability; physical disabilities and complex psychosocial issues (eg. homelessness, poverty, social isolation, at risk sexual behaviour)) contribute to poorer outcomes.

This project aimed to develop a model of care for people with HIV and complex care needs who utilise multiple service providers and present in crisis on multiple occasions to a tertiary treatment service. The model comprised the identification of a *key contact person,* the development of a process for the key team members to come together and discuss and review patients and the utilisation of a tool to be used by patient and community as well as hospital care providers as a means of communication of agreed care plan.

Evaluation of the project was based on patient outcome (weight, surrogate markers HIV, treatment adherence, unplanned admissions, social functioning {stable housing]), patient and hospital as well as community provider satisfaction; comparing 6 months prior to with 6 month post intervention.

The pilot project, from November 2002 to December 2003, provided care management for 9 consenting individuals. Compared to pre-intervention period the mean number of unplanned admissions over 6 months reduced from 6.4 before to 3 after the CCM; average days in any hospital bed from 47.1 to 24 days, failed outpatient assessment reduced form 3.9 to 2.6. Plasm HIV RNA reduced from 4 to 2.3 logs. and CD4 increased form 289 to 482 cells/μL. Patient satisfaction and staff satisfaction will be presented.
Community Service providers especially high case load GPs, Housing Agencies and Support Services may most efficiently utilise hospital services in this format. Patient outcomes and staff satisfaction improved during this project. Service requirement and ongoing processes will be assessed.

STRENGTHENING THE RELATIONSHIP BETWEEN HEALTH PROMOTION AND GENERAL PRACTICE

Ryan L[1]
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Social research indicates that individuals consider GPs to be a reliable and credible source of health information. General practice is a critical site for health education and holistic health care and as such GPs are considered key partners in HIV health promotion.

General Practitioners are well placed to translate population-level social marketing messages into personalised and accessible health education for individual patients. They are also well placed to provide health promotion practitioners with feedback on the impact that population-level programs have on individual knowledge and beliefs.

In recent years, specialist HIV/sexual health promotion practitioners have sought to develop programs that support the prevention and primary health care work undertaken in clinical settings. This has taken a variety of forms, including the establishment of training programs for GPs, development of print resources for patients and GP, and development of collaborative projects with Divisions of General Practice.

Strengthening these working relationships has been given additional priority following the recent increase in HIV notifications in NSW. Health promotion practitioners in those areas which have experienced the greatest increase have undertaken consultations with GPs to identify current issues in HIV prevention and more effective ways of supporting prevention in clinical settings.

This paper will outline the findings of those consultations, provide an overview of models currently in place for strengthening HIV/sexual health promotion in General Practice, comment on the effectiveness of these models in supporting prevention and primary health care, and highlight future directions for strengthening the collaboration.

HIV MANAGEMENT AND TREATMENT: WHERE ARE WE AT & WHERE ARE WE GOING? AN UPDATE OF THE QUEENSLAND EXPERIENCE

Lambert S M[1], Allworth A[2], Clare K[3], Marriott K[4], McCormack J[5], Murray J[6], Stodart J, Paten J[7], Patten J[6], Waldeck C, Wall P[8], Zimitat C[9]
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After 7 years of operation of the 'Prescribers' Course in HIV Medicine', designed to provide accreditation for prescribing of HIV antiretroviral therapies in Queensland, 78 medical practitioners had completed training. A review of course attendees describes the current status of those 44 who are not currently accredited to prescribe HIV antiretroviral therapies and the already mentioned survey describes the current status of those 34 who are currently accredited to prescribe HIV antiretroviral therapies. In 2004, 30/34 community-based medical practitioners accredited to prescribe HIV antiretroviral therapies in Queensland responded to a survey about their prescribing practices. Of the 30 respondents: 4 had no patients with HIV; 7 managed patients with HIV but do not prescribe, and 19 prescribed HIV antiretroviral therapies.

The survey was designed to support debate on models of care in HIV medicine at the annual HIV prescriber update organised by the HIV & HCV Education Projects of the School of Medicine. The focus of the debate was on the current system of education / assessment / accreditation, conducted within a broader discussion of various 'models of care' such as formal shared care in HIV medicine; accreditation to prescribe only maintenance scripts; specialist only care as they operate in Queensland.

The debate also included discussions about the management and care of people with HIV in Queensland. One primary issue of concern was the continuing suitability of the education / assessment / accreditation system for prescribers of HIV antiretroviral therapies in Queensland. Participants in the discussion reached consensus that the present system, although rigorous and set at a high standard, met the needs of medical practitioners seeking more training in HIV Medicine. This presentation will examine both the findings of the survey that prompted the discussion and the range of 'models of care' raised in the discussion: eg - formal shared care in HIV medicine; accreditation to prescribe only maintenance scripts; specialist only care (and who is a 'specialist) etc.

MENTAL HEALTH IN PRIMARY CARE

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The HIV, Hepatitis C and Mental health in primary care (H2M) service was formed in 2002, in response to a need expressed by local General Practitioners (GPs) for access to a liaison mental health service for people with HIV and/or HCV. GPs reported that patients often presented with many complex mental health problems which were having a negative impact on their general health and could not be adequately managed in a brief consultation. They requested a mental health service which could follow up, assess and treat referred patients, and could also provide advice and recommendations for GPs themselves, to help them manage patients with complex problems.

This presentation will provide an overview of data collected on the presenting mental health problems of people who have attended the H2M service since it began operating. The relative frequencies of various presenting problems will be discussed, highlighting the number and complexity of mental health problems often seen in primary care in people with HIV and/or HCV. The presentation will also outline some methods which we have found helpful in working with people with complex mental health problems.

THERAPEUTIC CONVERSATIONS IN HIV/AIDS CARE

Curran G[1]
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Poststructural ideas can help explore the diverse relationships that develop in the care of HIV-positive clients and their support networks. This presentation considers the therapeutic potential carried in conversations between client and practitioner (counsellors, doctors, educators, nurses, and so on).

The presentation draws on the proposition 'the map is not the territory' where the maps of clinical practice (treatment and management) needs to also resonate with the territory of the client's lived experience to improve therapeutic outcomes. What personal history, ethics, belief and values does the practitioner bring to the therapeutic relationship? And how might these influence therapeutic outcomes?

These ideas arise from a PhD study interested in reflective practice, poststructural narratives, anti-narratives, pathographies, relational ethics, the social construction of identity, and the impact of HIV/AIDS in a postmodern world on the therapeutic relationship.

Concurrent Session or Symposia – Clinical Medicine – Treatment Issues

THE SMART (STRATEGIES FOR MANAGEMENT OF ANTI-RETROVIRAL THERAPY) STUDY – ADHERENCE TO STRATEGY

Drummond F[1], Neuhaus J[2], Hoy J[3] on behalf of the SMART Protocol Team and the SMART Study Investigators
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The SMART Study is an international, randomised, clinical endpoint trial studying the long-term effects of two strategies for antiretroviral treatment (ART) in patients with CD4 T-cell counts > 350 cells/mm^3. The two strategies are:

- The Viral Suppression (VS) strategy aimed at suppressing viral load irrespective of CD4 count.
- The Drug Conservation (DC) strategy, aimed at conserving drugs by using ART episodically to maintain a CD4 count >250.

The protocol sets out standards for monitoring non-adherence throughout the study. For the VS arm the standard is that < 10% of patients will have stopped therapy for > 4 weeks during the first year of follow-up. For the DC arm the standard is that the cumulative percentage of patients restarting therapy at 6 months is < 50%.

The VS strategy was reviewed to see the number and percentage stopping ART for > 4 weeks since randomisation.

	Sydney Region	Other Sites	Total
N randomised	44	853	897
N stopping ART for > 4 weeks	1	98	99
N stopping ART by 12 months	1	76	77
Estimated % stopping ART by 12 months and 95% CI	0.1 (0.0, 0.4)	12.0 (9.4, 13.6)	12.2 (9.6, 14.8)

The DC strategy was reviewed to see the number of patients who had restarted therapy for non-protocol mandated reasons.

	Sydney Region	Other Sites	Total
N randomised	55	850	905
N initiated	13	326	339
N initiated for non-protocol reasons	4	68	72
Estimated % of non-protocol initiations at 12 months and 95% CI	14.6 (8.6, 20.6)	8.9 (8.6, 9.1)	9.0 (8.8, 9.3)

To allow the study to assess the clinical effect of these two strategies in reducing disease progression it is important that the difference in the time on therapy between the two arms is maximal. Data on the reasons for this non-adherence to assigned strategy will be discussed in this paper.

CONTINUOUS THERAPY IS DEFINITELY THE ONLY WAY TO TREAT HIV – ISN'T IT

Drummond F[1], Hoy J[2], Kelly M[3], Machon K[4]
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Continuous antiretroviral therapy results in significant reductions in HIV-associated mortality and morbidity and is the standard of care for patients who commence antiretroviral combination therapy. Limitations of this strategy are increasingly apparent and include long-term toxicities, drug resistance and failure, cost and adherence fatigue. Intermittent antiretroviral therapy [CD4 count driven] has been proposed as an alternative strategy to continuous antiretroviral therapy and potentially offers equal clinical efficacy with less toxicity. However several concerns exist following the initial experience of these strategies including the development of drug resistance and HIV disease progression, and the public health implications of HIV transmission during a treatment interruption.

After almost half a decade of debate no consensus exists regarding the roles of continuous versus intermittent antiretroviral therapy. New data mandates review and debate. This forum has been organized to assist clinicians to update their knowledge regarding the pertinent issues relating to this critical topic and to provide an opportunity to challenge their opinions about this question.

The debate will be lead by two eminent internationally renowned speakers who will review the current literature from both sides of the debate. This will be followed by a panel discussion involving high-case load general practitioners and community-advocates. Conference delegates will then have the opportunity to add their voice to the debate when the discussion is opened to the floor.

The practice of HIV medicine continues to evolve through informed debate and clinical research. You are invited to this forum to challenge your opinion regarding the allegation that "continuous therapy is definitely the only way to treat HIV".

Symposium – Epidemiology – Rises in New Infections

RISES IN NEW INFECTIONS: SOCIAL RESEARCH FINDINGS

Rawstorne P[1]
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As part of the Symposium, up-to-date social research data will be presented on trends in the following key indicators (mainly based on surveys of gay men): unprotected anal intercourse (UAI) with regular partners; unprotected anal intercourse (UAI) with casual partners; strategic positioning with serodiscordant regular partners and casual partners; negotiated safety relationships which are compromised (ie involve UAI with casual partners); HIV testing; use of HAART; proportion of people using HAART who report undetectable viral load; relationship between sexual practice and viral load; 'recreational' drug use; injecting drug use (IDU); awareness of post-exposure prophylaxis (PEP).

RISES IN NEW HIV INFECTIONS – GAY MEN'S EDUCATION RESPONDS

Wentzlaff-Eggebert M[1]
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This paper reports on the main strategies used so far in translating the news of rises in new HIV infections among gay and homosexually active men into a prevention education response.

It will describe the outcomes of educators' analysis of the science and of current gay men's culture as they strive to respond sensibly. Examples of health promotion strategies from larger and smaller Australian states as well as from the national education effort will illustrate current educational approaches. The paper will put these into the context of the education effort required for the maintenance of a culture and ethic of behavioural HIV prevention over certainly many years, and possibly many rises and falls in infection rates.

BEYOND THE ACTION PLAN: BUILDING THE LONG TERM RESPONSE TO INCREASES IN HIV INFECTIONS IN NSW

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There was a 15% increase in HIV notifications in NSW from 2001 to 2002. This was followed by a 6% increase from 2002 to 2003.

The NSW HIV sector quickly responded to the increase in HIV notifications by establishing a cross-sector HIV Prevention Interagency and Action Plan identifying immediate priorities for collective action. This Action Plan focused on three areas: social marketing to inform gay men of the increase and promote condom use; supporting HIV prevention work undertaken in clinical settings; and addressing sexually transmissible infections.

Preliminary analysis suggests that this was an appropriate and effective response to the increase in HIV notifications. However, the Action Plan did not address longer-term or more complex issues such as the relationship between alcohol and drug use and HIV risk, and the relationship between mental health and HIV risk.

This paper will outline the issues identified as long-term strategic priorities for gay men's HIV prevention and health promotion in NSW, and the strategies put in place to address those issues.

RESURGENT SYPHILIS IN GAY MEN: WHERE TO FROM HERE?

Grulich A[1], Jin F[1], Prestage G[1], Van de Ven P[2], Mao L[2], Kippax S[2], Pell C[3,4], Donovan B[4,5], Kaldor J[1] on behalf of the Australian-Thai HIV Vaccine Consortium
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In this overview of studies, we describe the re-emergence of syphilis in Sydney, characteristics of men with newly diagnosed syphilis in central Sydney, and the incidence of and risk factors for syphilis in homosexual men.

Data were analysed from three sources:

1. Surveillance data on infectious syphilis
2. A descriptive study in men with newly diagnosed early syphilis at three medical practices in inner-eastern Sydney during 2003.
3. Syphilis prevalence and incidence from the HIM cohort study of HIV negative gay men in Sydney.

In South-Eastern Sydney alone, notified cases of infectious syphilis increased six fold between 2001 and 2003. More than 95% of cases were in men. Increases have also occurred in gay men elsewhere in Australia. In the descriptive study, we recruited 57 homosexual men with early syphilis. Of these, 54% were HIV positive, and 26% were asymptomatic and were diagnosed by a screening test. Compared to men in gay community cohorts in Sydney, these men were more sexually active, were heavier users of recreational drugs, and were more likely to report using "dry" sex-on-premises venues. In the HIM study, 1292 HIV negative men (97% of the study total) underwent syphilis testing at recruitment and 3.0% tested positive. The prevalence of past infection increased with age to 19% in those aged over 55. Of these men, 793 attended at least once for an annual follow-up, and there were 8 syphilis seroconversions, (incidence 0.7%/year). The mean age of these men was 34. They reported a greater number of sex partners in the past six months (HR=2.33, 95% CI 1.16-4.68), and were more likely to report HIV positive regular partner(s) (HR=11.03, 95% CI 1.30-93.43) and engaging in unprotected anal intercourse (UAI) with HIV positive partners (HR=10.83, 95% CI 2.58-45.41). A variety of sexual practices that are classified as safe with respect to HIV transmission were associated with acquiring syphilis.

Syphilis is becoming re-established in the gay male population in Australia's cities. Most, but not all, men with syphilis report behaviours that put them at high risk of HIV infection.

THE IMPACT OF THE TREATMENTS PREVENTION NEXUS ON PEOPLE WITH HIV

Duffin R[1]
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This presentation will focus on the impact of the treatments-prevention nexus on people living with HIV.

At an individual level, people with HIV may use knowledge of clinical markers to influence decisions about risk practice and how 'transmissible' they see themselves. These practices are often frowned upon.

The knowledge that treatment uptake and compliance influences 'community viral load' and thus community vulnerability to further HIV infections may influence individual prescribing decisions, treatments guidelines and even how scientific findings are interpreted and translated into clinical practice. The possible 'conflict' between best individual clinical management and broader public health goals will be explored.

The increasing focus on the role of treatments, other mechanisms of biological prevention, changes in education prevention policy, rises in new HIV infections and increased pressure to disclose all act to focus on the role of people with HIV. Some of the problems this creates will be explored.

Concurrent Session – Basic Science – Molecular Biology

THE HIV ACCESSORY PROTEIN VIF AND THE SUPPRESSION OF AN INNATE ANTI-VIRAL DEFENCE MECHANISM

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The HIV Vif protein is a positive regulator of infection that is essential for virus growth in cultured T cells and, presumably, for the development of AIDS in infected persons. Earlier work demonstrated that Vif acts by suppressing the action of a host gene, *APOBEC3G* (formerly called *CEM15*), with natural anti-retroviral function. In the absence of Vif, APOBEC3G is packaged into nascent viral particles and carried forward into newly exposed cells. Here, this enzyme catalyses the purposeful and destructive deamination of deoxycytidine (dC) to deoxyuridine (dU) in viral cDNA replication intermediates, thereby terminating productive virus infection through hypermutation and the induced degradation of viral cDNA. In contrast, when Vif is present in virus-producing cells, APOBEC3G is recruited to a cellular ubiquitin ligase complex and degraded by the proteasome. As a result, the cellular pool of APOBEC3G is diminished and virus particles are produced that no longer contain APOBEC3G and are, therefore, spared from cytidine deamination.

Recent data have now shown that APOBEC3G is not the only member of the APOBEC family of cytidine deaminases with an anti-viral phenotype. The closely related human proteins APOBEC3F and APOBEC3B, as well as two rodent enzymes murine APOBEC3 and rat APOBEC1, are each potent suppressors of HIV infection *in vitro*. Moreover, examination of HIV sequence variation in HIV infected persons indicates that both APOBEC3G and APOBEC3F contribute to viral sequence diversification *in vivo*. Thus, cytidine deamination is not only a novel mode of regulated cell-mediated resistance to viral infection, but is also a means by which viral sequence variation can be generated. Together, these observations indicate that perturbation of Vif/APOBEC function should be investigated as a potential therapeutic approach.

THE ENGAGEMENT OF ALTERNATIVE CHEMOKINE RECEPTORS BY R5X4 ENV OF HIV-1 EVOKES DISTINCT CONFORMATIONAL SIGNALS TO THE GP120-GP41 ASSOCIATION SITE

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Binding by gp120 to CD4 and the chemokine receptors (CKR), CCR5 and CXCR4, leads to the transmission of a conformational signal to gp41, activating its membrane fusion function. These events precede viral entry. The core CCR5- and CXCR4-binding residues of R5 and X4 gp120s map to a conserved $R^{419}IKQ$ motif in the bridging sheet, and to conserved basic residues in the V3 loop. The sequence of V3 plays a dominant role in conferring CKR specificity to R5 and X4 viruses, CXCR4 utilization correlating with net positive charge. In contrast, CKR utilisation by R5X4 strains is determined by complex interactions among multiple gp120 segments, which engage distinct CCR5 and CXCR4 domains. Recently we proposed that residues within the disulfide-bonded region of gp41, including Trp-596 and Lys-601, have a conserved role in associating with gp120 and in sensing conformational changes in gp120 on CD4/CKR engagement (J. Biol. Chem. **278:**42149, 2003). Here we extend these studies by showing that W596L and K601E mutations in the R5X4 strains 89.6 and aBL01, respectively, led to a marked decrease in CD4/CCR5-dependent fusion but not CD4/CXCR4-dependent fusion. Thus, in these strains, Trp-596 and Lys-601 function in sensing the CD4/CCR5-induced conformational change in gp120 that leads to gp41 fusion activation. The induction of distinct conformational signals in R5X4 Env may be due to the engagement of different subsets of gp120 residues by different domains of CCR5 and CXCR4. In support of this notion, 89.6-W596L was rendered non-functional by a 32-residue deletion in the N-terminal domain of CXCR4 and a D187A substitution in the receptor's second extracellular loop. We propose that the engagement of alternative chemokine receptors by R5X4 gp120 evokes distinct fusion-activation signals to gp41 through the site of glycoprotein association. We speculate that complex gp120-gp41 signalling pathways coevolve with broadening CKR binding specificity in R5X4 Envs.

INVESTIGATING THE ROLE OF THE SPACER PEPTIDE P1 IN HIV-1 REPLICATION

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HIV-1 uses ribosomal frameshifting to express the precursor polyproteins Gag and GagPol. The frameshift required for GagPol translation is promoted by an RNA stem-loop. This frameshift stem-loop and the open reading frames for two proteins (P1 from Gag and transframe (TF) from GagPol) overlap. With a novel mutagenesis strategy we have successfully isolated P1 function from the RNA frameshift signal and from TF and demonstrated a critical role for P1 and its two highly conserved proline residues (position 7 and 13) in HIV-1 replication. It is unclear how P1 influences viral replication. The importance of proline residues to protein conformation suggests P1 may be critical for the overall folding of Gag or an intermediate cleavage product, such as NCp15 (NC-P1-$P6^{Gag}$). It is also unknown whether P1 acts independently or if it can be influenced by other viral proteins. P1 is critical for replication in two HIV-1 strains as double P1 proline mutations in the strains BH10 and NL4.3 abolish infectivity. Interestingly, the P1 proline mutants in BH10 displayed dramatic alterations to protein processing and genomic RNA dimer stability that were not seen in NL4.3. The major difference between the two strains is that BH10 lacks the viral proteins Nef and Vpr. However, supplementing BH10 P1 mutants with functional Nef and Vpr does not rescue the phenotype. The majority of the residues in P1 are highly conserved, with the exception of the residue at position 9 which is histidine in NL4.3 and tyrosine in BH10. We are currently investigating this difference to see if this residue contributes to the disparity in phenotype between BH10 and NL4.3. This will answer the question of whether the observed difference between the P1 mutants in BH10 and NL4.3 is a local or global effect.

ACETYLATION AND METHYLATION PATHWAYS ARE REQUIRED FOR PROCESSING OF HIV-1 TAT PROTEIN BY THE VIRAL PROTEASE

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Australia

Our lab has demonstrated an important role for Tat in reverse transcription, which can be genetically segregated from other roles of Tat in HIV-1 replication such as transcription by RNA polymerase II. Tat function in reverse transcription is essential for virus replication. Mutational analysis of four different domains of Tat showed that each contributed to Tat function. A surprising result from our studies was the discovery of a non-consensus HIV-1 protease (PR) cleavage site located in the Tat basic domain that was essential for Tat reverse transcription function (J Virol. 2003;77:9912). Mutation of this region down-regulated PR cleavage of Tat and also down-regulated HIV-1 reverse transcription. New experiments have shown that *in vitro* cleavage of Tat by PR can be completely inhibited by histone deacetylase (HDAC) activity indicating that acetylation of Tat is required for PR cleavage. HDAC inhibition was specific for Tat as other HIV proteins such as Gag-Pol are efficiently processed by PR in the presence of HDAC. We also examined whether protein arginine methyltransferase (PRMT) activity, may contribute towards cleavage of Tat by PR. Our in vitro experiments showed that Tat could be methylated, but it was not clear if this activity was essential. RNAi experiments directed at specific cellular enzymes including p300, PCAF, and PRMT1 are in progress in order to determine if these cellular factors influence virus infectivity and reverse transcription.

HIV VIF IN REVERSE TRANSCRIPTION COMPLEXES

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The actions of HIV Vif as an essential factor that negates APOBEC3G mediated host anti-viral defences late in viral replication in producer cells has received much attention. However, the potential biological roles of Vif in early replication in target cells has received less consideration. In this study we have investigated the presence of Vif in the incoming reverse transcription complex (RTC) in target cells.

Infections in Hut-78 cells were initiated by cell free infection (centrifugal enhancement) or cell-cell mixing with infected donor cells (H3B). Cell lysates were taken at 0, 2 and 6 hr post infection and subjected to sucrose gradient fractionation and fractions analysed for Vif protein (Western) and reverse transcription (RTn) products (real time PCR). RTC's were identified based on density and association with RTn products. Cell lysates were also analysed by immunoprecipitation (IP) followed by analysis of precipiated protein for co-association with RTn products. Vif was detected by Western in sucrose gradient fractions consistent with the size of a RTC and co-incident with HIV RTn products following either cell free or cell-cell infection. Further, IP experiments indicated that vif was bound to RTn products in RTC's. Vif containing RTC's were present in both the cell cytoplasm and in association with the nucleus.

Thus, we have demonstrated the presence of Vif in HIV RTC suggesting a role in early viral replication. Analysis of the properties of Vif defective RTC's will be pursued to investigate the potential roles of Vif in target cells.

HIV RECOMBINANT FOWL POX VIRUS/ VACCINIA VIRUS MUCOSAL AND SYSTEMIC PRIME BOOST VACCINE TRIAL IN MICE

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Developing vaccines that generate immune responses at the initial viral entry site, (i.e. mucosal surfaces such as cervico-vaginal tissue, rectal tissue) could be more effective in controlling diseases such as HIV. It has been shown that a direct mucosal application of a vaccine is necessary to induce high-quality mucosal immune responses in animals. Our previous work on mucosal HIV-DNA/Fowl poxvirus (FPV) prime boost vaccines future corroborates these findings. We have shown that, combined mucosal/systemic prime boost vaccines induce good mucosal and systemic T cell responses in mice as well as in macaques. In the current study 8 week old BALB/c mice were immunized with recombinant HIV-FPV followed by recombinant HIV-vaccinia virus (VV) boost. These animals were sacrificed 2 weeks post VV and B /T cell responses were measured respectively by ELISA and IFN-g ELISPOT assay and/or Intracellular staining of TNF-a and IFN-g and tetramer staining. In this study, a) number of systemic and/or mucosal vaccine delivery routes were tested in order to assess the vaccine route that generated both mucosal and systemic immune responses in mice and b) effect of co-expression of stimulatory molecules such as IL-12, IFN-g was also evaluated. Our results indicated that, route of vaccination influenced the immune response generated. And out of the vaccine routes tested, intranasal/ intramuscular HIV-FPV/HIV-VV prime boosting generated the best mucosal and systemic immune responses in mice and high avidity CD8+ T cells were also observed for the HIV antigens tested. Priming with co-stimulatory molecules such as IL-12 enhanced the T cell responses, and in contrast IFN-g decreased these responses to target antigens. Current data also indicated that, due to better up take of the FPV, intranasal HIV-FPV priming was much more effective than intranasal DNA priming.

A single recombinant FPV prime and VV boost vaccine can generate similar or better immune responses to HIV antigens in mice, compared to the previously tested lengthy DNA/FPV prime-boost regime.

Concurrent Session – Emerging Issues in Indigenous Sexual Health

Shannon C #467

INVESTIGATING THE SOCIAL WORLD OF ABORIGINAL PEOPLE LIVING WITH HIV: ABORIGINAL AND TORRES STRAIT ISLANDER COHORTS IN THE AUSTRALIAN "FUTURES" STUDIES

Saunders M[1], Willis J M[1], Grierson J[1], McDonald K[1], Hurley M[1], Pitts M[1] [1]ARCSHS, La Trobe University, Melbourne, Victoria, Australia

The HIV Futures study aims to provide HIV, health and funding agencies, as well as people and communities affected by HIV with a picture of the overall situation of people living with HIV/AIDS in Australia.

Data are collected every two years via a self-completed survey of PLWHA in all Australian States and Territories in 1999.This paper presents a secondary analysis of survey responses from a cohort of Aboriginal and Torres Strait Islander men and women who completed the survey in 1999, 2001 and 2003. Although there was no specific targeting of Indigenous respondents, the Aboriginal respondents represent about 30% of the Indigenous Australians known to have contracted HIV from 1992 to 2001.

Our analysis examines Indigenous responses to questions about health, use of antiretroviral and complementary treatments, use of information and support services, and housing and financial situation. It also presents data about sex and relationships, people's social supports, recreational drug use, work situation and future planning.

Key issues that the analysis addresses are whether Indigenous PLWHA are disadvantaged in relation to access to treatments and other care and support services, the impact of complex practices of discrimination on their experience of living with HIV, and alternative sources of support and care specific to Indigenous PLWHA.

LIVING AND LOVING ACROSS THE SERODIVIDE

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This paper responds to my partner Dr Jon Willis's 2003 ASHM paper, "Till Death Do Us Part: Living in a serodiscordant relationship". Like his paper, the presentation uses autoethnography, with my lived experience as data, to try to unpack some of the issues for negative partners of HIV positive gay men. In my case, my lived experience includes my identity as a Torres Strait Islander and Aboriginal man, and the particular cultural issues for me, my family and my community of my partnership with an HIV positive whitefella.

The paper examines the problems of living and loving across the serodivide using similar categories to those used by Willis in his 2003 paper. I look at how fear of death, health surveillance, guilt and responsibility, fear of transmission, the consequences of fear, symptoms and medications, sex and compromise, and work affect me as the negative partner.

I also explore the operation of stigma in my life. Living in a serodiscordant relationship is really not as bad as I thought it might be. If anybody had told me four years ago that I would be in this relationship, I would've laughed them down. I was just as paranoid about HIV/AIDS as the next person. Education and love have made it easier over time. My community is hostile to homosexuality, and when they find out that my partner is positive, they sometimes falsely decide that I too must have the virus. It is hard being stigmatised for associating with positive people, but when your partner and most of our friends are positive, stigma comes from all my communities, gay included. But with the stigma comes a lot of support from my brothers and sisters who are positive, black and white, and in the end, this support means more to me than the stigma.

JUST GETTIN' ON WITH MY LIFE WITHOUT THINKIN' ABOUT IT: ABORIGINAL EXPERIENCES OF LIVING WITH HIV IN WESTERN AUSTRALIA

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The incidence of HIV in Aboriginal people in WA now exceeds that of the non-Aboriginal population. Indigenous people with HIV have been largely invisible, a small minority whose experience differs from the mainstream HIV epidemic in many ways. Aboriginal people who are HIV positive may experience a range of social, geographic and other barriers to effective health care and quality of life. This qualitative research project provides a means of gauging the extent of any barriers as well as providing the opportunity for participants to tell their story.

Interviews were undertaken with 20 Aboriginal people with HIV of whom 80% were female, 90% acquired their infection through heterosexual contact, and 70% lived in rural/remote areas. Their age at diagnosis ranged from 16-49 years. The presentation will cover the characteristics of the participants and their experience of living with HIV including ways of coping, social supports, the economic impact of living with HIV, and their views on access to services, health care and treatment.

Some participants reported no knowledge of HIV prior to being infected but a few had relatives or friends with HIV. Disclosure was a major issue, with some individuals having disclosed to no family or friends, years after being infected. Family was a major source of social support. The need for confidentiality was paramount in small communities where discrimination was anticipated. Not thinking about HIV, ignoring it, was a common theme for coping with HIV both in the short and long term. This was not perceived as denial, rather an acceptance of the diagnosis but a refusal to allow it to dominate their lives.

All twenty participants were on very limited incomes, yet the majority did not believe that HIV had adversely affected their financial situation or their accommodation. For these participants, low incomes were expected and appear to be the norm for many Aboriginal people.

Implications for prevention, education, treatment compliance and health service provision will be discussed.

THE TERRITORY TWO STEP – ENHANCING DETECTION OF LATENT MTB IN HIV CLIENTS

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The Northern Territory (NT) has the highest rate of TB of any Australian jurisdiction with the burden of disease predominantly in the Indigenous and overseas born populations. High proportions of these groups also have latent TB infection (LTBI), and coinfection with HIV is the greatest known risk factor for reactivation to TB disease. Previously the NT AIDS and STI Program has screened HIV seropositive clients who are newly diagnosed or newly arrived in the NT for TB. This screening varied depending on the preference of the incumbent physician.

A review of screening practice identified 2 concerns - the risk of missing latent TB infection (LTBI) due to false negative single-step mantoux tests in immunosuppressed clients, and the lack of ongoing screening for LTBI in patients who may have further exposure to TB.

A screening algorithm was developed which included a two-step mantoux test when initial mantoux results were negative, indications for referral to the TB unit for assessment, and management guidelines for those in whom the initial two-step mantoux was negative. Additional fields and capacity were requested in SHIP (Sexual Health Information Program) to record serial mantoux, chest x-ray results and to generate recall lists.

From July 2003 to April 2004, 35 clients (55% of regular attendees to our clinic) have undergone mantoux testing. Positive results (≥ 5mm induration) were detected in 5/35 (14%) clients – at the first step in 2 (40%), and after the second step in a further 3 (60%). The remaining 30 clients had negative results after the two-step mantoux test. Of 5 with a positive test, one case of asymptomatic culture-positive pulmonary TB has been detected, and 3 out of 4 clients (75%) with LTBI have commenced preventive treatment.

Currently, ongoing screening for LTBI is thought to be a low priority in HIV management in Australia. These results should stimulate reconsideration of its importance, particularly in other regions with high rates of TB.

HIV Futures 4 Workshop

HIV FUTURES 4: STATE OF THE [POSITIVE] NATION

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Other panel members yet to be finalised, will include representatives of NAPWA, AFAO and ASHM

This workshop will give an overview of the key findings of the **HIV FUTURES 4** study and discuss the implications for PLWHA, community organisations, service providers, and policy directions.

The HIV Futures Survey is a national project examining the lived experience of HIV for Australian PLWHA. Data collection in this study is undertaken every two years using a self-completed, anonymous questionnaire. Core modules of the questionnaire include health status, treatments, service utilisation, social support, information management and sexual practice.

HIV Futures 4 was conducted in late 2003 and the main community report will be launched in August 2004. The survey was completed by 1061 PLWHA from all parts of the country.

The workshop will concentrate on 6 key areas:

1. Treatment breaks and the health management issues associated with them;
2. Experiences of discrimination in health services, the workplace and other settings;
3. Issues of poverty and finance;
4. Pre and post test counseling;
5. Engagement with the HIV sector including community organisations and health services; and
6. Sex and relationships.

Researchers will present an overview of the findings for each key area followed by commentary by the other panel members. A general discussion will follow.

ashm2004canberra
16TH AUSTRALASIAN CONFERENCE 2–4 SEPTEMBER 2004

ORAL PRESENTATION ABSTRACTS

SATURDAY 4 SEPTEMBER 2004

SATURDAY 4 SEPTEMBER 2004

Plenary

MEDICALISATION OF PREVENTION

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This paper takes up two main issues with reference to the 'medicalisation of prevention': the technologising of prevention; and the positioning of prevention within the context of treatment delivery. Both of these relatively recent 'moves', I argue, are placing prevention at risk. The first, the technologising move, while central to the fight against HIV and AIDS, has led to a down-playing of the social and behavioural in the transmission of HIV. The second move, the move to roll-out prevention with treatments and the concomitant emphasis on voluntary counseling and testing (VCT) is destabilising prevention efforts – especially in the developing world – by bypassing and undermining the important role that civil society plays in combating HIV. VCT has moved prevention from the community back into the clinic.

HIV is transmitted by sexual and drug injection practices that are heavily imbued with social meanings, with pleasure and with pain. To be successful, prevention efforts must engage with these meanings – to avoid them or treat them as irrelevant is to court disaster. Prevention – at least in some countries – has worked and it will continue to work as long as we address the human and social aspects as well as the biological and technological ones.

HAART: WHEN TO START AND WHAT WITH

Sax P E[1]
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Combination antiretroviral therapy using at least 3 potent agents has led to dramatic reductions in HIV-related morbidity and mortality. However, the clinical benefit of such treatment is proven only in those with advanced HIV-related immunosuppression; specifically, treatment prolongs life for those with HIV-associated opportunistic infections and/or a CD4 cell count < 200 cells/mm3. Starting therapy during earlier stages of HIV disease, where the short-term prognosis is excellent even without treatment, has no proven benefit; hence the optimal time to start for these individuals remains uncertain, with current guidelines deriving data from recent observational cohort studies. Once the decision is made to start therapy, there are presently 20 available antiretroviral agents from which to choose. The best outcomes in clinical trials have been from regimens that contain either efavirenz or lopinavir/r; these should be combined with two nucleoside (or nucleotide) reverse transcriptase inhibitors, of which one should be lamivudine or emtricitabine. Despite the availability of treatment guidelines, antiretroviral therapy must be individualized for each patient, and no single regimen is suitable for all clinical settings. The purpose of this presentation will be to review data on the timing of antiretroviral therapy as well as the selection of individual agents.

RECENT ADVANCES IN UNDERSTANDING HIV REPLICATION

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As an obligate intracellular parasite, HIV is dependent upon many cellular factors for effective infection, replication and dissemination. Recent years have seen an avalanche of information regarding newly discovered interactions between HIV and the infected host cell. In some cases, these interactions benefit virus replication, whereas in others they can impede replication. This presentation will discuss recent findings concerning two aspects of the dynamic interface between HIV and the human host:- 1) the role of APOBEC-mediated DNA editing in innate resistance to HIV replication; and 2) the role of cellular TRIM proteins in blocking the early steps of HIV infection. By expanding knowledge in these areas, it is possible that new approaches for anti-HIV/AIDS therapeutics can be designed.

Concurrent Session – Epidemiology of STI's

PREVALENCE AND RISK FACTORS FOR GONORRHOEA AND CHLAMYDIA IN THE HEALTH IN MEN (HIM) COHORT

Jin F[1], Prestage G[1], Van de Ven P[2], Mao L[2], Kippax S[2], Pell C[3,4], Donovan B[4,5], Cunningham P[6], Kaldor J[1], Grulich A[1]on behalf of the Australian-Thai HIV Vaccine Consortium
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While many studies have reported increases in gonorrhoea and chlamydia in homosexual men, few studies have been either community based or prospective. We aimed to determine the prevalence and risk factors for gonorrhoea and chlamydia in a community-based cohort of HIV negative gay men in Sydney.

Participants were offered annual sexual health screening. Nucleic acid amplification testing for urethral, pharyngeal and anal gonorrhoea and chlamydia (BDProbeTec) was performed from March 2003. Throat swabs were taken by the study nurse, and urine samples and anal swabs were self-collected by participants.

By the end of 2003, 1,020 participants had been tested. Overall, 86 men returned a positive gonorrhoea test (8.5%): 3 (0.3%) men tested positive in the urine, 73 (7.2%) in the pharynx and 12 (1.2%) in the anus. For chlamydia, 60 (6.0%) men tested positive at any site; in the urine in 9 (0.9%), pharynx in 14 (1.4%) and anus in 43 (4.3%). Younger men were at higher risk of gonorrhoea ($p<0.001$). For those aged under 25, 17.5% tested positive at any site, compared to 2.0% for those aged above 55. In univariate analysis, gonorrhoea was also significantly associated with number of casual partners, and the use of ecstasy, LSD or other party drugs in the past six months. After controlling for confounders, age (p trend<0.001) and number of casual sex partners ($p =0.009$) remained significant. No significant association with age was seen with chlamydia. In univariate analysis, detection of chlamydia was associated with number of sex partners, number of casual partners, unprotected anal intercourse (UAI) with casual partners and receptive UAI in the past six months. In multivariate logistic regression, reporting any receptive UAI (OR=3.04, 95% CI 1.62-5.71) and reporting UAI with casual partners (OR=1.95, 95% CI 1.13-3.35) remained significant.

The prevalence of both gonorrhoea and chlamydia is high among HIV negative gay men in Sydney, with substantial differences in the epidemiology of the two conditions. The findings in this community-based sample strongly support the need for screening homosexually active men for sexually transmissible infections.

EPIDEMIOLOGY OF HIV AND GONORRHOEA IN VICTORIA, 1993-2003

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HIV and gonorrhoea notifications have increased markedly in Victoria in recent years, especially among males reporting homosexual contact. We present the findings of a data analysis of Victorian HIV and gonorrhoea surveillance data for 1993-2003.

Between 1993 and 2003, there were 6648 notifications of *N. gonorrhoeae* and 2188 notifications of new diagnosis of HIV. Annual notifications of gonorrhoea gradually declined between 1993 and 1997 (from 479 to 359) but in 1998 there was an upturn in notifications (n=556) and figures have continued to increase with 1160 notifications reported in 2003. For HIV, annual notifications declined between 1993 and 1999 (from 236 to 140) and in 2000 there was a substantial increase in notifications (n=197) which had continued until 2002 (n=234). For both diseases, the majority of notifications were reported among males reporting homosexual contact (51% for gonorrhoea and 70% for HIV). This proportion increased from 37% to 54% for gonorrhoea notifications, but has remained steady for HIV. For both diseases, the majority of infections among males reporting homosexual contact were acquired in Australia (98% for gonorrhoea and 73% for HIV) and since 1997 (when source partner was first routinely recorded) the majority of infections among males reporting homosexual contact were reported to be acquired from a casual or anonymous sexual partner (69% for gonorrhoea and 64% for HIV).

In Victoria, the increase observed in HIV and gonorrhoea has occurred with a backdrop of increasing numbers of STIs, especially among males reporting homosexual contact. These data are of concern because they suggest an increase in high-risk sexual behaviour in this group. Gonococcal infections have been shown to increase the transmissibility of the HIV virus by up to five times and as shown in this analysis the last time an upsurge in gonorrhoea notifications was observed in Victoria (1997-2000), an increase in HIV diagnoses followed soon after (1999-2002). These data therefore highlight the urgent need for interventions to control the spread of gonorrhoea, HIV and other STI's in men who have sex with men.

THE HIV/HSV NEXUS

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Increasingly, Herpes simplex virus type 2 (HSV2) is being recognised as a potent factor in the transmission and acquisition of HIV infection. Having HSV2 antibodies (whether or not the individual is symptomatic) approximately doubles the risk of acquiring HIV. This risk is much greater in the first 12 months following the acquisition of HSV2.

In addition, HSV2 leads to an increase in HIV plasma viral load, and this effect is mitigated by treatment with aciclovir. Studies in the early 1990s suggested that treatment of HIV-infected individuals with aciclovir led to a decreased mortality – this may not hold true in the era of effective antiretroviral therapy.

In Australia, HSV2 is common in the people most at risk of acquiring HIV, namely homosexually-active men. In this population, a study published in 2001 showed a seroprevalence rate of 28% in HIV-negative gay men, and 61% in HIV-positive gay men. More seroprevalence data are needed.

Serotesting for HSV2 is now possible with the Focus™ ELISA test, augmented by Western Blot testing. This should form part of the routine serological testing of HIV-positive individuals. Transmission of HSV2 infection can be reduced by a combination of diagnosis, education, condom usage, and the use of antiherpes agents.

Furthermore, the population-attributable risk of HSV2 for HIV infection may be 25% in the Australian context, and HSV2 should be viewed as a modifiable risk factor for the acquisition and transmission of HIV infection in Australia. Studies are underway in the USA, Peru and Zimbabwe to asses whether treatment of HSV2 will reduce the transmission of HIV.

MANAGING SEXUALLY TRANSMISSIBLE INFECTIONS IN GAY MEN

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Sexually Transmissible Infections (STIs) are one of the key health issues facing sexually active gay men. There has been a sustained gonorrhoea and chlamydia epidemic in inner city Sydney gay men since 1999 and recently Syphilis notifications have risen dramatically.

Managing STIs in this population requires a multi faceted approach, utilising a variety of strategies.

These strategies include:

- Print media campaigns and materials
- Web based learning and information provision
- Working with general practice to incorporate education into clinical interactions
- Workforce development
- Reorientation of sexual health services
- Group work and individual interventions

This paper will focus on the application of a range of strategies to address the issue of sexually transmissible Infections in gay men as well as outline some of the barriers to sexual health.

SCREENING FOR SEXUALLY TRANSMITTED INFECTIONS IN INDIVIDUALS RECEIVING NON OCCUPATIONAL POST EXPOSURE PROPHYLAXIS

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Non Occupational Post Exposure Prophylaxis against HIV (NPEP) is routinely prescribed after high risk sexual exposure. This provides an opportunity to screen and treat individuals at risk of concurrent sexually transmitted infections (STI). Our clinic offers routine screening for gonorrhoea, chlamydia, syphilis and hepatitis B to all individuals on NPEP. The aim of this study was to assess the efficacy of STI screening in this cohort.

All individuals undergoing STI screening between March 2001 and May 2004 were included in the analysis. STI results were compared to type of sexual exposure and baseline patient characteristics. For individuals receiving NPEP on more than one occasion the first screen only was included in the analysis.

A total of 253 individuals were screened. This represents 84.6% of the target population. All were men who had sex with men (MSM). Exposure risk were as follows: receptive anal sex (RAS) 61%, insertive anal sex (IAS) 33%, receptive oral sex (ROS) 4%, mucous membrane exposure 0.40 %, other 1.6%. 12.6% had one STI or more. The most common STI was rectal chlamydia in 4.3% followed by rectal gonorrhoea in 2.4%. There was a significant association between infection with rectal chlamydia and rectal gonorrhoea (OR 13.2 95% CI 2-86; $p<0.001$). There was no association between presence of a rectal STI and age or exposure risk. Exposure risks of IAS and ROS were significantly associated with urethral STIs ($p=0.015$).

These data, with high numbers of positive STI results, highlight the importance of full STI screening in MSM after high risk sexual exposure.

SECONDARY STUDENTS AND SEXUAL HEALTH

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Secondary students in Years 10 and 12 students were surveyed in 1992, 1997 and 2002. The surveys examined key aspects of sexual health and can be used to chart changes in sexual behaviours and knowledge over time. The survey in 2002 involved 2,388 young people from all States and Territories and from all school sectors.

Knowledge of HIV transmission is very good; however the 2002 survey identifies a decline in HIV knowledge. Knowledge of STIs remains poor. Knowledge of hepatitis A, B and C is also poor, but has improved somewhat over the past five years. There has been a clear trend since 1992 for students to perceive themselves to be less at risk of contracting an STI; there has been no change in perceived risk of HIV.

The proportion of young people who are sexually active has increased over the time of the three surveys. Condom use is common; there is now a marked change between Years 10 and 12, with fewer Year 12 students reporting regular use of condoms; this can be accounted for by higher rates of oral contraception. More than one in five students reported being either drunk or high on their most recent sexual encounter.

The implications of these findings will be discussed.

Concurrent Session – Models of Primary Care

THE SOUTH AUSTRALIAN PRIMARY HEALTH CARE PROGRAMME FOR PEOPLE WITH HIV AND PEOPLE WHO MAY BE AT RISK

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The Care and Prevention Programme (C&PP) began in 1998 under time-limited commonwealth funding. In 2000 it became an activity of the Department of General Practice at the University of Adelaide and it has been funded since that time by the HIV, Hepatitis C and related programs unit of what is now the South Australian Department of Health.

The Programme collaborates closely with a general medical practice to provide an integrated primary health care service for South Australians living with, or at increased risk of, Human Immunodeficiency Virus (HIV) infection. It arose from collaboration between general practitioners, the Aids Council of South Australia and people living with HIV/AIDS SA Inc, and has maintained its community-based perspective through strategic development and governance procedures that emphasise the input of participants in the programme. It employs a primary health care model, has a commitment to multidisciplinarity and conceives of health holistically in its biological, psychological and social dimensions, according closely with current state and national policy on HIV.

Since it began, the C&PP has had a deliberate focus on the group most affected by HIV infection in Australia, gay-identifying and other homosexually active men. Its ability to care for both infected and uninfected members of a target community in the same setting is seen as a strength, since it minimises stigma associated with use of a designated HIV service.

State funding provides multidisciplinary services, health assessment, care coordination, oversight and data management, together with educational, professional and personal support for GPs and other health care workers engaged with the Programme. The integrated medical practice provides GPs and some specialist medical services funded through Medicare.

While the C&PP has now operated effectively for over six years, with clear and measurable health benefits for participants, its sustainability is threatened currently by the shortage of GPs in South Australia. This has resulted in extreme difficulty is recruiting GPs to take part in an area of medicine that is seen to be both difficult and poorly remunerated.

HOLDSWORTH HOUSE MEDICAL PRACTICE, A SYDNEY MODEL FOR HIV PATIENT CARE

Quan D[1]
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Holdsworth House Medical Practice established in 1992 recognises the evolving needs of those affected by HIV and those at risk of HIV. The practice has been growing to provide as many choices and as many services as possible for these changing needs of the community.

Based on patient surveys and a mission to overcome barriers to optimal HIV care, the Holdsworth House model aims to deliver advances in technology [IT], Care Planning and a diverse complement of health professionals to yield the care that our patient population needs.

With Dentists, psychologists, podiatrists, counsellors, nurses and medical specialists who have an interest in HIV Health as well as working with complementary therapists: Chinese herbalist, acupuncturist, chiropractor, physiotherapists, dietician, a comprehensive choice of practitioners are available to deliver better health outcomes to diverse community of patients.

Key to the approach is developing our own customized computerized record system designed to monitor , communicte and provide access to the multidisciplinary approach that Holdsworth House Medical Practice views necessary in patient care.

THE HIV/AIDS PROGRAM IN CANBERRA

Soo T M[1]
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Different areas in Australia have come up with different ways to address the issues involved in managing HIV in general practice. In the ACT, the HIV/AIDS Program run by the ACT Division of General Practice plays an invaluable role in supporting general practice in the management of HIV.

This program started in 1992 as one of the general practice projects funded by the Federal Government. Since 1994, it has been managed by the ACT Division of General Practice. The Program employs an HIV nurse full-time based in general practice and also contracts with a counsellor to provide counselling sessions. It also employs a general practitioner to oversight the project. The project also organises monthly education sessions as well as quarterly peer discussion meetings. These are invaluable for maintaining contacts between the different health providers and NGOs working in the HIV area in the ACT. The program also helps pay for ongoing education to meet the accreditation needs of the general practitioners as well as the training costs of new GP S100 prescribers. This project plays an invaluable role at supporting general practice in the ACT in managing HIV in the ACT community.

A PRIMARY HEALTH CARE PROGRAMME PROVIDES LONG-TERM BENEFITS FOR HOMOSEXUALLY ACTIVE MEN: SIX-YEAR OUTCOMES OF THE CARE AND PREVENTION PROGRAMME

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The Care and Prevention Programme has provided a comprehensive Primary Health Care service for homosexually active men (HAM) in South Australia (SA) since the beginning of 1998. 562 HAM have enrolled over that time, of whom 368 have so far been reviewed an average of eighteen months after enrolment, 224 have been reviewed a second time an average of 36 months after enrolment and 80 have been reviewed a third time an average of 55 months after enrolment.

As we have reported previously, enrolment data for the Programme show a pattern of social and health disadvantage that identifies HAM participants as subject to serious health inequity when compared with SA men generally.

Extended follow up of the cohort demonstrates high levels of satisfaction with the Programme (62% "Completely Satisfied", 27% "Largely Satisfied" and only 1% expressing any level of dissatisfaction).

Outcome measures, particularly those at the psychosocial end of the health spectrum, show a pattern of steady continuing health improvement across the period of participation suggesting therapeutic benefit associated with participation (eg: proportion with suicidal ideation in prior two weeks = 12.9% at enrolment, 6.2% at first review [P<0.05], 4.3% at second review [P<0.01]; proportion with Major Depressive Episode 26.2% at enrolment, 15.2% at first review [P<0.01], 12.9% at second review [P<0.001, all repeated measures analysis, n = 210]).

The proportion of men reporting unprotected anal intercourse with a casual partner in the prior six months fell marginally from 11.6% at enrolment to 9.7% at first review [NS] but had returned to 11.6% by second review [n=210, repeated measures]. However, while the rate at enrolment was not significantly different from that in the roughly contemporaneous 1999 Adelaide Periodic Survey (12.1%), the rate at second review was significantly lower than that in the roughly contemporaneous 2001 Periodic (15.9%, P<0.001 by Fisher's Test) suggesting an effect of participation compared with the prevailing community rate at the time.

Qualitative data suggest that any beneficial effect has resulted from perceived improvement in access to care, information and support resulting from a sense of acceptance and "comfort" for gay-identified men attending the Programme.

HIV HYPOCHONDRIA: A WORKSHOP TOWARDS A COMPASSIONATE APPROACH

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People who present for HIV testing with low stated risk, high anxiety associated with fear, guilt or shame, and are unrelieved by appropriate testing and reassurance, could be described as being hypochondriacal. These people present a unique challenge to both sexual health and HIV practitioners as we struggle to meet their needs, at times perpetuating their anxiety by inappropriately re-testing or taking out our frustrations on them.

This workshop that brings the perspectives of a psychologist, social worker and physician to the condition, aims to develop in participants:

- a recognition of the seriousness of the condition
- an understanding of the spectrum of illnesses
- an appreciation of how we may perpetuate anxiety in our clients
- an exploration of the social context that contributes to the illness, and
- an understanding of therapeutic approaches appropriate to the spectrum of illnesses

Workshop facilitators will use the information collection technique of real-time capture on a big screen, to both collect and organise findings, the printout of which will be presented to participants at the end of the session.

Symposium – International Policy Initiatives

BEST POLICIES; WORST EPIDEMIC

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This paper will look at the paradox of the South African AIDS epidemic – where the country has excellent policies and programmes to address HIV and AIDS, along with some of the most progressive legislation in the world and a constitution that protects and guarantees rights crucial to fighting the epidemic – but continues to have an epidemic that is 'out of control'. Why is it, that, despite a strong NGO sector, sound policies in government and an acclaimed National AIDS plan the country still has very high levels of infection, stigma, prejudice and discrimination.

What is it about the South African society that produces this paradox and how can the recent response from the President and the Health Minister be understood?

This paper looks at the disjuncture between policy, implementation and action and analyses what went wrong in the South African response.

IMPACTS OF REGIONAL AND BILATERAL TRADE AGREEMENTS ON ACCESS TO MEDICINES

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Members of the World Trade Organisation have long been debating access to medicines through the Trade Related Aspects of Intellectual Property Rights (TRIPS) Agreement. Where the United States Government has not been able to gain ground though this multilateral forum, it is now using regional and bilateral trade agreements to be able to extend pharmaceutical patent monopolies beyond what is required under TRIPS. In the Asia-Pacific region the US has, or continues to be, in FTA negotiations with Singapore, Australia and Thailand. The US has plans for FTAs with other countries in the Asia Pacific through its ASEAN regional trade initiative.

US trade strategy involves establishing model FTAs and replicating them in other countries. US bilateral and regional FTAs recently concluded, or in negotiation with, developing countries include several common provisions that seek to extend pharmaceutical patent monopolies and limit generic competition. These include extension of patent terms, limitations on the use of compulsory licences and other provisions for delaying entry of generic competition into the market. Such provisions should be excluded from FTAs.

The net effect of such provisions in FTAs will often mean that prices for originator drugs will remain high for longer periods as generic competition is obstructed. In developing countries that enter into FTAs with the US, these high prices could keep medicines out of reach of many in the population. The result, a significant impact on the health of a population, many of whom may be unable to outlive the delays in accessing affordable medicines introduced by the FTA.

EXTERNAL DONOR RESOURCES AND THEIR IMPACTS ON NATIONAL HIV/AIDS RESPONSES

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There is now a long history of western donor agencies providing valuable assistance to address the requirements of HIV/AIDS responses in resource poor countries. As well as established bilateral and multilateral projects, there are more recent activities that include the WHO 3 x 5 program and the Global Fund for HIV/AIDS, Tuberculosis and Malaria. In many countries these activities are having profound effects on the administration and focus of national HIV/AIDS responses. This paper will consider some of the ways in which external donor support programs might hinder or help national responses. What are the implications for recipient countries in terms of program management to ensure a unified and coordinated national HIV/AIDS program? What are the ways in which donor agencies can channel their support to achieve this goal? Evidence indicates that in many places, donor agency projects have on the one hand, provided excellent support and resources in particular locations or to counterpart organisations, but on the other hand, have failed to build national capacity to respond to HIV. How can these projects continue to provide technical and strategic resources in ways that also build capacity to sustain national responses?

In a context of growing regional epidemics and growing numbers of multilateral and bilateral agencies willing to contribute to efforts to stop those epidemics, it is essential that available resources be coordinated. This will better ensure that national responses are consistent, sustainable and avoid duplication.

Symposium – ACON & NSW Health – Gay Men & Condoms: The Relentless Pursuit of Rubber less Sex

GAY MEN AND CONDOMS: EXPLORING THE RISE IN UNPROTECTED SEX

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[1]AIDS Council of New South Wales, Sydney, NSW, Australia; [2]National Centre in HIV Epidemiology and Clinical Research, Sydney, NSW, Australia; [3]Albion Street Centre, Sydney, NSW, Australia.

In 2004 very few gay men in Australia don't know that consistent use of condoms and water-based lube will prevent transmission of HIV and other sexually transmissible infections. Yet in 2002 51% of gay men reported at least one event of unprotected anal intercourse in the last six months up from 35% in 1996. HIV prevention is obviously just one factor in gay men's decisions about condom use.

The speakers on this panel will discuss condom use in the context of such factors as: educational messages, erectile dysfunction, psychological issues, drug and alcohol use, long term relationships, intimacy and community attitudes.

Stevie Clayton: The factors that impact on gay men's decisions about condom use are many and varied. They range from the pursuit of sex without condoms as better sex, through mistaken beliefs about risk practices and a desire for greater intimacy, to external factors such alcohol and drug use. Many of the commonly held beliefs about these factors are not borne out by research findings. This paper examines the different influencing factors, contrasts anecdotal justifications with research findings and explores the ramifications for a health promotion response.

Jeanne Ellard: The *Seroconversion* study identifies a range of factors that influence sexual practice. These include location, assumptions about serostatus, level of familiarity with the partner, ideas about intimacy, sexual attraction and romance. This paper examines gay men's attitudes towards and experiences with condoms in order to glean an understanding of why some men sometimes decide not to use them. Many participants viewed condoms as an integral part of safe sex, not always desirable but necessary in the era of HIV/AIDS. Participants articulated a variety of attitudes toward condoms including: 'disease control'; 'it definitely feels different'; 'I've never really seen them as a hassle'; 'I hate them'; 'it's, a passion killer.'; 'It's just part of my routine'; 'I get an allergic reaction to latex'; 'I could never use a condom, could never maintain an erection'; 'a condom was just the natural function of sex and that's that'. Their responses reveal a range of practical and interpersonal issues that are likely to impact on sexual practice and more specifically decisions about protected and unprotected anal intercourse.

Garrett Prestage: 'Gay men make various 'arrangements' with their sex partners to make the sex they have with each other more pleasurable and stress-free. With their boyfriends these 'arrangements' often include the kind of sex they have with each other, as well as under what conditions sex with other men is permitted. With fuckbuddies they might agree on what sort of limitations there should be to emotional entanglements. And with a casual partner they might ask 'what are you into?' before figuring out what they're going to do with each other. In all of these situations, HIV and condoms are just one factor, and often not the most important factor, guiding their decisions. These sorts of arrangements are largely based on what they know about the other person, how well they know them, and how much they care about them. HIV-prevention is just a part of that picture.'

Alan Brotherton: The central role of positive people in prevention is a much quoted maxim in HIV strategy documents at all levels. What this looks like in practice is far from clear, and a source of contention both in Australia and overseas. Although there are a number of "explanations" circulating for positive gay men's failure to use condoms, research and discussion on HIV positive men's motivations **for** condom use is somewhat more limited. This presentation will look at some of the possible motivations and rationales for condom use as well as condom non-use amongst HIV positive gay men, with a view to identifying productive approaches to the inclusion of positive people in prevention strategies and activities.

Dr Derek Chan: Erectile dysfunction is commonly experienced by HIV positive men. Apart from the normal decreases in sexual function and performance men experience with age, there are numerous other physical and psychological factors that may exacerbate the problem. An overview will be provided about the biological mechanisms of erectile dysfunction as well as the available treatment options in the light of the HIV epidemic.

Concurrent Session – Community – HIV Prevention and Peer Education

SOCIAL CAPITAL AND THE PHENOMENOLOGY OF BAREBACKING

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This paper will describe Social Capital theory and discuss applying this theoretical framework to the practice of unprotected anal intercourse known within gay community vernaculars as 'barebacking'. The paper will suggest ways in which educators might take advantage of the social capital attached to barebacking cultures to reinforce HIV prevention. The paper will look at the phenomenology of barebacking and define the meaning of the term within Australian sex cultures. This will include a discussion of safe sex culture as well as the oppositions to that culture as a community 'norm'. It will describe the advent of a safe sex culture that had, as its foundations, social mobilisation and activism and how, over time, safe sex practice has been layered with moralism and institutionalised instruction. The paper will further describe the development of the sexual maverick and sexual adventurism as it applies to bareback-ing as it is understood in this country.

THE GEOGRAPHY OF THE GAY COMMUNITY 'GHETTO' IN SYDNEY

Madeddu D[1], Prestage G[1], Grierson J[2], Smith A[2], Richters J[3], Allan B[4], Grulich A[1]
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Whilst it is generally acknowledged that gay identifying men tend to live in the inner eastern suburbs of Sydney, very few attempts have been made to calculate the concentration of gay men, and estimate the size of the population of homosexually active men within this location.

The Australian Study of Health and Relationships (ASHR) was a survey of the sexual behaviour, sexually transmissible infection (STI) prevalence and STI knowledge of a random sample of Australian adults aged 16 – 59. An over-sample of this survey was performed amongst 1000 males in eastern Sydney, within the five most commonly reported postcodes of residence in studies of Sydney gay men.

Postcodes 2010, 2011, 2016, 2021 and 2026 were included in the over-sampling exercise. The proportion of males who reported:

- that that they identify as 'gay or homosexual' varied from 5.9% in 2026 to 36% in 2010;
- having sexual experiences exclusively with men varied from 4.2% in 2021 to 10% in 2010; and
- only ever having feelings of sexual attraction towards men varied from 3.3% in 2026 to 15.5% in 2011.

In this presentation we examine the proportion of men who report same sex behaviour, same sex attraction and who identify as 'gay or homosexual' and provide an illustration of the boundaries of the population of gay and homosexually active men in inner city Sydney

These findings provide a valuable source of information for health promotion intervention and policy planning, particularly regarding resource targeting and allocation decisions.

GAY COMMUNITY: SUBCULTURES, RISK AND 'COMFORTABLENESS'

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This paper will report on how gay men's perceptions of risk in the context of their differential paths of engagement with gay community life. Reference will be made to data from the Sydney Gay Community Periodic Surveys.

Gay men engage in gay community life in a variety of ways. These different paths can represent very different ways of living and being 'gay', sometimes intersecting with each other and sometimes not. In 2003-2004, some men reported using various types of venues or methods (bars, dance parties, sex venues, beats, gyms, internet) to meet sex partners, while others used only some of these: 27.7% used only gay social venues such as bars or dance parties, and 5.0% only used sex venues; Very few men reported using all types of methods or venues, but 21.2% indicated they used none of them. HIV prevalence and risk behaviour data vary across different samples: Men recruited at gay bars were less likely to be HIV positive ($p<.001$) or to engage in unprotected anal intercourse ($p<.001$) than men recruited at sex venues, but they are likely to have more gay friends ($p<.001$). Can subtle differences in how gay men engage with gay community subcultures, and the differences in their experiences of HIV prevalence and risk behaviour tell us anything about how they make calculations of risk and where they place HIV in their lives?

Gay men experience different levels of connectedness and notions of 'community' depending on the particular ways they interact with other gay men. Awareness of higher prevalence of HIV among their peers may not be as important as the degree to which they feel 'connected to' and, therefore, able to trust those peers. Their decisions about risk behaviour may reflect their own risk calculations and the extent to which they feel confident of their own capacity to 'handle it'.

WORKING WITH GAY MEN WHOSE SEXUALITY AND DRUG USE IS CULTURALLY SPECIFIC

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The debate around drug use and sex, particularly crystal methamphetamine and its putative link to the recent HIV increase, continues to happen as community health organisations and other health services and gay community grapple with limited data and few effective treatment models in formulating a response.

One of the emerging challenges is balancing a response that adopts a harm reduction approach aimed at the broader community of users with a demand reduction or abstinence approach for men who are experiencing adverse affects of their drug use.

Drawing on our service delivery and health promotion experience, this paper will outline some of the current debates around drug use and gay men. with a particular emphasis on men who use crystal methamphetamine, and discuss some of the service challenges, health promotion programs and clinical services necessary to reduce or eliminate the adverse effects of use.

The paper will also explore some of the barriers to implementing an effective response and outline the required policy and advocacy work needed to ensure that the political environment is enabling and supportive of a harm reduction approach to drug use.

NEW APPLICATIONS OF PEER EDUCATION IN YOUNG GAY MEN'S SEXUAL HEALTH PROMOTION

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Peer educators have contributed enormously to the spread of knowledge about prevention of HIV transmission and the changing of attitudes to HIV positive people and safe sex. In the context of community education of young gay men, this has most frequently been executed through their facilitating peer-run workshops or acting as informal sources of information among their peer group.

This presentation will consider means of extending the utility of peer educators beyond their traditional or most widely applied roles. In particular it will look at ways that peer education might be adapted to respond to challenges in young gay men's health and wellbeing. Possible areas of application may include the promotion of routine sexual health testing, knowledge and uptake of non-occupational post-exposure prophylaxis, vaccination against hepatitis A and B, and HIV seroconversion. The potential of peer education to more greatly affect young gay men's social environment will also be discussed. Influencing social networks to be more supportive of young men living with HIV and to more naturally engage with HIV prevention will also be discussed.

POSITIVE IN PREVENTION

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Recent rises in new HIV infections has led some commentators to comment that prevention education has failed and has led to some considerations of the place that disclosure by HIV positive people has played as a factor influencing these rises.

In the US, the Centre for Disease Control (CDC) in May 2003 has adopted a prevention model which places increased focus on identification of those at risk and testing; increased surveillance of positive people and getting them onto treatment together with promotion of a disclosure ethic for HIV positive people.

This new CDC prevention education model has the very real potential to create division and if you like viral apartheid between those who bear the virus and the uninfected and is strenuously opposed by NAPWA.

NAPWA considers that there are some very important education and policy questions which need examining so that the needs of positive people and their individual rights are not at odds with the needs of negative men and the agendas of public health.

If a model such as the CDC were it to be adopted in Australia by policy makers and government, it would have the effect of leading to further stigmatisation and discrimination of positive people with the very real potential for this approach to be to the detriment of HIV positive people, their health and well being.

This paper builds upon the recent work that the National Association of People Living with HIV/AIDS (NAPWA) has conducted with its own membership on the desired roles and responsibilities of positive people in prevention and includes some of the points of discussion from the 2004 national HIV Educator's conference Search Stream on positive in prevention.

In this paper NAPWA argues that there are compelling reasons for the continuation of a national response for prevention under the 5th National HIV Strategy, which is based upon shared responsibility, and a partnership model of combination prevention.

Concurrent Session – Social Research – Multicultural & IDUs

CULTURAL CHARACTERISTICS AND VULNERABILITY TO BLOOD BORNE VIRUSES OF ETHNIC VIETNAMESE INJECTING DRUG USERS

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There is increasing concern about the potential for a sudden and significant increase in HIV among ethnic Vietnamese injecting drug users (IDUs) in Australia. The current study aimed to systematically explore the cultural beliefs and behavioural practices of Vietnamese IDUs, to identify barriers to accessing health and preventive programs and to determine the prevalence of antibody HIV and HCV in this population. We present here qualitative data on cultural characteristics or sensibilities that influence vulnerability to blood-borne viruses.

Snowball sampling strategies, including ethnographic fieldwork and street outreach, were used to recruit Vietnamese-Australian IDUs (n = 44) in South Western Sydney. Eligibility criteria for the study were: Vietnamese cultural background, aged 16 years and over and injected drugs in the last six months. In-depth interviews were tape-recorded and transcribed and open coding was used to classify data into themes. Data were examined for regularities and variations in relationships between and within themes.

We identified four main cultural characteristics that appear to influence vulnerability to HIV and other blood-borne viruses: trust and obligation, a reluctance to discuss problems with outsiders, stoicism and a belief in fate. The paper discusses how these culturally shaped sensibilities impact on health beliefs and practices, including risk and preventive behaviours. Results suggest that service providers working with Vietnamese IDUs need to be aware of and to understand these sensibilities in order to work effectively with this group.

WHAT ROLE DO KEY INFORMANTS PLAY IN HELPING US TO UNDERSTAND AND ADDRESS BLOOD BORNE VIRUS PREVALENCE AND RISK BEHAVIOURS AMONG ETHNIC-VIETNAMESE INJECTING DRUG USERS IN MELBOURNE?

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Key informants or "experts" are often asked to estimate the prevalence of a disease, the numbers in particular risk groups, or the frequency of particular risk behaviours. The figures derived from key informant estimates often used become accepted as "the truth" and used to inform the direction of social and public health policy and resources.

As part of a larger study responding to an increasing concern regarding ethnic-Vietnamese injecting drug users (IDUs) in Melbourne being at high risk of HIV infection, a modified Delphi technique was used. The Delphi is a method for the systematic collection and aggregation of informed judgments from a group of experts (or key informants) on specific questions or issues. The study objective was to examine the role and usefulness of key informant information in an area such as injecting drug use where the populations are often marginalised and difficult to identify, and the illnesses (HIV and hepatitis C) associated with the risk behaviour can lead to discrimination by the general community as well as within the social group.

The study selected a panel of key informants from various sectors, with knowledge and skills in the area of interest, who were asked to answer a number of questions relating to ethnic-Vietnamese IDUs in Melbourne. The panel were also asked to indicate the level of confidence they had in their responses to the questions asked of them.

The results and outcomes of this study indicate a lack of specific knowledge and confidence in key informant responses to the questions asked by the study. Our study results highlight the limitations of relying upon key informant information alone to provide specific information or accurate data about ethnic-Vietnamese IDUs, without also obtaining sound evidence. Whilst exercises such as the Delphi technique can be used to generate the broad view of what is occurring in marginalised populations, we argue that care must be taken when using such information as "evidence" on which to base the direction and design of social and public health policy and resources.

CULTURE AND INTERDEPENDENCE: NEGOTIATING HIV DIAGNOSIS AND DISCLOSURE AMONG PEOPLE FROM CULTURALLY AND LINGUISTICALLY DIVERSE BACKGROUNDS

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The project "Living with HIV and Cultural Diversity" investigates the experiences of living with HIV among people from culturally and linguistically diverse (CALD) backgrounds. This group has been identified in the National HIV/AIDS strategy 1999–2004 as having specific needs relating to education, prevention and health promotion. People from CALD backgrounds made up 22% of HIV notifications in Australia in 2002.

Participants were recruited among the clients of the Multicultural HIV/AIDS and Hepatitis C Service and a sexual health clinic in Sydney. Data were collected through in-depth, open-ended interviews.

One major theme emerging from the narratives was interdependence between the individual, family and ethnic communities. Because of the association of HIV with 'shame' in many ethnic communities, an HIV diagnosis affected not only the person with HIV but the whole family. Disclosure required the careful balancing of individuals' needs for support, their obligations within the family, and their desire to be free from stigmatization A sense of interdependence was experienced as a barrier to disclosure where the family needed to be protected from negative judgements. However, it could also be a catalyst for disclosure out of a sense of obligation. Disclosure was described by some as a process which required mutual support between the person with HIV and those who had been disclosed to.

Support services for people from CALD backgrounds need to be sensitive to family and cultural dynamics within ethnic communities. The role of bilingual and bicultural co-workers was highly valued. They provide participants with a relationship where they can communicate in their own language. They also provide a relationship that is culturally sensitive, free from negative judgements and ensures confidentiality.

HIV AND INJECTION DRUG USE: IS HAART A REALITY?

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Sudden outbreaks of HIV in injecting drug users have occurred across the globe with the prevalence rising in just a few years. Victoria has seen a disproportionate number of ethnic Vietnamese injecting drug users with newly diagnosed HIV infection. Since January 1999 over 40% of the IDUs diagnosed with HIV have been ethnic Vietnamese. Although the numbers are small there remains apprehension about the potential for a sudden and significant increase in the number of cases of HIV in the injecting drug using population, particularly within the ethnic Vietnamese subgroup.

A recently completed cross-sectional study among ethnic Vietnamese IDUs found three HIV positive cases. One of these was a new notification; and, despite all being eligible for HAART, none of the three HIV cases in our study were in current contact with any HIV services . Our participants remain in complex and unstable social situations and are not well linked into available services. Our research highlights that these people are not accessing health services to the same extent as other HIV positive people.

Drug related crime and arrest, lack of opiate treatment, ambivalence about HAART, and issues of disclosure are a few of the social issues which mark the difficulties this group of HIV positive people have in dealing with their infection. Despite having case workers who are experienced, culturally aware and well known to the participants follow up has been problematic. Streamlined and flexible access to the infectious disease clinic has not increased compliance to attending appointments or to HAART.

This paper describes the difficulty the authors have had in sustaining primary health care for HIV positive IDUs. It will present a case study to outline the ways the authors have struggled with offering and maintaining a harm reduction focused health service.

ADHERENCE AND DIVERSITY

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People from culturally and linguistically diverse (CALD) backgrounds made up 22% of all new cases of HIV in Australia in 2002. Living with HIV/AIDS they experience many similar issues to others living with the virus – physically, socially, and psychologically. But their experience is often compounded by their migration, culture, language, and family, which in turn influence their experience of treatment and adherence.

The Multicultural HIV/AIDS and Hepatitis C Service uses bilingual/bicultural workers to provide a culturally relevant support to people living with HIV/AIDS (PLWHA). It currently targets 20 language backgrounds and the annual number of new referrals roughly equals half the new HIV notifications in NSW from people of CALD backgrounds.

This paper presents case studies from the cumulative experience of the Service to show that culturally relevant support can result in a series of positive outcomes, including 'better' adherence.

The paper argues that, contrary to some assumptions, CALD clients are often highly accepting of medical 'authority' and treatments, and their 'non-adherence' is usually a response to situational constraints, eg disclosure, residency, etc. Even where disclosure is an issue, negotiating these constraints in a culturally sensitive manner can result in positive outcomes.

The paper suggests that clinicians responding to the cultural diversity of their clients need to be sensitive to these issues.

HIV/AIDS MULTILINGUAL RECORDED LINES FOR PEOPLE FROM CULTURALLY DIVERSE BACKGROUNDS

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According to the most recent National Centre in HIV Epidemiology and Clinical Research (NCHECR) surveillance report, 22 per cent of HIV cases in Australia in 2002 were among people born in non-English speaking countries. In NSW for the two years 2001-2002, 18% of HIV notifications were among people who spoke a language other than English at home.

Data from the NCHECR has consistently found that people from Culturally and Linguistically Diverse (CALD) Backgrounds are more likely to present late with HIV when compared to people born in Australia - i.e. a diagnosis of an AIDS–related illness within 3 months of being tested for HIV. Late presentation has important public health implications, as well as personal implications for people from CALD backgrounds, who may not access HIV treatment early.

The Multicultural HIV/AIDS and Hepatitis C Service (MHAHS) carried out a consultation process with service providers and with people living with HIV/AIDS from CALD backgrounds to get their views on late presentation with the overall aim of reducing late HIV presentation, mainly by promoting access to HIV testing. The consultation process strongly supported the development of HIV/AIDS multilingual recorded information lines. The consultations indicated that people from CALD backgrounds, especially those who have language difficulties, want anonymous ways to access accurate information in their own language.

This paper will present the strategies implemented with the HIV/AIDS Multilingual Recorded Information Lines over the past year. The paper will focus on the strategies implemented since the information lines – in 21 community languages - were launched in November 2003. These include an ethnic media campaign data on the number of hits to the lines and the evaluation of the lines using HIV testing data from sexual health clinics in the Sydney region.

The paper will also explore the difficulties and successes encountered in working with a diverse range of stakeholders, developing the lines and point to strategies which services may be able to use to engage these communities on health issues.

Symposium – Basic Science – HIV Immunology

HIV AND HEPATITIS C ADAPTATION TO HLA-RESTRICTED IMMUNE RESPONSES

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HIV has an almost unprecedented ability to adapt rapidly to HLA-restricted immune responses both within an individual and at a population level. This appears to be a major driver of HIV Clades and the enormous global HIV diversity that is a major challenge to HIV vaccine design. On the other hand, this capacity for HIV genetic mutation and recombination is so great that it is possible to analyse HLA-viral mutation associations at the single amino acid level and we have been able to exploit this predictable relationship for vaccine design and evaluation. Specifically the relationship between HLA alleles and HIV polymorphism in chronically infected patients may be used to predict protective responses to a preventative vaccine in a population with similar HLA diversity exposed to a similar range of HIV diversity. Importantly, the innate advantage provided by intense human HLA diversity can then be exploited to ameliorate problems posed by HIV diversity. Analyses of real and theoretical candidate vaccines suggest that "polyallelic" vaccines will most effectively exploit HLA diversity to cover HIV diversity. The degree to which these principles can be generalised to Hepatitis C and other organisms that can adapt rapidly to the host is being examined.

PROLIFERATING ANTIGEN-SPECIFIC CD4+ WITH A CCR5, CYTOTOXIC T LYMPHOCYTE PHENOTYPE DURING PRIMARY HIV-1 INFECTION

Zaunders J[1], Munier M[2], Ip S[2], Grey P[2], Smith D E[2], Kaufmann D[3], Walker B D[3], Kaldor J[2], Cooper D A[1,2], Kelleher A D[1,2] on behalf of the Phaedra Study Team
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Antigen-specific CD4+ T lymphocytes are believed to be generated during primary HIV-1 infection (PHI), but are lost early in the course of infection, unless treatment is initiated. We have recently found, in a long-term non-progressor, that HIV-specific CD4+ T cells expressed CCR5, and were also cytotoxic T lymphocytes (CTL). Therefore, we investigated whether such cells could be detected during PHI.

Fresh peripheral blood samples were obtained from subjects enrolled in the Phaedra observational study of PHI. Immunophenotyping of whole blood CD4+ T cells for CCR5, activation antigens (CD38, HLA-DR), markers of CTL (TIA-1, Granzyme B, Perforin), proliferation (Ki-67) and cell survival (Bcl-2) were analysed by flow cytometry. Antigen-specific CD4+ T cells were identified by intracellular cytokine assay following incubation with HIV Gag or Nef peptide pools, or with CMV lysate.

In samples from 16 subjects with PHI, there was a significant elevation in the proportion of CD4+ T cells which were CCR5+CD38^{bright} compared with 12 uninfected staff controls (medians: 2.5 vs 0.3%, respectively; $p<0.001$). Ki-67+ proliferating CD4+ T cells were also elevated in PHI compared with controls (6.4 vs 1.6%, $p<0.001$). Approximately one quarter of the Ki-67+CD4+ T cells were CCR5+TIA-1+. Also, the proportion of CD4+ T cells which were TIA-1+Perforin+Granzyme B+ was increased during PHI compared with controls (15.2 vs 2.6%; $p<0.01$).

In 2 subjects with very early PHI (negative for HIV Western Blot at presentation), 0.3 and 0.8% of CD4+ T cells, respectively, produced IFN-γ in response to HIV Gag. These antigen-specific CD4+ T cells were predominantly CD38^{bright}Bcl-2^{dim}, TIA-1+Ki-67+, IL-7R- and CD57-negative, consistent with a phenotype of newly derived, activated, proliferating CTL effectors. These cells expressed CD40 ligand, and a subset also expressed IL-2, suggesting helper function. In the same subjects, CMV-specific CD4+ T cells exhibited a resting, non-proliferating, long-term memory phenotype. However, in another 2 subjects with later presentation (3 and 6 bands on Western Blot, respectively), antigen-specific CD4+ T cells could not be detected.

These results suggest that during PHI, the early anti-viral response includes activated CCR5+CD4+ T cells with a CTL and helper phenotype, but are probably highly susceptible to cytopathic infection with HIV-1.

T CELL DECLINE AND IMMUNE RESTORATION IN HIV DISEASE

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The human immune system responds to T-cell loss, by increasing T cell production either via peripheral expansion or through de novo T-cell production by the thymus. During HIV disease, thymic dysfunction and thymic involution occur as well as enhanced activation, proliferation and death of T cells in the periphery, all of which contribute to progressive T cell decline in untreated HIV infection. T cell receptor excision circles (TREC) and more recently CD31 expression on naïve T-cells have been proposed as markers of new thymic emigrants. Antiretroviral therapy (ART) is associated with an increase in TREC concentration and a reduction in T cell proliferation, activation and apoptosis. However, T cell activation rarely returns to levels seen in HIV-uninfected individuals. In fact, the level of T cell activation in individuals on ART is a strong predictor of subsequent CD4 T cell reconstitution. Individuals treated with ART who remain viremic with drug-resistant HIV often experience a durable increase in CD4 T-cell counts. This sustained immunologic benefit occurs even after controlling for the level of viremia and is associated with decreased levels of immune activation, increased HIV-specific T-cell responses and reduced proliferation in CD4+ T-cells. In individuals with drug-resistant virus, who fail ART immunologically, HIV regains replicative fitness. Proposed mechanisms for the restoration of viral fitness include compensatory mutations in gag or protease and/or a change from an R5 to X4 virus. Potential future approaches to novel immunotherapeutics for the treatment of HIV disease may include agents that enhance thymus output, reduce immune activation or reduce viral replication capacity.

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POSTER ABSTRACTS

POSTER ABSTRACTS

Clinical Medicine Posters

P1
GETTING TO THE BOTTOM OF ANAL ITCH – A CAUTIONARY TAIL

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Anal cancer is relatively rare in the general population. However, epidemiological data suggest that it is more common in individuals infected with HIV, particularly men who have sex with men. Unfortunately anal cancer frequently presents at an advanced stage, as the early phase of the condition is usually without symptoms. Anal intraepithelial neoplasia (AIN) is postulated to be a pre-cursor of anal cancer, and there have been calls to promote cytological screening in high-risk groups, However, there are currently no accepted screening guidelines.

We report a case of a homosexually active HIV-infected man with two pre-cancerous lesions of the anal region and suggest that it may be useful to offer targeted screening for anal cancer.

A 44 year old homosexual man presented with persistent pruritus ani and a diagnosis of "chronic eczema" of the perianal skin for 12 months. Physical examination revealed lichenified perianal skin. Histological assessment of a biopsy from this area revealed the characteristic histological changes of "atypical condyloma" – an unusual variant of human papilloma virus lesion, first reported in the cervix in 1977, now known to be associated with "high risk" viral subtype and increased risk of neoplastic transformation compared to "usual" condylomatous lesions. The patient was referred to a colorectal surgeon for excision of the lesion.

Anal cytology was performed at the time of biopsy, and revealed high-grade squamous intra-epithelial changes. Subsequent anoscopy with biopsy of acetowhite areas in the anal mucosa confirmed the presence of AIN 2.

This case demonstrated the so-called 'field effect' of human papilloma virus – a well-recognised phenomenon in women, where cervical intraepithelial neoplasia is frequently found in association with intra-epithelial ("dysplastic") changes in the vagina and vulva. We believe that the changes described in this man represent a similar phenomenon occurring in the anal region and suggest that peri-anal lesions may provide a useful indicator of individuals at increased risk of intra-epithelial neoplasia in the anal canal.

Furthermore, this case also emphasises the need to thoroughly investigate persistent anal symptoms in HIV positive men, no matter how insignificant they may appear.

P2
BASELINE RESISTANCE TO TENOFOVIR (TFV) AND ATANAZAVIR (ATV)IN A HIV CLINIC POPULATION

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The ability of HIV-1 to evolve resistance to antiretroviral drugs leads to treatment failure. Some HIV infected individuals who have never received antiretroviral therapy also carry resistance mutations. A study was conducted to assess the prevalence of antiretroviral resistance mutations in treated and untreated HIV patients in a clinic environment at Westmead Hospital. The impact of current resistance mutations in these patients was studied for two newly introduced antiretroviral drugs; TFV and ATV. The study included 157 patients who had failed treatment and another 107 who were treatment naive. The PR and RT region were sequenced and results interpreted using the Stanford database. The primary TFV resistance mutations K65R or T69SS were uncommon in our study (K65R/T69SS-0.7%). In our clinic, 25% (39/157) of antiretroviral experienced patients had the M41L or L210W mutations plus 3 other TAMs, with half the patients also having the M184V mutation. None of the treatment naive patients had these combinations. The high proportion of M184V in patients with multiple TAMs may enhance TFV efficacy in this heavily pretreated population. With ATV, the signature mutation 150L was absent in this study. ATV resistance can also develop with the accumulation of 5 or more amino acid substitutions at codons 10I/V/F, 20R/M/I, 24I, 33I/F/V, 36I/L, 46I/L, 48V, 54V/L, 63P, 71V/T/I, 73C/S/T/A, 82A/F/S/T, 84V and 90M. Thirty-two percent (50/157) of antiretroviral drug experienced patients had 5 or more of these substitutions, but none of treatment naive patients. In our clinic, 25% of the antiretroviral experienced patients may not get long-term benefit with TFV (although M184V may reverse this), and another 32% may have impaired ATV responses. The prevalence of resistance mutations in a particular region or country depends on local antiretroviral treatment practices; these data can be used to assess the value of new drugs introduced into clinical practice.

P3
COMPARISON OF THE FREQUENCY OF HIV-1 DRUG RESISTANCE MUTATIONS IN TREATED AND UNTREATED PATIENTS FROM VARIOUS COUNTRIES

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The development of antiretroviral drug resistance mutations is a serious obstacle to sustained suppression of HIV during HAART. Antiretroviral drug resistance testing allows clinicians to choose appropriate therapeutic options. A retrospective study was conducted to assess the prevalence of antiretroviral resistance mutations in treated and untreated HIV patients in a clinic environment, and results compared with overseas data. Resistance to at least one PI was fairly similar (approximately 2%) among treatment naïve patients in different countries, except for Canada (3.8%). More variation was observed with NRTI, with resistance to 1 or more NRTI ranging from 1.2% in Argentina to 28.9% in Warsaw. NNRTI resistance ranged from 0.2% to 4.9%. Warsaw had higher frequency of resistance mutations in M184V (17%), K70R (42%) and M41L (9%). In pretreated patients, the proportion of PI resistance among the various countries varied from 12% to 58%. The percentage of NRTI resistance mutations ranged from 48 to 77%. Westmead had a higher frequency of L74V (19%) and Y181C (18%) mutations, Brazil-T69D/N (47%), Canada-M41L(50%), M184V (65%, D67N (43%) and L90M (46%), Spain-T215Y (51%), G190A/S (13.6%) and Puerto Rico -K103N (40%). Thailand had a lower frequency of PI resistance mutations-L90M (7%), I54V/L (6%), V82A (8%). The prevalence of primary and secondary resistance mutations in different regions or country will depend on the local treatment practices and antiretroviral drug availability, the patterns of cross-resistance, the presence of different HIV-1 subtypes, and the frequency of resistance mutations in treatment naïve individual.

P4
VALIDITY OF A NEW COMPUTERISED BATTERY FOR THE ASSESSMENT OF NEUROCOGNITIVE FUNCTIONS IN ADVANCED HIV-INFECTION AND AIDS DEMENTIA COMPLEX

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The early identification of AIDS Dementia Complex (ADC), the most severe manifestation of HIV-associated neurocognitive impairment is essential, as several studies have demonstrated the benefit of Highly Active Antiretroviral Therapy (HAART). Conventional neuropsychological assessment is costly in time and resources. A practical brief screening tool is needed.

Sixty individuals with advanced HIV-infection (stage CDC C3, 1993) were randomly selected from a tertiary referral hospital outpatients clinic. Eleven were currently diagnosed with ADC stage 1 or 2. Twenty-one seronegative individuals were recruited as controls. Participants were examined with a comprehensive standard neuropsychological examination and a brief computerised examination, lasting ten to fifteen minutes, assessing psychomotor speed, attention, decision-making and memory learning.

Computerised assessment showed that advanced HIV-infected individuals were significantly slower ($p<.000$) and less accurate ($p<.03$) than controls. ADC patients demonstrated worse performance when compared to non-demented patients on most speed measures ($p<.000$) and the most demanding accuracy ($p<.03$) measures. Computerised measures were correlated with standard measures of complex attention and processing speed ($r=.45$ to $.62$). Computerised total reaction time ($p<.003$) and learning accuracy ($p<.02$) were significant predictors of neuropsychological impairment and ADC. When using the standard neuropsychological measures as a gold standard, the brief computerised examination had a sensitivity of 83.8% and specificity of 47.8%.

In conclusion, our study showed that a short computerised battery was sensitive to the neurocognitive deficits associated with HIV-infection. The use of this battery could help screening patients at risk for ADC.

P5
MEANINGFUL DATA – THE CHALLENGE FOR ALL CLINICIANS

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The effective treatment of HIV and hepatitis C (HCV) in recent years has resulted in increased life expectancy and quality of life for HIV and HCV patients. However the number of patients who present to non-inpatient services with complex needs has grown enormously. South Eastern Sydney Area Health Service (SESAHS) is well recognized as being at the epicentre of the HIV/AIDS epidemic in Australia. However it was also recognized that there was a need for improvement in the collection and reporting of the HIV/AIDS, HCV and Sexual Health data arising from non-inpatient attendances to hospital based services in the area. In 2001 Working Groups of interested, representative multi-disciplinary clinicians, including HIV specialists and Allied Health, of the six high caseload hospital based services were established. The aim was to formulate a Minimum Dataset for HIV/AIDS, HCV and Sexual Health for the ambulatory care, outpatient and Community Health services in SESAHS. The initiative was supported, and the database funded, by the AIDS/Infectious Diseases Branch, NSW Health.

A uniform core set of definitions encompassing 22 broad categories of demographic, clinical and service utilisation was established. Patient profile data items include Sex, Age, Country of Birth, Aboriginality, Postcode, Source of Referral, Risk Category together with and health outcome data relating to Diagnosis, Intervention, Treatment etc. In addition, the database also encompasses CD4, viral load and anti-retroviral graphical functions and preliminary Clinical Indicators in HIV and HCV care. The minimum dataset dictionary has been piloted area-wide and refined over the past two years and at the end of 2003, culminated in the development of a computerized database for utilisation by all HIV, HCV and Sexual Health services across SESAHS. In February 2004 data extraction was commenced area-wide. We report on the collaborative process of developing such a database and on the challenges encountered in the development, implementation and outcomes of the first Australian area-wide Minimum Dataset and computerised database in these three important clinical areas.

P6
THE PHAEDRA COHORT UPDATE: BASELINE CHARACTERISTICS AND TREATMENT UPTAKE IN PRIMARY HIV INFECTION

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The Phaedra cohort was established to provide a structured mechanism to recruit and follow people identified with primary HIV infection (PHI) whether they are treated or not. The long-term follow-up of study participants will help to define immunological, virological and therapeutic factors that influence disease progression.

Individuals diagnosed with acute and early HIV infection in Sydney and Melbourne have been enrolled in an ongoing cohort. Clinical and laboratory variables were collected intensively during the first year of seroconversion and 6 monthly thereafter with additional blood samples taken for storage.

Since recruitment into Phaedra commenced in September 2002, 232 individuals have been enrolled to May 2004. Within the cohort 133 individuals have been newly diagnosed with acute or early infection and a further 99 were retrospectively recruited from other clinical studies in PHI. Of the newly diagnosed seroconverters 59% were identified with acute and 41% with early HIV infection. The cohort has enrolled approximately 50% of all newly infected individuals identified during this period by the Centre for Immunology, and 21% of notifications to VIDRL in Melbourne.

All study participants were male with a median age of 35 years and had been infected mainly via homosexual transmission (96%). Within the 133 newly diagnosed patients, concurrent infections at the time of HIV seroconversion were: syphilis 6 (4.5%), herpes simplex 3(2%), gonorrhoea 6 (4.5%), chlamydia 2 (1.5%) and HSV-2 4 (3%) The median viral load and CD4 T-cell count at baseline of this group was 204,000 copies/ml (range 50->750,000 copies/ml) and 504 cells/µl (range 168-1360 cells/µl), respectively. Ninety two % presented with PHI signs or symptoms. Sixty nine % of newly identified seroconverters had commenced treatment within a median of 9 days (range 1-377 days) from HIV diagnosis. Seventy six % of treated participants have commenced on a regimen containing two-nucleoside reverse transcriptase with a protease inhibitor. Thirty one % (31 early and 10 acute) of individuals did not commence treatment within 8 weeks of diagnosis, of which 22% remain untreated after 6 months follow-up.

The clinical and immunological characterisation of this well-defined cohort will provide the opportunity to assess long-term outcomes related to pathogenesis and treatment in primary HIV infection.

P7
ATAZANAVIR SPECIAL ACCESS SCHEME: INTERIM SUMMARY OF AVAILABLE DATA

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Atazanavir (ATV) is a potent once daily protease inhibitor (PI) that has demonstrated clinical comparability to standard of care in naïve and treatment experienced patients, with a superior metabolic profile. ATV was made available through a Special Access Scheme (SAS) in Australia in 2003. Presented is an interim summary of mandatory safety data for patients enrolled in the Scheme. Data has not been independently monitored and sites have adopted different timelines for submission of data. Parameters such as HIV RNA, CD4 and lipids were not routinely collected.

733 patients enrolled in the Scheme from January 2003 to May 2004. Patients are treatment experienced. Patients were eligible if experiencing virologic failure (74.4%), toxicity (65.8%) and/or severe, refractory hyperlipidaemia (31.4%) with previous therapy. The average age of participants is 46.1 years (SD ± 10 years) and the majority (91%) are male. 539 (73.5%) of patients are receiving Atazanavir (ATV) 300mg plus 100mg ritonavir, once a day.

Sites involved in the Scheme were asked to submit safety data one month (OT1) after commencement of Atazanavir and every 2-3 months thereafter. On average the visit interval for data collection is 60-70 days.

ALT and bilirubin are the mandatory laboratory parameters collected. The proportion of patients that experienced concurrent ALT and bilirubin rises was low, with the rate at baseline being nil and increasing to approximately 9% (OT1-OT5). At baseline 12.9% of patients reported an ALT of 55-100 U/L, this increased to 21.3% at OT1 and was stable at 18.3% at OT5. At baseline 8.3% of patients reported a bilirubin 20-59μmol/L, this increased to 49.4% at OT1 and 53.8% at OT5.

The most common Non Serious Adverse Events (NSAE) considered to be related to ATV by the treating doctor were gastrointestinal symptoms (n=32) and hyperbilirubinaemia (n=21). The most common reasons given for patients discontinuing treatment with ATV were adverse events (n=34) and patient withdrawal of consent (n=22). Fifteen Serious Adverse Events (SAE) considered certainly, probably or possibly related to ATV were reported, including 3 hyperbilirubinaemia and jaundice, 2 rash, 2 pancreatitis, 2 vascular occlusions (same patient) and 2 palpitations. Hyperbilirubinaemia seen with ATV has not been associated with hepatotoxicity.

P8
HS-CRP IS ELEVATED IN HIV POSITIVE PATIENTS WITH A TREND TO INCREASED LEVELS IN PATIENTS IN THE TWELVE MONTHS PRIOR TO CORONARY EVENTS

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Cardiac events occurring in HIV infected individuals may be related to traditionally recognised risks, HIV treatments or other factors. A Case Control examination of HIV related factors was undertaken in those with and without defined symptomatic cardiac disease treated at the Alfred Hospital.

Cases were defined as having a documented myocardial infarct, angiogram demonstrating vascular disease, a positive nuclear medicine scan or exercise test or clinical disease with or without ECG changes treated as angina. Controls were selected from those individuals with no CVD matched age (± 2 years), era and gender (before and after HAART (1996) without documented cardiac events. Thirty three cases and sixty six controls were identified.

CD4 at admission and nadir, HIV RNA at event/ matching date and prior peak, antivirals, and cardiovascular risks were analysed. There was no difference in recorded smoking history, diabetes mellitus, cholesterol, triglycerides, hypertension, HAART therapy, HIV viral load or days of protease inhibitor therapy.

As a substudy of this study we examined the HS-CRP (highly sensitive C reactive protein) levels in our cases and controls in the twelve months prior to censoring from stored viral load samples usually taken at routine outpatient vists. The CRP level has been shown to be one of the stronger predictors of a cardiac event in n HIV negative population and postulated to be a direct player in the pathogenesis of coronary disease. Wheras the normal levels in an HIV negative population are less than 5 the levels in our study were a mean of 7.83 (N=22 SD= 13.8) for controls and 12.87 (N= 13 SD=24.56) for cases. The difference between cases and controls did not reach statistical significance by univariate analysis. This data in a small population suggest further examination in a larger population is warranted.

P9
AN ANALYSIS OF THE TIME TAKEN FOR CLINICAL TRIAL DATA TO BE SUBMITTED TO CENTRAL DATA MANAGEMENT

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Early review of data by central data management (CDM) enables sites to promptly clarify data queries and reduces time to completion of study. This study aimed to summarise the time taken for clinical trial data to be sent from investigator sites to CDM. Ongoing drug supply was dependant on CDM receiving data.

A review was undertaken of the first 48 weeks of data received by CDM for an open label, multicentre, phase III study. Data were faxed to the CDM following each patient visit. Records were reviewed to assess the time for the CDM to receive study related data. Data was summarised according to week of study visit and study site; Hospital or General Practice (GP). Significance was tested using a two-tailed T test.

There was a mean time of 16 days between a patient's visit and CDM receiving the initial data relating to that visit from the site. There was a mean time of 29 days between a patient's visit and the final piece of data for study visit. Over the 48 week duration of the study, the mean time for completed study data to be received by the CDM lengthened from a mean of 12 days at the patients screening visit to 22 days at week 48 ($p = 0.002$). The mean number of days to submit their data to the CDM was 17 days for hospital sites and 34 days for GP sites ($P = 0.0001$).

Faxing data to CDM provided an efficient mechanism for sites to transmit data. However transmission of data became slower over the duration of the study, possibly due to changing priorities. There was a significant difference between hospital and GP sites to submit data, this may be related to the large number of studies for which individual coordinators at GP sites are responsible. Timely receipt of data enables the CDM to assist the site in adhering to the protocol and may influence the completeness of the study data.

P10
TWO CASES OF NON PERINATAL TRANSMISSION OF PAEDIATRIC HIV IN THE AUSTRALIAN SETTING

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Almost 600,000 children are believed to acquire Human Immunodeficiency Virus (HIV) worldwide annually. HIV is transmitted via blood to blood, sexual exposure and vertically. Approximately 90% of infected children worldwide acquire HIV from mother to child, during pregnancy, labour or breastfeeding. This is also the most common route of transmission in children in Australia in the era of blood donor screening and usually occurs when HIV status of the mother is unknown and vertical transmission reduction strategies such as the PACTG076 protocol are not implemented. If prevention strategies are implemented, the mother to child transmission rate drops to 1-2%.

Historically, blood transfusion was also a common route of transmission of HIV but has been almost eliminated since the introduction of routine testing of blood donations in the mid 1980's.

Case one is a teenage female who presented with Pneumocystis Carinii Pneumonia (PCP). There was a history of repeated sexual abuse. It emerged that the alleged perpetrator was a HIV infected male. This child has done well on HAART and quickly achieved undetectable viral load. In case two, the mode of acquisition is unknown. Both parents and both siblings of this teenage female are HIV negative. She was found to be repeatedly reactive on Enzyme-Linked Immunosorbent Assay (ELISA) testing for HIV antibodies and for HIV antigen/antibodies. Her HIV-1 Western blot was positive on three occasions. She denies sexual contact. She received several immunisation injections in a developing country. Her CD4 count is normal and her HIV viral load is undetectable using an ultra sensitive assay.

These two case studies will be used to explore the issue of non-typical acquisition of HIV in the paediatric setting. These case studies will be compared and contrasted with data from overseas.

The aim of this presentation is to draw attention to the issue of non-typical acquisition of HIV in the paediatric setting in Australia and overseas.

P11
PARA/POST-KALA-AZAR DERMAL LEISHMANIASIS (PKDL) IN AN HIV-INFECTED INDIVIDUAL WITH VISCERAL LEISHMANIASIS (VL).

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VL, caused by *Leishmania spp,* is a zoonotic infection widespread in Africa, Southern Europe, India and S.America. It is an emerging opportunistic pathogen in HIV-infection in areas where both are common. VL is characterised by depressed cellular immune responses to the pathogen. Para- and post-Kala-azar dermal leishmaniasis (PKDL) presents with maculopapular/nodular lesions to the face, limbs, and trunk in those with a recent/remote history of treated VL and probably represents a form of immune restoration disease (IRD). PKDL is common with *L.donovani* and rare with *L.infantum*. Treatment depends largely on geographical location i.e. no therapy in areas where spontaneous remission is common (Sudan) or long periods of appropriate antimicrobials (India). PKDL has been very rarely reported in HIV-infection.

To describe the clinical presentation of PKDL in a patient with chronic VL-HIV co-infection and the use of PCR for species identification.

Promastigotes were cultured from skin biopsies and PCR performed using primers specific for the repetitive sequence *Leishmania* nuclear DNA and the SSUrRNA region of *Leishmania*. PCR-RFLP analysis was undertaken using primers targeting the repetitive sequence *Leishmania* nuclear DNA with subsequent digestion of *Hae*III for speciation.

This HAART-treated HIV-VL co-infected individual, developed nodular lesions on the head and neck during induction/maintenance therapy for VL with liposomal amphotericin. The development of these skin lesions correlated with clinical and immunological improvement i.e. weight gain, defervescence of fever, significant decrease in spleen size and doubling of the CD4+ count from 176 to 374 cells/μL. Skin Biopsies on separate occasions revealed amastigotes confirmed as *L.infantum* on PCR (n=2) and inflammatory changes only (n=1).

Rapid tests for Leishmania speciation are clinically relevant as some currently available antimicrobials have higher treatment-failure rates for *L.infantum*. The incidence of *L.donovani*-PKDL appears to be lower when liposomal amphotericin rather than sodium stibogluconate is used. However, even allowing for these treatment differences in *L.infantum*-endemic areas, *L.infantum*-PKDL is still very uncommon. Several features of this individual's presentation are suggestive of *L.infantum*-PKDL, a form of IRD; however, it is unclear how best to manage this condition as so little is currently known about treatment outcomes in both immunocompetent and immunocompromised hosts.

P12
CUSHING'S SYNDROME AND SECONDARY ADRENAL SUPPRESSION IN HIV-1-INFECTED PATIENTS WITH THE "HIV-LIPODYSTROPHY PHENOTYPE" RECEIVING INHALED FLUTICASONE WITH RITONAVIR-BOOSTED PROTEASE INHIBITORS (PI)

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Ritonavir, a Protease Inhibitor (PI) used in the treatment of HIV-infection, is an extremely potent inhibitor of cytochrome P450 3A4 activity and "boosting" doses of ritonavir (200mg/day) with other PIs leads to large increases in area under the curve (AUC) of the second PI. This drug-drug interaction is used advantageously to simplify antiretroviral (ARV) regimens and increase adherence. Asthma and chronic airways limitation (CAL) are common conditions in HIV-infected and uninfected populations with inhaled corticosteroids prescribed for moderate-severe asthma as per current treatment guidelines. All 17-OH sterols are metabolised through P450 3A4 and in healthy adults given low-dose ritonavir with fluticosone, significant increases in AUC for fluticasone (200mcg od) and decreases in plasma cortisol AUC (by 86%) were observed within 7 days. Iatrogenic Cushing's syndrome with secondary adrenal suppression has been reported with high dose ritonavir (>800mg/day)–fluticasone co-administration in HIV-infection, however, there are relatively few reports of Cushing's syndrome with "boosting" doses of ritonavir co-administered with fluticasone.

To describe the clinical and biochemical features of HIV-infected individuals (n=5) presenting with Cushing's syndrome and secondary adrenal suppression during receipt of a ritonavir-boosted-PI and inhaled fluticasone.

Cushing's syndrome was confirmed by an Endocrinologist. Standard early morning short synacthen tests were used to confirm the diagnosis and monitor adrenal recovery.

The individuals in this small cohort (n=5) had chronic HIV-1-infection, were on an ARV regimen that included ritonavir (100-200mg/day), had body shape changes associated with HIV-lipodystrophy and were receiving inhaled fluticasone 500-1000mcg/day for CAL. Various clinical manifestations of Cushing's syndrome including abdominal distension, "moon" face, proximal weakness, striae, fatigue and altered mental state were observed. Baseline cortisols were extremely low i.e. 0-76 nmol/L (NR 200-650nmol/L) and short synacthen responses were indicative of adrenal suppression. Each developed symptomatic hypoadrenalism managed with low-dose oral prednisone replacement following the withdrawal of ritonavir and/or fluticasone. Adrenal recovery was delayed by week to months in all five individuals.

Co-administration of inhaled fluticasone with boosting doses of ritonavir and other PIs that inhibit P450 3A4 can negatively impact on the adrenal axis. The diagnosis of Cushing's syndrome may be masked/delayed in patients with HIV-lipodystrophy.

P13
A LABORATORY'S EXPERIENCE IN THE USE OF THE COMBINED ANTIGEN/ANTIBODY ASSAY FOR DETECTION OF SEROCONVERSION TO HIV

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Recognition of seroconversion to HIV generally requires 14-22 days ('the window period') from the time of infection for detection of antibodies. Strategies to shorten this time include detection of virus either by demonstration of viral nucleic acid or proteins. The latter can be added to an HIV antibody immunoassay system and used for routine diagnostic screening of patient samples. Such combination assays are reported to decrease the window period by up to 7 days.

Our laboratory introduced the Abbott Axsym® HIV Ag/Ab Combo assay in July 2003 as a screening test for HIV. Introduction of the test necessitated a change in our strategy for HIV testing as we now need to distinguish between detection of HIV antigen (p24) only, as expected in early infection prior to seroconversion, and the detection of antibody with or without detection of antigen, as occurs following seroconversion. Therefore, in addition to a second antigen/antibody test for all reactive samples, we also perform an antibody-only test (Abbott Axsym HIV1/2 gO) to determine if the reactivity could be due to the presence of p24. Confirmatory testing includes a separate p24 antigen test as well as a Western Blot.

We have performed 33,553 tests in a mixed risk population using this strategy and detected six patients with evidence of seroconversion to HIV. In three of these patients HIV infection would not have been detected at the first sample with the previously used antibody-only assay. Our experience also indicates that for samples above the sample to cut-off rate (S/CO) positivity threshold, the degree of elevation of S/CO in the Abbott Axsym® Combo assay is less predictive of the final outcome of testing than with the HIV antibody only assay. In the seroconverting patient positive Western blots may be associated with only slightly elevated S/CO values and detection of p24 antigen may be associated with either high or marginally elevated S/CO.

P14
THERAPEUTIC DRUG MONITORING (TDM) OF ATAZANAVIR

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Atazanavir (ATV) a potent once-daily PI has demonstrated clinical comparability to standard of care in naïve and treatment experienced patients. A previous pharmacokinetic study has shown that ATV exposure measured by area under the curve (AUC) was a significant predictor of viral suppression and serum bilirubin elevation. St Vincent's Hospital, Sydney has derived a target ATV trough concentration of 300μg/L from these data; however this target requires further validation.

ATV therapeutic drug monitoring (TDM) became available at St. Vincent's Hospital, Sydney, in December 2003 and to date 160 requests (110 patients) have been received. Patients were receiving ATV 300mg + 100mg RTV (ATV300/r) daily (n=92) or ATV 400mg (ATV400) daily (n=26), in combination with other antiretrovirals. 24-hour trough collection was preferred; however samples collected at other times were converted to troughs using standard pharmacokinetic formulae. Plasma concentrations were quantitated by an HPLC method developed and validated to good laboratory practice standards with a limit of detection of 25μg/L. Population pharmacokinetic analysis was performed using Kinetica V 4.2, (InnaPhase Corp. PA, USA).

Forty two (26%) requests were rejected because of insufficient information to interpret the result (eg missing time of last dose). ATV trough concentrations exhibited substantial interpatient variability, with a median concentration of 30 μg/L (range, <25-390 μg/L) for ATV400 and 476 μg/L (range, <25-2108 μg/L) for ATV300/r. Trough concentrations for 16(17%) samples where the patient was receiving ATV300/r, were >3 times the suggested target of effect. Thirteen (15%) samples from patients taking ATV300/r exhibited trough concentrations <150μg/L. Despite these apparently low concentrations, HIV RNA levels in most patients remained undetectable. In addition, 6/11 patients with plasma ATV concentrations <25μg/L were receiving contraindicated medications, therefore low concentrations of ATV were expected. Serum bilirubin concentrations correlated significantly with higher ATV trough concentrations ($\rho = 0.801$; $p<0.001$). Pharmacokinetic analysis in patients receiving ATV400 found the half-life varied from 2.2 to 9.8 hours and that 12(13%) patients receiving ATV300/r had a half-life <4 hours. TDM may prove to be a useful tool in the optimal management of ATV therapy.

P15
THERAPEUTIC DRUG MONITORING OF ATAZANAVIR IDENTIFIES LOW EXPOSURE TO THE DRUG IN SOME PATIENTS

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Therapy for HIV is complex. Interpatient variability in drug absorption, distribution and elimination is substantial and drug interactions are problematic.

Plasma samples from 110 highly treatment experienced patients were submitted for therapeutic drug monitoring. ATV plasma concentrations were quantitated by HPLC with a limit of detection of 25 µg/L and pharmacokinetic data analysis was performed using Kinetica V 4.2, (InnaPhase Corp. PA, USA). A number of patients (18%) had trough plasma ATV concentrations below the limit of detection (25µg/L) of the assay and were selected for further evaluation. Patients were interviewed to assess adherence and medical records were examined for interacting drugs. Furthermore, pharmacokinetic analysis was performed on eleven patients who had plasma samples collected 0,3,6,9 and 24 hours after an observed ATV dose was taken with a standard meal. The solubility of ATV decreases as gastric pH increases and seven patients were given ATV with 100 mL of classic cola drink (which is known to have a pH of 3.0) and a 3 hour blood sample was collected to observe the effect on ATV concentrations.

This study confirmed low exposure in 8 people with HIV receiving ATV 400 mg daily when compared to population pharmacokinetic data for HIV infected patients; mean area under the curve (AUC_{0-24}) was 13,027 µg/L.h (range 3499 – 23,354) compared to the population average (AUC_{0-24} of 23,500 µg/L.h). Furthermore, the mean half-life of ATV was reduced in this group (3.8 h; range 1.7-5.1) compared to healthy subjects (half-life 6.3 h). Reasons for low ATV exposure in this cohort of people include administration of interacting drugs, including an unexpected dual drug interaction (RTV, fluticasone and ATV), impaired ATV absorption secondary to suspected achlorhydria and potential interactions with colchine or nandrolone that need further investigation. Viral load remained undetectable in most of these patients with low ATV exposure. The frequency of low ATV results appeared to decrease (4%) after early intervention by the pharmaceutical manufacturer, reminded prescribers of the potential for contraindicated medications to lower ATV exposure.

TDM and pharmacokinetic studies should be viewed as fundamental tools in the development of ART, to improve pharmacotherapy for people with HIV.

P16
HEPATIC HISTOPLASMA CAPSULATUM CAUSING FEVER OF UNKNOWN ORIGIN IN A WOMAN WITH ADVANCED HIV INFECTION

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A 28 year old woman presented to several GPs with high fevers and weight loss. She reported negative HIV tests in the recent past, but a test performed locally was diagnostic for HIV infection with a CD4 count of 20 cells/mm^3. In spite of full investigation, and empiric pneumocystis and mycobacterial antibiotics, she had recurring high fevers and malaise. The only localising sign was of hepatomegaly. Liver biopsy was performed and sent for histology and culture. The histology was consistent with a non-specific reaction suggestive of drug reaction. Culture for bacteria and mycobacteria was negative, but extended incubation yielded a filamentous fungus. This was identified as *Histoplasma capsulatum* using 28S rDNA sequencing and review of the fungal morphology after prolongued incubation.

This case demonstrates the importance of sending tissue for culture as well as histology. It also demonstrates the need to be knowledgeable about diseases of travel.

P17
A SINGLECENTRE SIX-MONTH CLINICAL EXPERIENCE OF ATAZANAVIR IN A SPECIAL ACCESS SCHEME (SAS) IN AUSTRALIA

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Clinical trials have demonstrated atazanavir (AZV) to be potent, safe and well tolerated in both naïve and treatment experienced patients. However, little is known about how this drug performs in a clinic setting. This audit was performed to correlate our experience with published reports.

Patients commencing AZV at a designated HIV outpatient clinic from July 2003 to April 2004 were identified on the clinic pharmacy's database. Data were retrospectively collected from patients' medical records.

30 patients received AZV during the period. The reasons for commencing AZV were: virological failure in 6 (20%) of cases, toxicity to previous regimen in 13 (43%), restarting antiretroviral treatment following treatment interruption in 9 (30%) and simplify dosing regimen to once daily in 2 (7%). 6 (20%) discontinued AZV during the observation period. 1 due to virological failure, 2 due to toxicity to concomitant antiretrovirals, 2 patient's choice and 1 physician's decision.18 patients commenced AZV in combination therapy with a detectable viral load (VL). The mean baseline VL was log 3.8 ± 1.1 copies/ml and the mean period of observation was 6.9 ± 3.5 months. During this period 15 (83%) had >1.0 log decrease in VL with 11 (61%) achieving viral suppression to <50 copies/ml. 3 (16%) failures were recorded in this group.12 patients commenced AZV with undetectable VL. One (8%) virological failure was recorded in this group.

Mean bilirubin increased by 22.7µmol/L ($p < 0.001$). Significant decreases in serum cholesterol [1.3 mmol/L, $p=0.016$] and triglyceride [1.3 mmol/L, $p=0.031$] were observed in 12 patients who were switched to ritonavir-boosted AZV from other protease inhibitors and not on lipid lowering drugs.

Mild gastrointestinal disturbance occurred in 50% of patients. Jaundice was reported in only two subjects.

This audit found AZV to be safe, well tolerated and have good potency in treatment-experienced patients. In addition this audit found significant decrease in lipids in this group of patients. However considering there was one failure in the undetectable group and 3 failures in the detectable group, caution should be exercised in switching to AZV in some heavily pre-treated patients.

P18
THE USE OF A TRIPLE NUCLEOSIDE-NUCLEOTIDE REGIMEN FOR NON-OCCUPATIONAL HIV POST EXPOSURE PROPHYLAXIX

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Non-occupational HIV post-exposure prophylaxis (NPEP) is recommended for individuals after high-risk sexual exposure. Furthermore, published surveys reveal more than 75% of physicians would prescribe a triple antiretroviral regimen containing a protease inhibitor (PI). Due to the high incidence of intolerable side effects observed with PI based and zidovudine-based NPEP regimens, our department changed standard NPEP treatment to 28 days of stavudine-lamivudine-tenofovir (d4T-3TC-TDF) in December 2002. The aim of this study was to compare side effects and number of individuals completing NPEP before and after this change.

Parameters were compared between individuals commencing the following NPEP regimens: zidovudine-3TC (Combivir, group 1) and Combivir-nelfinavir (group 2) both between August 1999 and November 2002 and d4T-3TC-TDF (group 3) between December 2002 to November 2003. The clinic protocol for prescribing NPEP and follow up did not change between these time periods. Episodes where individuals received a NPEP regimen on more than one occasion were excluded.

A total of 398 individuals received NPEP in the above time period with 36, 225 and 137 individuals in groups 1, 2 and 3 respectively. There were no differences in age or sex between groups. Non-completion rates for the prescribed regimens were 25%, 32% and 15% respectively for the three regimens ($p<0.001$) with odds ratios for non-completion 2.0 and 2.7 in groups 1 and 2 relative to group 3 ($p=0.008$). Adverse events were generally less common with d4t–3TC–TDF with total event rates in groups 1 and 2 versus group 3 as follows: nausea 53%, 42% and 23% respectively ($p<0.001$), headaches 17%, 12% and 0.7% respectively ($p<0.001$), but not peripheral neuropathy, which was more common in group 3 (0%, 0% and 8% respectively, $p=0.001$). There was no HIV seroconversion in any group.

d4T-3TC-TDF is significantly better tolerated than Combivir or Combivir-nelfinavir as NPEP and results in greater numbers of individuals completing 28 days of treatment.

P19
MANAGEMENT OF THE HIV-PREGNANT PATIENT: USE OF TENOFOVIR

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36 year old pregnant HIV positive female presented for antiretroviral therapy at 5/40. CD4 count 630, viral load 9730 copies/ml. The plan decided on was suppressive therapy from the second trimester. She was commenced Combivir and Nevirapine at 16 weeks. Liver function tests (LFTs) were normal after 2 weeks. She developed a rash; medications were discontinued. After 10 days she became jaundiced with abnormal LFTs. Liver ultrasound was normal. Symptoms settled spontaneously. Recommenced AZT, 3TC and Tenofovir (compassionate release from Gilead) at 28 weeks. LFTs remained normal. Viral load undetectable at 36 weeks. Ruptured membranes at 38 weeks, AZT IV infusion started. The patient had requested elective caesarean section, regardless of viral load. LSCS under spinal after 4+ hours. Baby delivered with membranes intact. Post-op course uncomplicated. The infant was provided with oral Zidovudine for 6 weeks.

Antiretroviral therapy was not initiated on the patient prior to pregnancy, because she was asymptomatic, had a stable and relatively low HIV-1 viral load with normal CD4 counts. We initially followed the US Public Health Service recommendations (2002) for an HIV-infected pregnant woman who had not received prior antiretroviral therapy and who had an HIV RNA of over 1000 copies/ml (regardless of clinical and immunologic status), and provided triple antiretroviral therapy. As the patient was intolerant to Nevirapine, she was switched to Tenofovir for the following reasons: 1) her HIV-1 viral load did not warrant putting her on a protease inhibitor, 2) Tenofovir is an FDA Category B drug- "animal reproduction studies fail to demonstrate a risk to the foetus and adequate and well-controlled studies of pregnant women have not been conducted", and 3) continued triple antiretroviral therapy would prevent the development of resistance, should she require antiretrovirals in the future. Newer studies though show that Tenofovir in a combination with other nucleoside analogues are not effective in producing a sustained viral load response. Tenofovir was well tolerated, and in combination with Combivir, resulted in an undetectable viral load prior to delivery.

Primary Care Posters

P20
INVOLVING GENERAL PRACTITIONERS IN HEPATITIS C CARE & PREVENTION

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General Practitioners (GP's) are pivotal to any program of best practice hepatitis C care. They play a crucial role in detecting and diagnosing the infection and many cases of uncomplicated hepatitis C can be managed entirely in general practice. If referral is required, GP's are best placed to play the central role in the shared - care management of their patients.

The C Clearly program was established to assist people with hepatitis C, and those at risk of infection, to maximise their health and well-being. One of it's principal aims was to support GPs recruited by the program to become and remain involved in a primary care and prevention response to hepatitis C. The program has found that:

- There is considerable ignorance of hepatitis C and misinformation being propagated by many GP's
- There is great variability in the numbers of patients being seen and actively managed by different GP's
- People with HCV infection pose particular challenges for GP's as they are generally a very mobile group with complex issues – clinical, mental health, social, and drug use
- There is poor uptake in the use of Medicare Extended Primary Care (EPC) items as a way of managing and financing hepatitis C care
- GP's see themselves as generalists and there is limited enthusiasm for more extended specialised involvement in HCV management

The C Clearly program has succeeded in engaging over 160 GPs in a series of professional development seminars and through direct Project Officer support in managing program participants. This paper describes issues involved in engaging GP's in this area, outlines some successful strategies, and explores problems identified with establishing an adequately resourced primary health care response to hepatitis C care and prevention.

Nursing And Allied Health Posters

P21
BENEFICIAL EFFECTS OF INTERACTIONS BETWEEN ANTIRETROVIRAL AGENTS

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The therapeutic options for human immunodeficiency virus type 1 (HIV-1) patients have dramatically improved with the availability of highly active antiretroviral therapy (HAART). Protease inhibitors (PIs) are metabolised by the cytochrome P450 enzyme system in the gastrointestinal tract and liver. When PIs are used in combination, significant drug interactions may occur that are useful in practice.

Ritonavir, a protease inhibitor, is increasingly used in low doses in HAART to augment the plasma concentrations of other concomitantly administered protease inhibitors such as atazanavir, saquinavir, lopinavir, and indinavir.

The combination of ritonavir with other PIs offer many advantages such as utilisation of lower doses with longer dosing intervals (eg: daily instead of twice a day), better patient compliance to therapy and higher treatment potency. These concepts have led to the implementation of prescribing guidelines (eg: drug interaction charts) at our institution that will help practitioners to use these drug combinations in their practice.

P22
DELAYED DIAGNOSIS OF HIV/AIDS

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The Holden Street Clinic is situated on the NSW Central Coast. The clinic has a relatively high proportion of clients who were diagnosed HIV positive with an AIDS defining illness. The demographics of this client group are similar to that found in previous studies. Variables associated with delayed diagnosis of HIV were found to be: male gender, heterosexual and age over 44. The Holden St cohort supports these finding.

The majority of clients presented with opportunistic infections and were subsequently found to be profoundly immunosupressed. In addition, testing for HIV had occurred as a 'last ditch' option after multiple investigations failed to determine cause of illness. These clients did not fall into an obvious high risk group therefore HIV infection was not immediately considered.

An HIV diagnosis was associated with multiple psychosocial problems when clients had to come to terms with an unexpected, potentially life threatening outcome and face the daunting task of disclosing their diagnosis to family and friends. HIV incidence in Australia remains, to a great extent, an infection restricted to men who have sex with men, occurring mainly in metropolitan areas. Therefore the potential remains that individuals not falling into a specific category will continue to have delayed diagnosis and associated adverse health outcomes in an era where antiretroviral therapy has significantly reduced the incidence of AIDS.

P23
SEXUAL HEALTH: A RESPONSIVE PARTNERSHIP APPROACH

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Griffith University, in collaboration with Queensland Health, has offered a Graduate Certificate of Sexual Health Nursing since 2001. This program provides sexual health nurses with the theoretical knowledge and clinical competency to achieve Sexual & Reproductive Health Endorsement - Drug Therapy Protocol (DTP) with the Queensland Nursing Council.

Recent evaluation of the program indicated the need to revise content and restructure the program to meet the changing higher education needs of sexual health clinicians, provide a mechanism of training for beginner practitioners entering the speciality field and target a broader multidisciplinary cohort of students.

This paper describes the ways in which the program will provide flexible pathways for clinicians from a broad range of disciplines and a variety of health care settings to advance their expertise in the specialty of sexual health. The challenges of flexible on-line internet delivery mode will be discussed as well as strategies to enhance interactive student learning and provide highest quality sexual health education. Courses aim to promote best practice and research for a diverse range of students both nationally and internationally.

Policy Posters

P24
UGANDAN MINISTRY OF HEALTH POLICY ON INFANT FEEDING AMONG HIV+ PARENTS

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Policy guidelines on feeding of infants and young children in the context of HIV/AIDS were adopted in 2001 by the Ugandan Ministry of Health (MOH). The policy recommended infant feeding counseling (IFC) for all HIV positive (HIV+) parents.

We performed a comparative cross sectional study to assess the effect of IFC on infant feeding choices and practices among parents who had attended the prevention of mother to child HIV transmission (PMTCT) program in Bushenyi district, Uganda, East Africa.

By May 2003, 200 interviews had been conducted: 161 were of women and 39 were of male partners. In total, 61 mothers were HIV+, and 100 were HIV negative. Overall, 103 respondents had ever heard of IFC and 43 (42%) had ever attended an IFC session, of whom 5 were men. Of these, 35 (81.4%) were HIV+ women. Of the 38 mothers who attended an IFC session the majority (23, 61%) chose exclusive breastfeeding (EBF); 11 (29%) chose replacement feeding (RF) and were practicing RF at the time of the interview. This indicates the high adherence of these mothers to their choice of infant feeding option made during the IFC session. Adherence to EBF was lower with 18 (73%) adhering to this mode. Choice of feeding mode differed between HIV+ and HIV negative mothers ($p = 0.02$): 21.7% of the HIV+ women EBF, 21.7% mix fed and 15% complement the infant feeds compared to 15%, 53% and 23% respectively, among the HIV negative women. Overall, 36.7% of the HIV positive women were feeding contrary to Ugandan policy recommendations. As only 57.4% of the HIV positive women had attended an IFC session, this is not surprising.

These results have important infant feeding policy implications for this community: while IFC is crucial in the reduction of perinatal HIV transmission, more than 40% of HIV+ women had not attended an IFC session, and 37% were feeding contrary to policy recommendations.

Public Health And Prevention Posters

P25
THE MANAGEMENT OF PLWHA IN CORRECTIONAL SETTINGS FROM THE PUBLIC HEALTH NURSE/ADAHPT PARTNERSHIP PERSPECTIVE

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In response to referrals which highlight the management difficulties encountered in the correctional setting for PLWHA, ADAHPT, a state-wide tertiary outreach service for people living with HIV/AIDS and complex needs has been working in partnership with Public Health Nurses from Corrections Health Services. The experience of ADAHPT working with HIV positive people identified as potential risks to the health of other inmates and the use of case management was seen as an ideal model for the community management of clients who are currently incarcerated but are facing imminent release from correctional settings into the community.

ADAHPT has been working closely with Public Health Nurses from Corrections Health Services clinics in prisons around NSW. Ideally, referrals are accepted whilst a PLWHA is still in the correctional setting and the plan is to establish a relationship with the client prior to their release, to smooth the transition between prison and independent living in the community. A management plan is devised with the intention to support the client to live independently in the community. This involves assessment, planning, linking, monitoring and review of the client's needs from the time of referral up to and beyond their release from custody.

In the initial assessment process of case management for clients, it has been alleged by inmates that they have placed other inmates at risk of transmission of HIV/AIDS. Such allegations have raised difficult dilemmas for both services in deciding how to best manage the real or perceived risks involved when inmates allegedly place one another at risk.

By the use of a case study, we will describe how the assessment of the client for community follow up and case management revealed such a dilemma. The complexities of this situation and the pressure this has placed upon the partnership will also be described.

P26
NATIONAL HIV EDUCATION – THE AFAO NAPWA EDUCATION TEAM (ANET)

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The AFAO NAPWA Education Team (ANET) is funded to produce national HIV prevention campaigns and health promotion campaigns for people living with HIV.

This poster describes the work of ANET over the last 12 months including:

National campaigns to address rises in new HIV Infections
A booklet for people with a recent HIV diagnosis
A booklet of side effects of HIV treatments
A campaign on HIV Treatments Breaks
A number of discussion papers

Each major campaign will be described and discussed.

A brief discussion of some of the major issues and challenges facing both HIV prevention and health promotion for people with HIV will be included on the poster.

P27
EVALUATION OF INTERAGENCY ACTION PLAN IN RESPONSE TO THE REPORTED INCREASE IN HIV NOTIFICATIONS

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From 2001-2002 there was a reported 15% increase in HIV notifications in NSW. This was predominantly concentrated among gay and homosexually active men in the inner city of Sydney. This represented the largest increase in HIV notifications in NSW since the epidemic was brought under control in the late 1980s. This paper will outline the:

- responses to this increase by an interagency of government and HIV/AIDS community groups, metropolitan Area Health Services and HIV/AIDS research organisations;
- 'Action Plan' of specific short-term HIV health promotion activities carried out from September 2003 to March 2004; and
- range of evaluation measures that were developed to assess the progress and impact of the response.

The Action Plan included a comprehensive range of activities that:

- communicated with gay men about the HIV increase and prevention issues (including; a significant media campaign of target the gay community, telephone information line, prevention activities targeting sex on premise venues, etc.,);
- supported GPs and sexual health services to address HIV prevention; and
- addressed sexually transmitted infections.

The evaluation components to be reported on will include:

- analysis of the impact of the campaign activities;
- process evaluation of the development and implementation of the Action Plan/Interagency;
- evaluation of the Telephone Information Line; and
- assessment of the impact of the broad HIV/STI prevention activities conducted during the period of the Action Plan.

P28
PROVISION OF CARE TO HIV POSITIVE INMATES IN NSW CORRECTIONAL ENVIRONMENT

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There are clinics in 31 correctional centres, 11 periodic detention centres, two transitional centres, 8 police cell complexes, 14 court complexes and nine juvenile detention centres across New South Wales. The fulltime population is currently around 8,500. Twenty seven percent of people stay less than eight days, 17% eight to 30 days, and 56% longer than 30 days with only 10% longer than six months. Recidivism is high at about 69%.

Within the Corrections environment a large number of inmates are either already infected with a blood borne virus, or are at risk of acquiring one. In addition inmates are often in a situation whereby they are exposed to ongoing risk during their incarceration. Education and health promotion are important roles for staff working with these clients, as access to harm minimisation strategies is limited.

While only a small number of inmates are HIV positive, these numbers are steadily increasing. Often inmates have complex health needs related to co-infection with hepatitis C and/or hepatitis B, drug and alcohol and mental health related problems. They can be housed at any of the correctional centres around the state. These clients are managed by a team of experienced Sexual / Public Health Nurses in collaboration with Specialist Medical Services. CHS also works closely with Specialist Health Services and Community Based Organisations both in relation to the provision of care and transfer to the community.

Providing these clients with optimal care presents many challenges. These include potential movement of clients to any Correctional Facility in the state making follow up for specialist services and routine monitoring complex, in addition to presenting challenges related to the maintenance of confidentiality and privacy. Clients who are on antiretroviral therapy present particular challenges in relation to compliance and management of side effects. HIV positive inmates can also feel isolated and marginalised as access to their usual community support networks is limited. The issue of managing harm minimisation strategies within the correctional environment is also challenging when providing health care to HIV positive clients.

This poster will describe the provision of care to HIV positive inmates in a Correctional Environment.

P29
HARM MINIMINSTATION IN AN EVIRONMENT OF ZERO TOLERANCE: THE AUSTRALIAN PRISON EXPERIENCE

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Over 22,000 prisoners reside in Australia's prisons and 40,000 prisoners are released back to the community annually. It is important to examine how the experience of incarceration has impacted on these people given the prevailing policy of zero tolerance within the prison system.

In recent years there has been a significant strengthening of partnerships across Australia of those in the prisoner health sector who actively work towards the introduction of harm minimisation strategies. Resistance to harm reduction initiatives is gradually shifting among custodial services from a policy of zero tolerance to acceptance of a harm minimisation framework.

The prison system is often criticised for its lack of progress in the introduction of harm reduction strategies, however progress is being made and innovative strategies are in place in the different jurisdictions across Australia – only some of the examples to be presented include methadone maintenance programs, henna tattooing and conjugal visits for prisoners. This paper takes a national perspective on these achievements, their implementation milestones, and obstacles.

Importantly the paper also examines how the sometime uneasy partnership between health and custodial services can be strengthened in relation to the introduction of demand and harm reduction strategies.

P31
SAFER SEX-RELATED KNOWLEDGE, RISK PERCEPTIONS AND BEHAVIOURS AMONG YOUNG MENTAL HEALTH CLIENTS WHO HAVE EXPERIENCED A FIRST EPISODE OF PSYCHOSIS

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To describe and cross-sectionally analyze sexual health knowledge, risk behaviour and sexually transmissible infection (STI) screening history among young people who have been diagnosed with a first episode of psychosis, presenting to community based early psychosis programs in south-eastern
Sydney.

A self-report questionnaire was distributed among young mental health clients presenting with a first episode of psychosis to a south-eastern Sydney early psychosis programme. Sixty-two complete surveys were obtained from 110 approaches (56%). Among sexually active respondents, females were much more likely to report >3 partners than males (57% vs. 7%; x^2=13.3; P<0.0001). Comparison with available findings among adolescents without a mental illness suggests that this significant gender disparity is particular to young people who have a mental illness. Eighty two percent of respondents identified as safe sex knowledge confident, however 24% of males and 45% of females expressed concern that they had had unsafe sex in the past 12 months. Knowledge regarding STI transmissibility was fair and knowledge of risk associated with sexual practice was good, excepting anal and oral sex. Most respondents who were concerned about the occurrence of unsafe sex in the past 12 months reported undergoing a STI screen, however of 37 screens reported, only two (5%) were complete for both bacterial and viral sexually transmissible infections.

Young women with a mental illness may be significantly more exposed to STI risk than young men with a mental illness. Confidence in safe sex knowledge may not be predictive of actual safe sex practice. Current STI screening for young people with a mental illness is likely to be sub-optimal.

Community Program Posters

P32
LIVING WELL WITH HIV

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MOSAIC, a program of Relationships Australia (SA), provides an innovative counselling service for people affected by HIV and Hepatitis C. This lively, interactive workshop will provide an overview of how a counselling service underpinned by health promotion principles works with the HIV affected community to develop personal skills and resources, strengthen community action, and build collaborative partnerships as the foundation for a holistic, effective and responsive service for people living with HIV.

The workshop will showcase how best practice in counselling, group work, and the development of collaborative partnerships with HIV community organisations, hospitals, and other relevant services promotes the emotional and mental health and well being of people living with HIV.

P33
LOBBYING FOR LEGISLATIVE EQUALITY IN ORDER TO ESTABLISH AND MAINTAIN AN ENVIRONMENT FOR SUPPORTIVE PUBLIC POLICY IN HIV IN NSW

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Cultural and legislative discrimination against gay men, people who inject drugs and sex workers continue to be constant barriers to the delivery of effective health care interventions and education.

This presentation will draw on a range of lobbying interventions, social marketing campaigns and community mobilisation strategies utilised over the last 20 years in the NSW response to the HIV epidemic. Examples of the successes and failures in the response related to the decriminalisation of sex work, homosexuality and the provision of sterile injecting equipment in order to create a supportive environment to minimise the transmission of HIV will be used.

Legislation which discriminates against gay men, people who inject drugs and sex workers creates an environment where HIV can pose a serious public health threat to marginalised populations and the community at large.

In order for public policy to create an environment where individuals and communities can make the best health decisions and establish collective healthy normative behaviour, all levels of government, non-government advocacy agencies and affected communities need to be committed to an on-going response.

P34
A SENSITIVE, QUANTITATIVE REAL-TIME PCR ASSAY TO DETECT LAMIVUDINE RESISTANCE-ASSOCIATED MUTATIONS IN HEPATITIS B VIRUS (HBV)

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Rapid inexpensive detection of drug-resistant HBV quasispecies would be of benefit in the rational choice of antiviral therapy for HBV. The most common antiviral currently used for treatment of HBV is Lamivudine. Mutations leading to Lamivudine resistance are located within the HBV polymerase at the YMDD motif and are known as the rtM204I and the rtM204V mutation. Currently, detection of drug resistance requires sequencing of the HBV polymerase.

Discrimination between the 3 variants (wild type, rtM204I and rtM204V) was possible using a common forward primer specific for a highly conserved sequence in the coding region of the viral polymerase paired with reverse primers specific for each variant (separately) at the 3' terminal. Real-time PCR and a molecular beacon specific for a highly conserved region between the primer pairs was used to detect amplicons. External plasmid standards constructed with wild type HBV and with either the rtM204I or rtM204V substitutions enabled quantification of each quasispecies.

Using the plasmid standards as template we determined the degree of cross priming between mismatched template-primer sets. Cross priming occurred when the mismatched species was present in excess of 4 logs greater than the complementary quasispecies. This was factored into further analysis. Using mixes of known ratios of wild type to mutant template we confirmed the accuracy of the assay. Input and calculated copy numbers for each variant were identical, with the assay able to detect minority quasispecies at 1 in 1, 000.

Real time PCR was performed on sera from 24 individuals never treated with Lamivudine. Only wild type virus was detected by both real time PCR and sequence analysis. A further 59 plasma samples obtained from 21 HBV-infected individuals taking lamivudine were analysed by real time PCR, sequencing and line probe (LiPA) analysis. This collection of sera included sequential samples for 15 individuals and infection with wild-type, rtM204V and rtM204I mutations. A high degree of correlation between the techniques was observed, with the added advantage of quantification of each quasispecies with real-time PCR.

Discriminatory real-time PCR is a simple and rapid technique that can reliably detect and quantify Lamivudine-resistant HBV.

P35
MAKING, KEEPING AND BREAKING AGREEMENTS WITH REGULAR PARTNERS AMONG GAY MEN: THE HEALTH IN MEN STUDY

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This paper will report on negotiated agreements among HIV-negative gay men in Sydney.

Data from the Health in Men longitudinal study of HIV-negative men participating in Sydney's gay community will be used. 1333 men were interviewed between 2001 and 2003.

903 men had a primary regular partner during the six month period before their baseline interview. Most of these men had negotiated agreements with their partners about their sex with each other (76.0%) and with other partners (69.7%). They most commonly agreed not to use condoms with each other (39.0%); For sex with other partners they mainly agreed to always use condoms (33.3%) or to not have sex with other men at all (24.7%) – only 0.3% permitted unprotected anal intercourse (UAI) with other men. 73.9% found it easy to discuss sex with their partner; and 65.6% were confident their partner would tell them if he broke their agreement. However, 31.9% were less comfortable discussing with their partner their sex with other men. 21.8% of those with agreements with their partners reported ever breaking them. Those who found it more difficult to discuss their sex with other men were more likely to break their agreements ($p<.001$), and to have engaged in UAI with casual partners in the previous six months ($p<.01$). A quarter of the men who broke their agreements did not inform their partner. Otherwise, those who broke their agreements most commonly either returned to using condoms with their partner (27.1%), or re-negotiated their agreements (27.3%).

While most gay men are able to negotiate agreements with their partners about the kinds of sex they have inside and outside their relationship, a minority of men find this less easy, particularly when it comes to discussing sex with other men. Some men may have reported difficulty discussing these issues because they had broken their agreements. Nonetheless, difficulty discussing these issues with their partners may place some men at increased risk of breaking their agreements and may place both themselves and their partners at increased risk of infection.

P36
HOUSING PEOPLE LIVING WITH HIV: SUSTAINING TENANCIES IN COMMUNITY HOUSING AND LINKING PEOPLE WITH MULTIPLE SUPPORT SERVICES

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Secure tenancies and good health are closely linked, particularly for people living with HIV. The experience of the Bobby Goldsmith Foundation in provision of accommodation support aimed at achieving and maintaining tenancies for people living with HIV and multiple other needs is described, the challenge of maintaining networks of support to meet these multiple needs are discussed, and the critical success factors in assisting people to achieve and sustain tenancies in community housing, more congregate settings, and in emerging models of housing provision are outlined. Partnerships with other services and how they are developed, formalised and maintained are also described.

P37
DECA DURABOLIN: ESTABLISHING EQUITABLE ACCESS FOR TREATING HIV COMPLICATIONS

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HIV wasting occurs in 40–50% of the HIV population. While metabolic wasting usually occurs in advanced disease, wasting associated with quality of life issues can occur at any stage of HIV infection where people may have difficulty maintaining adequate nutritional intake. Reduced quality of life indicators can be associated with multiple factors such as reduced libido, depression, self-esteem and body image issues. Antiviral agents can assist in slowing or preventing HIV wasting in some people, but weight gains are often only fat and not muscle. In the era of HAART, muscle wasting continues to take place in 48% of people taking antiviral medication which is often masked by fat gains. Osteopenia and osteoporosis have been identified in people with HIV.

Deca Durabolin (nandrolone decanoate) has been shown to be a safe and effective treatment for all of the above complications. Prescribing of Deca Durabolin depends on the personal beliefs of treating physicians, leading to inequitable access to what could be considered to be an essential treatment for people with HIV. Some physicians believe that HIV wasting is a straight forward classification of weight loss > 10% from normal body weight which might be considered to be an outdated definition. This paper discusses possible new definitions for HIV wasting, along with potential uses of Deca Durabolin including results from a small ad hoc survey of doctors in Melbourne. Guidelines have been drafted in an effort to encourage a national standard of care for equitable access to Deca Durabolin for HIV positive Australians.

P38
CHANGING LIVES, GIVING HOPE

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The rapidly rising AIDS cases need to be addressed through innovative, cost effective interventions based at home and the community. The overburdened healthcare system is incapable of providing even basic care and support that ensure better quality of life for PWHA's.

Project Concern International, implements CDC, Atlanta /GAP, India funded home and community based care project for PWHAs viz. "Pathway – Positive Action for the health of People living with HIV/AIDS' in two Indian states; in Pune, Maharashtra with local NGO partners Sevadham Trust and NMP. In 2003, a second intervention site in Salem, Tamilnadu. The goal: 'to improve the quality of life of PWHA's and their families'; main objectives are (1) increase access to healthcare, psycho-social, economic support, prevention services (2) increase community support for PWHAs (3) increase capacity of partners and community groups to provide HBC services.

The services provided includes: VCTC, psycho-social counseling, palliative, prophylactic, curative treatment of OI's, TB/HIV treatment, self & family care, medical & nursing care, mobile clinics, home visits, DIC, community centers, nutritional supplementation, livelihood enhancement through micro-credit enterprises, mental health services, community sensitization & outreach, capacity building, trainings, referrals and networking. ARV therapy for selected clients through Government of India ARV program.

The outcome thus far are: **830** PWHAs identified, **4599** counseling sessions, **1532** HIV testing, **9417** visits by PWHA, **15119** general clients visit to mobile clinical services, **15943** home visits, **694** referrals, **274** PWHA's provided nutritional support, **1237** community programs, **85** micro enterprises development loans disbursed, **15** PWHA support group formed, **117** training workshops.

The lessons learnt: * Early diagnosis leads to better quality of life* Care and support to PWHA's at home improves mental well being* Community involvement reduces stigma and discrimination *Incorporating GIPA across the board leads to better programming* Integration of HIV and TB reduce the burden of disease * Nutritional supplementation foster greater PWHA's acceptances to services* Economic empowerment of PWHA's is key to revival of hope, family bonding, dignity* Good quality healthcare can be delivered by family members of PWHA's* Responding health needs of PWHA's at their doorsteps increases compliance* Care propels prevention.

Education Posters

P40
THE NAPWA INTERNATIONAL PORTFOLIO

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The National Association of People Living with HIV/AIDS (NAPWA) has been operating an International Portfolio since the early 1990s. Over the past five years, this activity has steadily increased, and the South-East Asian region has become more of a focus for the work of the networks.

NAPWA is the recognised Australian representative body for the Asian Pacific Network of Positive People (APN+), and has had representatives involved in this network for more than a decade. More recently, NAPWA has engaged with networks of positive people in the Pacific, to encourage "twinning" and similar support to those groups or organisations seeking such collaborations or alliances.

The work of the International Portfolio includes support for regional PLWHA groups by providing technical assistance, capacity building, skills development, study tours, mentoring, twinning, and specific resource development projects.

Specific resources have included production of organisational development manuals, guidelines for writing proposals, train-the-trainer workshops, and training modules to accompany the use of publications and written resources. Several projects have sought NAPWA's consultation for needs analysis, program design and the implementation of these programs.

Relationships currently established include APN+ and the Global network of Positive People (GPN+), Australian Red Cross, United Nations Development Program (UNDP), ASHM, and the Australian Foundation for Peoples of Asia and the Pacific (AFAP), Body Positive New Zealand, Pacific Islanders AIDS Foundation (PIAF), I GAT Hope network (PNG), and the beginning of contacts in East Timor.

This presentation will also discuss the broader policy objectives of the work of the NAPWA International Portfolio networks, and the underlying principles of HIV positive peer facilitation within community development for HIV positive people in the region.

P41
HIV & WELLNESS: A QUEENSLAND RESPONSE

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In June 2004 a workshop examining the management of complex cases in HIV in the era of HIV as a chronic disease was conducted in Brisbane, Queensland. The Workshop was titled: 'HIV & Wellness Workshop II: Examining Complex Cases'. The aim of the workshop was to increase knowledge, skills and confidence levels for the management of complex cases utilising a chronic condition self-management approach to healthcare.

The course was advertised through networks of sexual health and related organisations. This included 'invitations to attend' provided to all current HIV prescribers in Queensland and mail outs to hospitals, nursing organisations, divisions of general practice and HIV/sexual health service providers. The seminar was attended by over 40 health care workers.

The workshop centred on discussion of a complex case and provided summary presentations on topics relevant to that case. These included psychological issues with difficult clients; management tips for recreational drug use; pharmacology of HIV antiretrovirals and recreational drugs; neurocognitive effects of HIV; and an examination of evidence based management principles.

This poster will examine the responses to the evaluation question: What will I do differently in my clinical practice, as a result of attending this workshop?

Epidemiology Posters

P42
CHANGING FACE OF PAEDIATRIC HIV INFECTION: RETROSPECTIVE 20 YEAR REVIEW FROM A MAJOR AUSTRALIAN PAEDIATRIC HIV UNIT (1983-2003)

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The Paediatric HIV Service at Sydney Children's Hospital, Randwick has managed affected children and families since the beginning of the HIV epidemic. This retrospective review describes the changing epidemiology of paediatric HIV in a major paediatric HIV centre in Australia. The aims of the review were to document the mode(s) of paediatric HIV infection before and after the introduction of blood screening in NSW (1985), to document changes in mother-to-child transmission (MTCT) rates with the introduction of prevention strategies available since 1994, to document the clinical course of HIV infected children before and after the introduction of HAART (highly active anti-retroviral therapy,) and finally to document the current clinical status of perinatally exposed non-HIV infected and HIV infected children.

120 charts of HIV exposed or infected children were reviewed. Of the 42 infected children, 21% were from sources other than perinatal transmission. The vast majority of these were infected before 1985. Of those perinatally infected, the majority (70%) were born before intervention strategies were available. For HIV infected children managed pre HAART, growth was slower and mortality higher, compared to children managed in the post HAART era.

The review demonstrates that since the introduction of blood product screening in Australia in 1985, MTCT now represents the major mode of HIV infection in children. Preventative intervention strategies introduced in 1994 have dramatically decreased MTCT. The rate of perinatally infected children thus correlates with maternal knowledge of diagnosis prior to delivery and argues in favour of a universal antenatal HIV screening strategy. For infected children, the introduction of HAART has improved the quality of life and slowed clinical progression of disease.

P43
SEX IN THE CITY – CHAPTER TWO

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We have previously reported on a cluster of heterosexually acquired HIV infection in Sydney and now continue the story. In early January 1999 an 18-year old female presented to ASC following an HIV diagnosis by a General Practitioner. Two male partners, both from Pattern II countries and both having several of the female partners in common, were contact traced. One of the men was diagnosed as having HIV infection. Following that diagnosis, five women were contacted, and an additional two women were subsequently diagnosed as having HIV infection. The identified HIV infected male partner subsequently received care, including extensive counselling regarding his responsibility to future sexual partners, and also anti-retroviral therapy, until mid 2001 and was then lost to follow-up.

In early 2003 a female tourist was identified as having HIV infection and indicated the source of the infection as the original male contact. Coincidentally, and somewhat serendipitously, another female tourist was identified as being infected from the same source and ten male partners of this woman were also contact traced. At this time, four additional female partners of the index male were contacted in the context of a police investigation, and one was identified as having HIV infection.

In summary we report the heterosexual transmission of HIV to six women in Sydney, over a five year period. A number of significant issues were highlighted as a result of the investigation of this cluster of women, which impact on patients and services. These issues will be fully discussed and include: determinants of patient infectivity; heterosexual transmission identification in a low prevalence setting; clinician public health responsibilities; patient republic health responsibility and factors determining compliance; clinical service policies and procedures; confidentiality issues; and contract tracing in the context of HIV.

P44
PRESENTATION AND OUTCOME OF ANAL CARCINOMA AMONG HIV INFECTED AND HIV NON-INFECTED INDIVIDUALS

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Anal cancer is generally a rare malignancy. However, it is the 4th most common malignancy among the HIV infected, with a relative risk of 34 compared to the general population. Furthermore, anecdotal, and some epidemiological data, suggest that the incidence is increasing.

Little is known of the clinical behaviour of anal cancer, and its interaction with HIV in Australia. We therefore sought to investigate the characteristics of people presenting with anal cancer in Sydney.

A retrospective case note review was performed of patients presenting between January 1994 and January 2004 to St Vincent's Hospital in Sydney with a histological diagnosis anal squamous cell cancer. Cases were identified from the pathology database of the hospital.

Of the 82 cases of anal cancers identified, the proportion known to be associated with HIV infection rose from 16% (1 of 6) in 1994 to 68% (5 of 7) in 2003. Compared to the uninfected, those with HIV infection presented at an earlier age, were more likely to have poorly differentiated histology, had more frequent recurrences and had a higher rate of treatment-related complications.

Current management strategies for anal cancer have been developed for the HIV negative community. Our data suggest that the evolving HIV epidemic may significantly change the frequency and modes of presentation of people with anal cancer. Furthermore, treatment regimes may need to be modified in view of the higher rates of recurrence. Further research is required to confirm these findings, and to evaluate the possible role of preventative screening programs.

P45
ANAL SQUAMOUS INTRAEPITHELIAL LESIONS – DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

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Anal Squamous Intraepithelial Lesions (ASIL's), are the suspected precursors of invasive anal carcinoma. Although anal carcinoma is a rare malignancy, anecdotal and epidemiological evidence suggests that its incidence is increasing, particularly among HIV infected homosexual/bisexual men. It is now the fourth common malignancy among the HIV infected. Using the analogy of CIN (Cervical Intraepithelial Neoplasia), it has been suggested that early diagnosis and treatment of ASIL may reduce the incidence of anal cancer.

Little is known about the epidemiology and clinical characteristics of ASIL. We therefore sought to investigate the characteristics of people presenting with ASIL's. A retrospective analysis of medical files of 90 patients who had a histological diagnosis of ASIL was carried out. The demographic details, HIV status and CD4 counts, presenting symptoms, initial and histology diagnoses were recorded.

The study population consisted mainly of young HIV positive, homosexual/bisexual males. Only 37% were clinically diagnosed as likely to have ASIL prior to biopsy with a wide range of differential diagnoses initially being considered. In particular, anal warts were difficult to differentiate from ASIL by macroscopic appearance alone.

These results indicate that ASIL's are often asymptomatic and are coincidentally found at biopsy. ASIL is therefore significantly under diagnosed. It is often diagnosed coincidentally at biopsy. The progression and regression rates of ASIL are currently poorly defined, and the clinical significance is unclear. However, our study suggests that a high index of suspicion should be maintained, especially in high risk patients, particularly those with anal warts.

P46
INCIDENCE AND RISK FACTORS FOR HIV SEROCONVERSION IN THE HEALTH IN MEN (HIM) COHORT

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[2]National Centre in HIV Social Research, UNSW, NSW, Australia

One of the primary reasons for setting up the HIM cohort was to estimate HIV incidence and to determine risk factors for HIV seroconversion. In this presentation, we present the first data on HIV incidence and risk factors from the cohort.

HIM is an open cohort study of HIV-negative gay men in Sydney. All participants undergo annual HIV testing and face-to-face interview regarding their sexual behaviour, sexual health, recreational drug use as well as demographics and gay community involvement. Hazard ratios (HR) were calculated using Cox regression.

By the end of 2003, 1,333 men had been recruited and 798 had completed at least one follow-up interview. Seven men were excluded at baseline because they tested HIV positive at their first interview. There were ten confirmed HIV seroconversions, and the incidence rate was 0.9 per 100 person years. The mean age at seroconversion was 38, ranging from 28 to 57. Despite limited power at this stage of the study, a number of factors were related to HIV seroconversion. Partners of HIV positive men were non-significantly more likely to seroconvert (HR 3.32, 95% CI 0.64-17.18). Seroconverters were significantly more likely to report more lifetime sex partners. Recent use of a variety of recreational drugs was related to HIV seroconversion. These included injecting drug use (HR1.80, 95% CI 1.02-3.18) and using viagra (HR 4.97, 95% CI 1.40-17.63). Those injecting drug users who seroconverted did not report needle sharing. Certain esoteric sexual practices such as using sex toys and sado-masochistic practices were also predictive of HIV seroconversion. A positive screening test for anal gonorrhoea was strongly associated with HIV seroconversion (HR 22.09, 95% CI 2.46-198.58), as was a self-reported history of pharyngeal gonorrhoea (HR 4.03, 95% CI 1.04-15.61).

HIV incidence in gay men in Sydney is around 1%, a lower rate than in the previously conducted SMASH study. Early analyses of risk factors in this cohort, based on only 10 seroconversions, point to a variety of risk behaviours involving esoteric sexual practices which are not in themselves high risk for HIV, heavier usage of recreational drugs, and the presence of sexually transmissible diseases.

P47
LONG TERM NON PROGRESSION IN SURVIVING SYDNEY BLOOD BANK COHORT RECIPIENTS AFTER > 20 YEARS OF INFECTION WITH A MUTANT *NEF* HIV-1 STRAIN

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The Sydney Blood Bank Cohort (SBBC) consisted of eight members; seven recipients with transfusion transmitted HIV infection, (TTH) and a common donor. All members of the SBBC were infected with a mutant *nef* HIV-1 strain. Four recipients are deceased after many years of infection from causes unrelated to HIV; none had progressed to symptomatic HIV disease before death.

The three remaining recipients C49, C64, and C135 have been infected >20 years, are therapy naïve with no signs of disease progression. C135 and C64 have CD4:CD8 ratios of 1:1, and C49 has a normal CD4:8 ratio. All have HIV-1 RNA consistently below detectable limits (<50 copies). C135 has host factors that favour slow progression; HLA B57, and is heterozygous for the CCR5Δ32 deletion. All recipients today have detectable HIV-specific CD4 and CD8 T cell responses, which have been associated with immunological control of viral replication.

The CD4:CD8 ratios for C49, C64 and C135 are in contrast to normal HIV-1 infection, where CD4:8 ratios are typically inverted, caused by elevated CD8 T cells consistent with an ongoing CTL response to replicating virus.

After 20 years of infection with HIV, LTNPs are extremely rare. From the137 people with TTH identified by the ARCBS, only five are true LTNPs, of which three are members of the SBBC. These three LTNPs, who share a mutant *nef* HIV-1 strain, are scientifically valuable individuals that are the subject of ongoing monitoring and study.

P48

FREQUENCY OF HLA TYPES IN THE AUSTRALIAN LONG TERM NON-PROGRESSOR COHORT

Middleton M[1], Merlin K[2], Guerin J[3], Kelleher A[1, 2], Cooper D[1], Kaldor J[1] on behalf of the LTNP Study Group
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The Australian Long Term Non-progressor (LTNP) cohort was established in 1994. Recruitment into the long-term non-progressor (LTNP) cohort is based on documented evidence of HIV-1 infection for at least 8 years with a CD4 count ≥500cells/μL and without any clinical evidence of HIV-related disease. The cohort has been followed to identify host genetic, immunological and virological factors associated with asymptomatic HIV infection and their influence on disease progression in LTNP individuals.

There are currently 102 individuals enrolled in the cohort with a median duration of infection of 16.1 years (range 8.6-19.4). Eighty-seven of these individual have had their HLA class 1 allelles typed. Further analysis was undertaken of 52 LTNPs with more than 5 years follow up to determine the relationship between HLA type and sustained long term non-progression and sustained viral control. Sustained non-progressors were defined by a CD4 T-cell count ≥350cells/μL for the duration of follow up and remaining treatment naïve and all other individuals were defined as progressors. Sustained viral control was defined as the maintenance of a viral load ≤28,000copies/μL and remaining treatment naive. Seventeen individuals were defined as sustained non-progressors and 19 individuals showed evidence of sustained viral control. There were 43 different types of HLA class I alleles found with in the cohort. The types that occurred mostly frequently in the cohort were A1 (17), A2 (25), A3 (19), B8 (10), B27 (14) and B44 (17). In univariate analysis, a significant association was found between the possession of a HLA class I A32 allele and sustained long term non-progression. Three percent of progressors had the A32 allele compared to 35% of non-progressors (P<0.003). No association was found between viral control and HLA type. There was also no relationship between the diversity of alleles found in an individual and sustained non-progression or viral control.

The association that was found between possession of a HLA A32 allele and sustained non-progression suggests that it may protect against HIV disease progression.

P49

LONG-TERM TRENDS IN CD4 COUNT CHANGES IN PEOPLE RECEIVING ANTIRETROVIRAL TREATMENT FOR MORE THAN THREE YEARS

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To investigate the long-term CD4 cell response in patients receiving HAART in the presence or absence of sustained virological response.

Analyses were based on patients who were recruited to AHOD up to September 2003, commenced HAART after 1 January 1997, and had at least 3 years of follow-up. Patients were required to have a baseline CD4 cell count at time of initiation of HAART and a series of follow-up CD4 cell measurements. Mean change in CD4 cell count was determined for every six-month period following HAART up to 5 years. Sustained virological response over time was defined in terms of the time-weighted area under the curve log viral load from one year after HAART initiation to last follow-up, stratified according to the following: <2.7 logs, 2.7 -< 3 logs; 3-<4 logs; and >4 logs. Trends in CD4 counts over time were examined overall and according to baseline CD4 count at HAART initiation.

By September 2003, 2311 patients had been recruited to the Australian HIV Observational Database (AHOD). Of these, 631 patients met the inclusion criteria as defined above. Mean baseline CD4 cell count was 371 cells/μl. Forty-three percent of patients had a viral load persistently below 2.7 logs copies, while 12% of patients had sustained viral load above 4 logs copies. Mean CD4 count increases at 3, 4 and 5 years in each strata were: <2.7 logs, 306, 334 and 383 cells/μl; 2.7- <3.0 logs, 260, 275 and 286 cells/μl; 3 - <4 logs, 179, 148 and 119 cells/μl; and 4+ logs, 23, -94 and - 65 cells/μl. Among patients whose viral load was continually below detection (<2.7 log copies), mean CD4 continued to increase over 5 years of follow-up, for all baseline CD4 strata.

Patients with sustained viral load below 4 log copies for extended periods of time displayed ongoing recovery of CD4 cells.

P50

ASSESSING REGIONAL DIFFERENCES IN TREATMENT UPTAKE AND HIV DISEASE PROGRESSION IN THE AUSTRALIAN HIV OBSERVATIONAL DATABASE

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The Australian HIV Observational Database (AHOD) recruits patients from both high and low caseload sites to ensure broad representation of the HIV-infected population within Australia. We aim to assess whether there is any evidence of differences in treatment uptake or access to treatment between people seen at metropolitan clinics compared to those seen at non-metropolitan clinics in AHOD.

Analysis included all patients recruited to AHOD to the end of September 2003. Metropolitan and non-metropolitan region was determined by post-code of treatment clinic. Patients were categorised into metropolitan or non-metropolitan region based on the clinic they were recruited through. Comparisons were made of baseline patient characteristics, HIV disease stage and uptake of antiretroviral treatment.

By September 2003, 2311 patients had been recruited to AHOD from 28 sites. Of these, 648 (28%) patients were recruited from non-metropolitan clinics. Patient demographics at baseline between metropolitan and non-metropolitan sites were comparable. HIV disease stage at the time of entry into the cohort was broadly similar between the regional groups. However, a slightly greater proportion of patients from non-metropolitan sites had lower CD4 cell counts (<200 cells/μl) (17% vs 14%), and higher baseline viral loads (>10,000 copies/ml), at time of entry into the cohort (30% vs 24%).

After 1 January 1997, 50% of patients from metropolitan sites commenced HAART (3+ antiretovirals), compared to 54% of patients from non-metropolitan sites. Patients from non-metropolitan sites were more likely to begin HAART therapy which included NRTIs and a PI (51% vs 46%), while patients from metropolitan sites were more likely to commence HAART therapy which included an NRTIs and an NNRTI without a PI (52% vs 45%).

Between July 2002 and July 2003, 69% of patients from metropolitan and non-metropolitan regions were receiving antiretrovirals, of which approximately 90% of both groups were receiving triple plus therapy. During this period both metropolitan and non-metropolitan patients received treatment regimens including a NRTI backbone with a PI, and excluding a NNRTI (40% each) or alternatively an NRTI backbone including a NNRTI, and excluding a PI (40% and 39% respectively).

There do not appear to be differences between patients recruited at metropolitan compared to non-metropolitan sites, in both uptake of antiretroviral therapy of indeed HIV disease stage. Further analyses assessing treatment responses and patient outcomes are ongoing.

P51

PREVALENCE AND RISK FACTORS FOR HIV INFECTION AMONG MEN WHO HAVE SEX WITH MEN IN BANGKOK

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HIV prevalence and associated risk behaviors among men who have sex with men (MSM) in Thailand are unknown. This information is crucial to inform and implement targeted preventive interventions for this population.

A cross-sectional assessment, using venue-day-time sampling, was conducted at parks, bathhouses and entertainment venues. Participants were 1,121 Thai men who were 18 years or older, residents of Bangkok, and who reported oral or anal sex with a man during the past 6 months. Oral fluid specimens were tested for HIV antibody. Demographic and behavioral data were collected using an interviewer-administered PalmTM based automated questionnaire.

HIV prevalence was 17.3% (194/1,121). Mean age was 26.9 years (median 25 years), and university education was completed by 42.5%. Sex with men and women during the past 6 months was reported by 22.3%; sex with a woman ever, 36%; and unprotected intercourse (anal, vaginal or both) during the past 3 months, 44.1%. Alcohol use during the past 3 months was common (73.7%); other drug use was rare (2.5%). Multivariate logistic regression analyses showed lower education, recruitment from a park, self-identification as homosexual, practicing both receptive and insertive anal intercourse, increasing years elapsed since first anal intercourse, and increasing numbers of male sex partners to be significantly and independently associated with HIV prevalence.

HIV infection is common in Bangkok MSM. HIV prevention programs are urgently needed to prevent further spread of HIV in this young and sexually active population. Development of user-friendly HIV voluntary counseling and testing, and access to care services are warranted.

P52
DATA SAFETY MONITORING BOARDS IN NCHECR CLINICAL TRIALS

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To ensure patient safety, virtually all clinical trials have regular monitoring of safety data. Many clinical trials also have interim inspection of efficacy data, so that if there is early evidence of overwhelming treatment superiority (either efficacy or safety), continued treatment of patients with the inferior treatment is minimised. These decisions regarding continued trial conduct are increasingly being made by independent Data Safety Monitoring Boards (DSMBs). In this paper we will discuss how DSMBs have been implemented in NCHECR clinical trials, and also the merits of DSMBs in some circumstances.

In NCHECR clinical trials, DSMB members are chosen so that they are independent of both the trial, and also from NCHECR. Members are chosen from a range of disciplines, as dictated by the trial, including HIV clinicians, clinicians fom other specialities, behavioural researchers, biostatisticians, and representatives of the affected community. Of the DSMB members, one is elected as chair, and given the responsibility of chairing meetings. To avoid any possibility of external pressures, membership of NCHECR DSMBs have been kept confidential from the trial clinicians and patients. Although timing of DSMB meetings will have been specified in the protocol, detailed terms of references, including data summaries to be reviewed, formal efficacy stopping rules and format of meetings, are discussed and agreed with the DSMB.

Data summaries for DSMB meetings are generated by the trial statistician, usually in a semi-blinded format, and are kept strictly confidential from all NCHECR and external personnel involved in the conduct of the trial other than the statistician. DSMB meetings have been attended by the trial statistician in an *ex officio* capacity, with clinical project leaders available for questionning if points of clarification arise. Recommendations of the DSMB are made in writing to the trial Principal Investigators.

Although there is a clear role for DSMBs in long-term clinical trials, their role in short term investigator lead studies, and particularly safety studies, is less clear. The work involved in organising and running DSMB meetings, both for NCHECR and the DSMB members themselves, can be quite substantial, and frequency and timing of meetings needs careful consideration.

SOCIAL RESEARCH POSTERS

P53
ROLE OF LEGAL LAW AS STRATEGY TO IMPROVE THE QUALITY ACCESS TO HEALTH CARE FOR PLHA'S IN PAKISTAN

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The research has been made to many Government Hospitals and private ones that PLHA's are provided a poor health care especially when a person exposes his status of being positive. The stigma and discrimination is highly encountered against health carers. Gaps in information and available medical treatment do exist and protect the human Rights of PLHA's and health care workers in Pakistan

There is a need to adopt and advocacy milestone for PLHA's. The legal and ethical protocols to form and integral component of the strategy to improve access to health care for PLHA's in Pakistan

These are the examples on how they are discriminated:

- Doctors test patients HIV without their consent
- Doctors and nurses breach confidentiality after the HIV testing (etc)

I would believe that people with AIDS need a really good support system. Be it from friends and family or counselors to help them to deal with this dreaded disease. They need medication to help slow down the disease's progress. They need people to be educated about this disease as well as people living with AIDS need to be educated as to what they are about to go through with battling this disease. I think that people with AIDS have the right to have affordable medication for them, the right to live their lives as they choose fit instead of being discriminated against.

P54
GENDER, A RISK FACTOR FOR HIV/AIDS INFECTION: PAKISTAN SITUATION

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Pakistan is a low prevalence (1,913 cases till March 2002) but high-risk country as regards HIV/AIDS. Most cases reported were between 20-44 years, with male: female of 7, two-thirds got infected through heterosexual transmission.

Global trend for sex distribution has dramatically changed over time; earlier predominance among men has now shifted. In 2001, 47% of all new infections were in women (in younger age than men). Although 75% of infections are transmitted through hetero-sexual routes, these trends suggest that HIV-positive young women may outnumber their male peers by almost six times.

Pakistan with similar vulnerabilities and pattern of risky behavior has a totally opposite sex ratio among HIV positives; this signaled the need to review and appraise the gender perspectives of this group.

Review focused on three core areas of Provincial AIDS Control Program's work in HIV prevention: prevention among young people, women especially pregnant women and, comprehensive condom programming. Out of 1970 women tested, 2% were found infected, all through sexual transmission. Among total identified, 60% were married Pakistani. Further analysis through in-depth interviews as well as details of programmatic intervention suggest, gender norms as risk factors. It also provides a strong basis for building gender-responsive HIV/AIDS programs.

P55
THERAPEUTIC USE OF MARIJUANA IN THE POSITIVE HEALTH COHORT

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This paper examines factors associated with the therapeutic use of marijuana in the *Positive Health* longitudinal cohort study of PLWHA from NSW and VIC. This paper focuses on a subgroup of participants (n=408) who completed interviews between February 2002 and August 2003.

Participants were asked their opinion on the effectiveness of medicinal marijuana, whether they used marijuana therapeutically, followed by questions regarding recreational use of marijuana. Participants were separated into two groups based on whether they reported "no use" (including recreational-only use) or "some use" of marijuana for therapeutic purposes.

Multivariate logistic regression analyses were used to determine which variables significantly contribute towards the use of marijuana for therapeutic purposes.

Most participants thought that marijuana was highly or moderately effective for reducing stress (74.8%), weight gain (59.8%), pain reduction (59.1%) and quelling nausea (53.2%).

Of all respondents, 26.5% reported using marijuana for therapeutic purposes. Of those who report some therapeutic use (n=108), 89.8% report that they also use marijuana for recreational purposes. Of those who report no therapeutic use of marijuana (n=300), 45.3% report using marijuana recreationally. At a bivariate level, therapeutic users of marijuana appeared to be sicker, more depressed and reported more problems with appetite and mood than those who did not report using marijuana therapeutically. At a multivariate level, logistic regression analyses showed that therapeutic use of marijuana was significantly associated with a lower income, more reported symptoms, greater use of other alternative therapies, not being on anti-retroviral therapy, and a larger number of friends who are also HIV-positive. Length of diagnosis was not significant.

These results suggest that therapeutic use of marijuana in PLWHA is not simply related experiencing symptoms such as nausea or sleep disruption. Marijuana, when used as therapy, appears to be associated with a range of factors including the social context of some PLWHA, illness or feeling unwell, as well as attitudes towards alternative and complementary therapies and modern ART.

P56
THE CONSORTIUM: BUILDING HIV AND HEPATITIS C RESEARCH CAPACITIES

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In Australia social research is a very delicate balancing act, requiring input from a diverse range of stakeholders. Two of the main stakeholders are the academics and the health sector groups that have to implement the policy outcomes from the research. Some of the key challenges facing social researchers are to ensure that the academics are doing the type of research that will be practical when implemented in the community; that health sector groups have the skills to help formulate good research questions; that they are able to contribute to the research; and that they have the analytical skills necessary to take the important messages out of the research into the community.

This paper will discuss the ways the Consortium aims to address these issues. It will focus on a number of initiatives that have been set up to assist both academics to understand what research is needed and give workers the skills to understand and participate in social research.

The initiatives include:

- Workshops where academics and community workers come together to discuss innovative research topics, techniques and trends, and to facilitate new research partnerships between academics and HIV/hepatitis C workers.
- Masters of Arts (MA) by Research which is run by the National Centre in HIV Social Research (NCHSR) and is designed to bring people with an HIV/hepC sector background in the sector into a research environment. Scholarships associated with the MA by Research are offered on a part time basis to attract students that are working fulltime in the sector already.
- An Internship program to allow HIV/hepC workers an opportunity to work closely with academics to improve their understanding of research.
- A Clearinghouse which will be a comprehensive research tool for people in the sector.

P57
'WE JUST DON'T KNOW': MANAGING MEDICAL UNCERTAINTY IN AUSTRALIAN HIV TREATMENTS MEDIA

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This paper explores how uncertainty about changes in HIV medical 'best practice' has been managed in Australian treatments journalism since the inception of antiretroviral therapy (ART) in 1996. This research forms part of the Treatment Histories Project which investigates HIV media, treatments campaigns and qualitative interviews from different time periods since the inception of ART. The focus of this paper is five Australian HIV media publications: Talkabout, Positive Living and HIV Australia, which continue to be published, and the National AIDS Bulletin and HIV Herald, which have been succeeded by HIV Australia. The field of HIV medicine has become increasingly complex since ART was first made available, with many different treatment strategies advocated and contested by clinicians, community organisations and people living with HIV/AIDS (PLWHA). Treatments media have reported and evaluated these many changes over time, assembling reviews of international research to assist PLWHA in making informed treatment decisions. Central to this translation of science into journalism is the use of discursive tools such as metaphor, and so this environment of constant change is typified by evocative images of HIV medicine as a fashion victim, rollercoaster ride, obstacle course or guessing game. An analysis of these kinds of journalistic strategies provides a unique insight into how the discourses of medicine, education, public health and community activism have intersected and changed over time, producing different treatment histories which significantly impact the contemporary field of HIV medicine.

P58
DETERMINANTS OF ENROLLMENT: WHY PEOPLE ENQUIRED, BUT CHOSE NOT TO PARTICIPATE IN AN AUSTRALIAN PROPHYLACTIC HIV VACCINE CLINICAL TRIAL

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A phase I/IIa clinical trial of an Australian-designed DNA-fowlpox prime-boost HIV vaccine strategy is underway in Sydney, Australia. The target recruitment of this randomized, placebo-controlled, double-blind study was 24 healthy HIV-negative adult volunteers at low risk of HIV infection. Recruitment commenced with a national media campaign in parallel with targeted solicitation in community, campus and research cohorts. Information was sought from those enquiring about participation, to develop a profile of the type of person likely to respond to vaccine trial recruitment promotion in Australia.

A self-administered questionnaire was distributed to 127 people who enquired about the vaccine trial. The questionnaire assessed demographics, behaviour, motivation and reasons for withdrawal from the recruitment process if appropriate.

A total of 78 questionnaires were returned (61% response) and 21 respondents ultimately participated in the trial. Respondents and those eventually participating differed in the means of recruitment; through media campaign (65%, 48%), campus (23%, 23%) and word of mouth (12%, 29%) for respondents and eventual trial participants, respectively. Respondents were primarily male (67%), employed (77%) and had attained a tertiary or university degree (80%). They were likely to associate with the gay community and have personal contact with people with HIV. 72% of respondents had undergone HIV testing in the past 2 years. 55% were gay or bisexual and 55% were professionally employed. Altruism was the primary reason for interest. Overall, 31% of respondents decided not to contact trial staff again: 27% of these were too busy, 20% were concerned about side affects, 10% saw no personal benefit and 10% had friends or family not happy with trial involvement. Of the 66% of respondents who did contact trial staff again, 29% of these were ineligible due to an HIV+ partner, 27% were outside the age range, 18% were not low risk and 18% were recipients of a prior HIV vaccine.

There was a good response from those willing to participate in the gay and HIV-affected community to this combined recruitment approach, although personal circumstance and stringent eligibility criteria prevented many from taking part in the trial. Over half of the eventual participants were recruited through campus and personal communication, which will assist to target recruitment into future Australian vaccine trials more efficiently.

International & Regional Issues Posters

P60
HIV/AIDS – MENTAL AND EMOTIONAL ASPECTS IN PAPUA NEW GUINEA

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The number of HIV/AIDS cases in Papua New Guinea (PNG) is on the rise and is becoming of increasing importance to mental health for a number of reasons. For those diagnosed with HIV/AIDS, there are problems of adjustment to a diagnosis of HIV and or AIDS with attached stigma, there is reactive depression and potential risk of suicide, personality disorder, shock and denial of the diagnosis, uncertainty of the prognosis and potential death in the absence of treatment. Inability to access limited health care due to factors such as geographical difficulties, diverse cultures and languages also increases the potential of death. The increasing use of marijuana and abuse of alcohol among Papua New Guineans poses an increasing risk to HIV infection. HIV/AIDS also has the capacity to induce psychological symptoms in those who are not themselves infected but are providing care for those living with HIV and/or AIDS. HIV infection also has direct neurological consequences. This paper highlights the mental and emotional aspects of HIV/AIDS in PNG as this area is not currently addressed and emphasises the need for a social research in mental and psychological aspects of HIV/AIDS among people living with HIV/AIDS in PNG.

P61
THE SOCIAL MARKETING APPROACH IN PAPUA NEW GUINEA

Movono I[1]
[1]Indistage

A two-streamed social marketing model was developed for Papua New Guinea to address the lack of knowledge and awareness of HIV/AIDS and increase risk perception and efficacy in a vast growing epidemic that has been impacted by a diverse cultural background, the existence of a vast range of risky practices in a mainly rural population .

The three campaigns since 2001 have been research-based and have been evaluated with the post-campaign evaluations contributing to the formative research of the next campaign.

While the social marketing campaign has been conducted largely through the mass media, it has included the development of small media with materials to support the campaign and to meet demands to knowledge and services created by the campaigns.

Four waves of evaluation have been conducted involving a total of 8000 respondents in the four regions of Papua New Guinea .

The impact evaluations have shown an increase in awareness and knowledge and some increase in behavioural intention. The increase in distribution of condoms and IEC materials since 2001 reflect an increase in the demand. As a result of the social marketing campaign the Karamap brand of condom which has been developed and promoted has been established as a condom for Papua New Guineans.

Evaluations and research have identified the need to develop a Stigma Reduction Campaign, to scale-up condom promotion and community strategies for behaviour change.

P62
PREVENTION AND CARE EDUCATION FOR TOWNSHIP YOUTH IN PRETORIA SOUTH AFRICA: THE YOUTH SKILLS DEVELOPMENT PROGRAM

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The Youth Skills Development Programme, funded by Ireland AID, developed a successful community outreach project for reaching young vulnerable men in the wider community setting. The outreach work has targeted youth groups and structures but has also extended to male and female sex workers as well as young gay men. It has developed an integrated programme which concentrates how young men and women in Pretoria understand: sexual behaviour and practices; the influence of culture, community, economic status; their knowledge and understanding of sexuality; and their need to make a personal investment in their future.

The YSD programme uses the methodology developed in the UNDP-funded Youth to Youth project with one of the university choirs. In this training young men were given extensive training which allowed them to develop skills in their understanding of HIV and AIDS, its transmission and impact on the communities from which they are drawn. It also allowed them to recognise and understand their sexual behaviour and sexual patterning, and their perceptions of risk and responsibility. They were trained as peer educators and counsellors and some as trainers themselves.

The training improved participants' ability to access health and social development services, to interact constructively with these services and to operate within other community programmes and in inter-generational projects. The method used successful and appropriate, especially where participants were already in established shared interest groups with a community of interest in and shared engagement in the training. It has developed ways in which young men and women, especially those who are marginalized, are fully brought into the establishment and creation of community based structures that deal with their personal health and well being and which address the issues of care.

Continuing work is needed with young men, marginalised youth and so called 'hard to reach' youth on sexual behaviour, sexual mapping, sexuality and access to services.

Basic Science Posters

P63
A NOVEL NUCLEAR IMPORT PATHWAY FOR HIV-1 VPR PROTEIN?

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In contrast to other retroviruses, the HIV-1 lentivirus can infect non-dividing cells via newly transcribed cDNA being transported into the nucleus through the intact nuclear envelope as a large DNA/protein complex, the pre-integration complex (PIC). The HIV-1 Vpr protein is believed to play a vital role in this process, but it is unclear whether Vpr interacts with the conventional cellular nuclear import factors, the importins (imps), or mediates nuclear entry though direct interaction with the nucleoporins (nups), that make up the nuclear pore complex, the pathway for all transport into and out of the nucleus.

This study set out to determine the cellular localisation properties of Vpr, focussing on interactions between Vpr and imps or nups. Mammalian cell transfection experiments using GFP- and DsRed2-Vpr fusion protein constructs indicated that both the N- and C-termini of Vpr possess nuclear targeting properties. An *in vitro* nuclear transport system using bacterially expressed GFP-Vpr fusion proteins, indicated that the N-terminus of Vpr is required for nuclear targeting, with the C-terminus having reduced import activity. Co-transfection experiments between GFP-Vpr and the infectious HIV-1 NL4.3wt virus showed an increase in cytoplasmic Vpr localisation, presumably through interaction with other HIV-1 components.

Yeast 2-hybrid analysis identified two human nups, hCG1 and hCAN as potential binding partners of the Vpr N-terminus, implying that Vpr can interact directly with nups without the requirement for imps. Antibody staining to Nup88, a member of the hCAN nup complex, but not nup62 (localised differently in the NPC), revealed colocalisation with hCAN.

This study provides evidence for the existence of a novel nuclear import pathway for Vpr through direct binding and interaction with nups via its N-terminus. Preliminary experiments using the specific nuclear export inhibitor Leptomycin B implicated a nuclear export sequence within the Vpr C-terminus. Vpr subcellular localisation thus may be modulated by competing import and export pathways; since Vpr plays a key role in PIC nuclear import, the results here may have therapeutic applications.

P64
HIV-1 PERSISTENCE IN DOUBLE NEGATIVE T CELLS FROM PATIENTS NOT RESPONDING TO ANTIRETROVIRAL THERAPY

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The establishment of reservoirs of latently infected cells is thought to contribute to the persistence of HIV-1 infection in the host. Studies so far have mainly focussed on the long-lived reservoir of HIV-infected resting $CD4^+$ T cells, however a discrete population of HIV-infected Double Negative (DN) T cells has been shown to exist and may also play a role in HIV-1 persistence.

DN T cells are CD3 positive, either TCR$\alpha\beta$ or TCR$\gamma\delta$ positive but lack both the CD4 and CD8 cell surface markers. We have developed a novel, magnetic column-based cell fractionation procedure for isolating >99% pure DN T cells. $CD4^+$, $CD8^+$ and DN T cells were purified from a cohort of 21 HIV-1 infected patients undergoing highly active antiretroviral therapy (HAART). Each fraction was analysed for levels of total (*gag*-PCR) and integrated (modified nested *Alu*-PCR) HIV-1 DNA. A correlation was observed between HIV-1 DNA in the DN T cell fraction and the patients' response to therapy (determined by plasma viral load [VL]).

Using a micrococulture technique, we saw an initial release of virus (assayed by p24 ELISA) from DN T cells of a patient with high VL. Analysis of *env* and *nef* sequence data suggested that the HIV-1 present in $CD4^+$ and DN T cells originated from a common infecting strain.

Contrary to the published literature, we have demonstrated the presence of HIV-1 DNA in DN T cells only in patients that are experiencing HAART failure. Our results therefore suggest a role for DN T cells in HIV-1 persistence in patients not responding to HAART. We believe that understanding the distribution of persistent HIV-1 is critical for the development of comprehensive therapies and the informed management of patient drug regimens.

This work was supported by an Australian Commonwealth AIDS Research Grant.

P65
MEASUREMENT OF HIV INTEGRATED VIRAL LOAD IN CLINICAL SAMPLES

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Many patients currently treated with HAART have undetectable circulating viral loads (VL). However, there may be circulating cells still harbouring HIV. In the presence of low circulating viral load, monitoring of this cell associated population, or the integrated viral load (iVL), may provide valuable information for consideration in patient management. We aimed to quantitatively measure iVL in routinely collected clinic samples from patient populations on HAART.

Samples are collected as for routine VL measurement from patients entering the RAH clinic with informed consent. Following removal of plasma for VL measurement the cell layer is isolated, leukocytes purified by density gradient centrifugation and total DNA extracted (Dneasy, Qiagen). iVL is quantitated by real-time Alu-PCR, with samples normalised for β-globin content and Alu- PCR controls to determine the contribution of unintegrated DNA to our measurement.

Our current laboratory methods for Alu-PCR have been adapted to real-time PCR analysis. Linear quantitation of an HIV specific product from 10-1000 copies/50,000 cells has been validated. Patient samples collected under normal clinical conditions for VL measurement have been successfully used to obtain real-time PCR compatible DNA. iVL has successfully been measured at less than 20 copies/50,000 cells in a limited number of patient samples. Results thus far indicate that our real-time Alu-PCR method can be applied to clinical samples to detect iVL from a total cell population, in patients on HAART. Further application to broader clinical samples will be performed to assess the correlation of iVL with circulating VL and clinical outcomes and validate the use of the technique in a wider patient cohort. The use of samples already taken for routine VL, the total cell population and total DNA fraction makes the extraction and quantitation method as simple as possible to assist adaptation to a rapid diagnostic setting.

P66
PROTEOMIC ANALYSIS OF DC-SIGN ON DENDRITIC CELLS DETECTS TETRAMERS REQUIRED FOR LIGAND BINDING BUT NO ASSOCIATION WITH CD4

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DC-SIGN (dendritic cell specific intracellular adhesion molecule 3 grabbing non-integrin) or CD209 is a type II transmembrane protein and one of several C-type lectin receptors expressed by dendritic cell subsets which bind to high mannose glycoproteins promoting their endocytosis and potential degradation. DC-SIGN also mediates attachment of HIV to dendritic cells and binding to this receptor can subsequently lead to endocytosis or enhancement of CD4/CCR5 dependent infection. The latter was proposed to be facilitated by an interaction between DC-SIGN and CD4. Endocytosis of HIV virions does not necessarily lead to their complete degradation. A proportion of the virions remain infective and can be later presented to T cells mediating their infection in trans. Previously, the extracellular domain of recombinant DC-SIGN has been shown to assemble as tetramers and in the current study we use a short-range covalent cross-linker and show that DC-SIGN exists as tetramers on the surface of immature monocyte-derived dendritic cells. There was no evidence of direct binding between DC-SIGN and CD4 either by cross-linking or by fluorescence resonance energy transfer measurements suggesting that there is no constitutive association of the majority of these proteins in the membrane. Importantly we also show that the tetrameric complexes, in contrast to DC-SIGN monomers, bind with high affinity to high-mannose glycoproteins such as mannan or HIV gp120 suggesting that such an assembly is required for high-affinity binding of glycoproteins to DC-SIGN providing the first direct evidence that DC-SIGN tetramers are essential for high affinity interactions with pathogens like HIV.

P67
METHODOLOGICAL APPROACH TO ANALYSING DENDRITIC CELL UPTAKE OF VACCINIA, AN IMPORTANT CANDIDATE HIV VACCINE VECTOR

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The delivery of viral antigens in a recombinant viral vector is a promising approach to successful vaccination against HIV, particularly in a prime-boost format. Professional antigen presenting cells, especially dendritic cells (DCs) play a key role in controlling the magnitude, quality and memory of the immune response elicited by such vaccines. This study-in-progress is designed to investigate the binding, entry and processing of the potential HIV vaccine vector, vaccinia virus (VV), into human monocyte-derived DCs. The cellular receptors for VV binding are yet to be elucidated but we speculate that C-type lectins receptors (CLRs) are important for initial binding of the virus to DCs, as is the case for HIV and a growing number of other viruses.

A technique called spinoculation, originally developed for HIV infection of CEM-SS T-cells, has been adapted to infect DCs with VV. This technique has overcome poor binding and infection rates of VV in DCs, enabling binding to be studied. A number of assays have subsequently been developed to analyse VV binding to DCs. A GFP-labeled VV was used to develop a real-time PCR assay, detecting the GFP gene within the viral genome. This assay allows for quantification of the number of copies of VV present in a sample. Together with real-time PCR quantification of the number of DCs present, by amplification of the albumin gene, the ability of the virus to bind under different culture conditions can be assessed. Secondly, a flow cytometric assay detecting GFP has been developed for quantifying the number of cells that have bound VV. VV binding to DCs has also been qualitatively analysed by confocal microscopy using virus-specific monoclonal antibodies.

These methods are being used to investigate VV binding to DCs in the presence of CLR blockers, as CLRs are likely to be important for initial binding and uptake by these cells. Further understanding of the receptors involved may lead to enhanced uptake and processing of VV vaccine vectors in DCs, currently recognised as a major hurdle in improving their efficacy.

P68
DISCOVERY OF A REVERSION OF A 100 AMINO ACID TRUNCATION OF THE GP41 CYTOPLASMIC TAIL AND IDENTIFICATION OF MATRIX MUTATIONS IN HIV-1 RFGP34

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The 150 amino acid (aa) cytoplasmic tail (CT) of the HIV-1 glycoprotein-41 (gp41) is highly conserved in both length and sequence amongst HIV-1 isolates. We have previously reported a 100 aa truncation of the CT of the laboratory strain RF (designated RFgp34). Compared with RFwt (which has a full-length CT), RFgp34 shows reduced and delayed replication kinetics, and giant syncytia. The Matrix (MA) protein is thought to interact with the CT and previous studies have shown that mutations within regions of MA can compensate for large CT truncations.

RFgp34 viral stocks were cultured in Hut78 cells for 11 days. Through Western blotting of viral lysates taken from the day 11 culture we discovered that one RFgp34 viral lysate (designated RFgp34rev) contained a mixed population of gp41 and gp34. DNA was extracted from the RFgp34rev-infected Hut78 cells on day 11 and the gp41 region was sequenced. A mixed base population (A and G) at position 740 of gp41 was present resulting in a mix of W and stop codon at gp41 aa 247. No other changes corresponding to the RFwt sequence were found.

The MA region of RFwt, and RFgp34 isolates was sequenced. Two mutations (E to K at aa 40 and F to I at aa 44) were discovered in MA which were unique to RFgp34. These mutations are in the second alpha-helix of MA, and were still present in RFgp34rev.

Here our data clearly showed that the mixed population of the RFgp34 isolate from day 11 (RFgp34rev) is the result of the TAG (stop codon) reverting to TGG (W) and not due to contamination from an RFwt culture. We have identified two unique MA mutations in our RFgp34 isolate that accompany the truncation of the gp41 CT.

P69
INVESTIGATION OF DENDRITIC CELL GENE EXPRESSION LEVELS IN RESPONSE TO HIGH TITRE HIV AND HIV ENVELOPE GLYCOPROTEIN

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Dendritic cells (DCs) are specialised antigen presenting cells that form a link between the innate and adaptive immune systems. Immature DCs are resident within epithelial tissues where they engulf microbial antigens via endocytosis then migrate to draining lymph nodes while differentiating into a mature phenotype, up-regulating MHCII. Here they present the antigen to and activate T-cells. Unlike T-cells, HIV replicates at low levels in immature DCs although epithelial DCs are probably the first cells of the immune system that HIV encounters after sexual transmission. The virus therefore uses these cells as a 'Trojan horse' to gain access to large numbers of T-cells where it establishes a productive infection. An understanding of how HIV interacts with and infects DCs is therefore of vital importance. Though the mechanisms of entry and the subsequent viral life cycle have been well studied in CD4 T-lymphocytes and macrophages, virus internalisation and replication in DCs is very poorly understood. The marked differences between these target cells are shown by the unique entry mechanisms for HIV into DCs.

We therefore used DNA microarray experiments in order to obtain a global picture of the gene expression profiles in Monocyte Derived Dendritic Cells (MDDCs) in response to HIV infection or exposure the HIV envelope glycoprotein. To this end MDDCs were either infected with high titre HIV (Bal strain) in parallel to an inactivated virus that can enter but not subsequently replicate inside the cell, or exposed to HIV (Bal) recombinant gp120 in parallel to untreated cells. RNA was isolated from these cells at various time points post exposure was subsequently amplified using the Eberwine technique before being labelling and hybridised to 8K human cDNA microarrays. Very few genes were differentially expressed in response to gp120 exposure however as expected, differential gene expression increased with time post infection with live HIV with most differentially genes occurring at 48hours post infection. Genes with consistently altered expression levels included those associated with transcription, RNA splicing, the endolysosomal pathway and vesicle trafficking, translational initiation and ubiquitination.

P70
EFFECT OF FLUORESCENTLY LABELED FULL LENGTH HIV-1 VPR AND VPR FRAGMENTS ON VIRAL INCORPORATION AND INFECTIVITY

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Co-transfection of infectious viral constructs with fluorescently labelled Vpr has previously been used to produce fluorescently labelled virus particles which can be followed by confocal microscopy during infection of cells. However, so far no studies have been able to follow the subviral particles upon their transport into the nucleus. Here we have evaluated the suitability of different fluorescent labels of Vpr as well as the N-terminal and C-terminal fragments of Vpr for studying nuclear import of the HIV pre-integration complex.

Virus produced in 293 cells co-transfected with fluorescently labelled Vpr constructs (EGFP-Vpr1-96, GFP-Vpr1-96, GFP-Vpr1-46, GFP-Vpr46-96, and DsRed2-Vpr1-96) and either NL4.3wt or NL4.3 lacking Vpr (NL4.3ΔVpr) was examined for the incorporation of the fluorescently labelled Vpr constructs into virions using Western blotting. Infectivity of fluorescently labelled virus was assessed using the MAGI assay in both dividing and γ-irradiated cells.

The full length Vpr constructs were incorporated into virions. However, the GFP-Vpr construct was proteolytically cleaved into GFP and Vpr. In contrast, the EGFP-Vpr construct appeared to be proteolytically cleaved from the C-terminus of Vpr. Interestingly, both the N- and C-terminal fluorescently labelled Vpr fragments were only present in virus co-transfected with NL4.3wt but not in virus co-transfected with NL4.3ΔVpr. Virus containing fluorescently labelled Vpr was consistently less infectious than NL4.3wt and this was more pronounced in γ-irradiated cells. Infectivity with fluorescently labelled Vpr containing virus was even lower than that of NL4.3 ΔVpr. Virus containing fluorescently labelled fragments had strongly decreased infectivity in γ-irradiated MAGI cells.

The results demonstrate that small differences in the constructs expressing GFP-Vpr and EGFP-Vpr such as the linker region between the fluorescent protein and Vpr affected proteolytic cleavage, virus incorporation of Vpr and infectivity. The fact that both N- and C-terminal Vpr fragments were incorporated into virus when full length wt Vpr was present suggests that the incorporation was facilitated via an interaction with Vpr rather than with $p6^{gag}$. The data question the suitability of the GFP-Vpr and EGFP-Vpr constructs for the study of PIC nuclear import. Alternatives for labelling of Vpr will be discussed.

P71
OPTIMISATION OF A HUMAN IMMUNODEFICIENCY VIRUS TYPE – 1 DERIVED GENE TRANSFER VECTOR

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Many different viruses have been used to develop gene delivery systems. For many gene therapy strategies the target cells are essentially non-dividing. Therefore the ideal virus/vector must possess the ability to infect non-cycling cells and preferably also result in the long term, stable genetic modification of the target cell. Human Immunodeficiency Virus type – 1 (HIV-1) naturally possesses such characteristics and accordingly we have used it as the basis of a gene transfer system. This gene delivery system comprises of a number of plasmids that separate the *cis* and *trans* functions of the virus. The *cis* functions are incorporated into a transfer vector construct, whilst the *trans* (protein coding) functions are distributed over a number of 'helper' or packaging plasmids, to prevent their transfer to target cells. A general strategy to improve the efficiency and safety of the vector construct is to reduce the viral sequence to the minimum required to maintain the desired characteristics of the virus whilst removing any unwanted ones. In addition, it is clear that HIV-1 sequence content can be further reduced by substituting certain HIV-1 *cis* functions with similar elements from heterologous sources. For some elements, such as the polyadenylation signal, this approach has been used to improve RNA processing efficiency leading to improvements in vector function. Currently detailed analysis of splice site function and the HIV-1 encapsidation signal are being performed and the use of alternate polyadenylation signals explored.

P72
IDENTIFICATION OF A NOVEL C-TYPE LECTIN RECEPTOR OTHER THAN MANNOSE RECEPTOR, DCSIGN OR LANGERIN WHICH BIND TO GP120 ON THE SURFACE OF MONOCYTE DERIVED DENDRITIC CELLS

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Peripheral mucosal DCs such as Langerhans cells (LCs) are one of the first cell types that are thought to interact with HIV-1 after infection and play a crucial role in the initial dissemination of the virus throughout the host. The main C-type lectin receptors (CLRs) expressed on the surface of DCs are DC-SIGN (dendritic cell specific ICAM-3 grabbing non-integrin), the mannose receptor (MR) and langerin (Langerhans cells) but other receptors are also expressed.

Previous studies have shown that CLRs on monocyte derived dendritic cells (MDDCs) and LCs bind viral gp120 preferentially compared to CD4 and its co-receptors CCR5/CXCR4. In particular, much focus has been placed on DC-SIGN as the primary CLR to bind gp120 on MDDCs. However, we have shown that there are multiple CLRs on different DC subsets that participate in binding gp120 by mannan inhibition studies. Inhibition of gp120 binding by mannan on immature dermal DCs implicates the possible involvement of one or more other viral attachment factors. Further evidence suggesting that multiple CLRs (and not langerin alone) are involved in gp120 binding on emigrant LCs was shown by a reduction of gp120 binding by 90% on these cells, despite the maintenance of langerin expression over a 24 hour period. The identity of these potential CLRs is yet to be elucidated.

To investigate the identity of these novel receptors, surface molecules on MDDCs were chemically cross linked to allow oligomer formation. Oligomeric DC-SIGN and MR were shown to bind mannan with higher affinity than their monomeric form. Cell lysates were then passed consecutively through columns containing anti-DCSIGN, anti-MR and anti-Langerin conjugated beads to eliminate these known mannan binding CLRs. To detect CLRs which bind with lower affinity or are expressed at lower quantities on MDDCs the eluate was then passed through a column containing mannan conjugated beads. Purified CLRs were then separated on an SDS PAGE gel and Coomassie-stainable proteins were identified by mass spectrometry and database searches. Using this technique, we have identified calreticulin as a surface mannan binding CLR on MDDCs. Further investigations using gp120 conjugated beads will be required for the identification of novel surface gp120 binding CLRs.

P73
INTERLEUKIN-23 AND INTERFERON-Γ DEFICIENCY IN SEVERELY IMMUNODEFICIENT HIV PATIENTS WHO HAVE ACHIEVED A LONG-TERM INCREASE IN CD4 T-CELL COUNTS ON HAART

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The pathogenesis of HIV infection and susceptibility to opportunistic infections has been associated with poor type 1 cytokine production. IL-23 is a recently discovered cytokine formed from the p40 subunit of IL-12 binding to p19, a novel homologue of IL-12p35. IL-23 has very similar functions to IL-12, notably induction of interferon-γ (IFN-γ) production in T-cells. However, IL-23 enhances memory rather than naïve T-cell proliferation and activation. We have measured the mRNA of IL-23p19 and other type 1 cytokine pathway components in peripheral blood mononuclear cells (PBMCs) from HIV patients with long-term immune reconstitution on HAART.

Purified CD4 and CD8 T-cell populations were isolated by positive selection using magnetic beads. Adherent cells were obtained by culturing PBMC on 6-well plates for 2 hours at 37°C. mRNA levels for IL-23p19, IL-12p35, IL-12p40, IL-12Rβ1, IL-12Rβ2, IFN-γ and IL-2 were determined using real-time PCR on a LightCycler (Roche).

In severely immunodeficient HIV patients who achieved increased CD4 T-cell counts on long-term HAART, we observed reduced spontaneous expression of IL-23p19 in adherent cells and IL-12Rβ2 in unfractionated PBMC compared to healthy controls. IFNγ was also decreased in purified CD4 and CD8 T-cells from patients. Spontaneous IL-12Rβ1 expression in unfractionated PBMC was low in patients and controls. IL-23p35 mRNA was detected in a few patients and controls but IL-2 and IL-12p40 mRNA could not be detected in any unstimulated samples.

Reduced IL-23 dependent production of IFN-γ by memory T-cell may be a complication of severe immunodeficiency that is not corrected after suppression of HIV infection by HAART. This may explain the occurrence of opportunistic infections seen in a minority of patients with substantial CD4 T-cell recovery on HAART.

P74
ANALYSIS OF FCRΓ CONTENT IN MONOCYTES AND PERIPHERAL BLOOD LYMPHOCYTES FROM HIV-POSITIVE BLOOD

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FcRγ is a small ~8 kDa protein which transduces intracellular signals in response to activation of immunoreceptors via its immunoreceptor tyrosine-based activation motif (ITAM). Receptors which have been shown to signal via FcRγ include the Fcε receptor expressed on mast cells, Fcα and Fcγ receptors expressed on NK cells and monocyte/macrophages, and the T-cell receptor expressed on effector CD4 T-cells. We have shown that HIV-1 infection of human monocyte-derived macrophages decreases Fcγ receptor dependent phagocytosis which is associated with decreased protein expression of FcRγ. Given the important role of FcRγ in NK cell, effector CD4 T cells and monocyte function we investigated whether FcRγ expression is decreased in monocytes and peripheral blood lymphocytes from HIV-1-infected individuals.

We developed an assay to measure FcRγ protein expression in cellular fractions obtained from 10-20ml of whole blood. Preliminary experiments suggested that HIV-1-positive individuals had decreased expression of FcRγ in both adherent cells (monocytes) and non-adherent peripheral blood lymphocytes (PBL; which consists of NK cells and other lymphocyte subsets). Further investigations showed that FcRγ expression is unstable in whole blood and significantly reduced in both monocytes and PBL within 24 hour. We therefore conducted a pilot study comparing FcRγ protein expression in 5 HIV-1 seropositive (whose viral loads varied from undetectable to 70,400 copies per ml) and 5 HIV-1 seronegative individuals, carefully matching the time between blood collection and sample processing. It was found that FcRγ expression in both monocytes and PBL was unchanged in these patients. As we have shown that FcRγ expression is decreased in HIV-1 infected macrophages, the lack of a decrease in monocytes suggests that HIV-1 exerts a direct effect on FcRγ expression rather than a bystander effect, although more work needs to be done to establish this. We are currently in the process of extending these observations.

We conclude that there is no evidence for decreased FcRγ protein expression in peripheral blood mononuclear cells from HIV-1-positive individuals.

P75
NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS CAUSE DECREASED ADIPOCYTE MITOCHONDRIAL (MT) MRNA TRANSCRIPTION IN THE ABSENCE OF CHANGES IN MTDNA COPY NUMBER OR CELL MORPHOLOGY

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Long-term NRTI therapy often leads to lipoatrophy. Although NRTIs may inhibit adipocyte DNA polymerase γ, affecting mitochondrial (mt) replication, it is unclear if mtDNA depletion is the primary defect in NRTI induced toxicity.

We examined mtRNA expression, mtDNA copy number and cell morphology in fat biopsies from 20 HIV-neg healthy adult subjects enrolled in a prospective, randomised trial of 6 weeks d4T/3TC or AZT/3TC followed by 6 weeks washout. Assessments included clinical history, fasting lipids and glucose, and measurement of body composition. Adipose tissue biopsies were performed at weeks 0 and 2. RNA and DNA were extracted and mtRNA expression and mtDNA copy number measured by real-time RT-PCR. Results are expressed relative to β-actin expression for mtRNA and relative to a nuclear gene copy number (2/cell) for mtDNA.

Median age was 41 yrs (IQR 14.5) and 90% of subjects were male. Both groups were matched for baseline parameters with no change in body composition or serum lipids by week 6. Adipose tissue mtRNA expression decreased significantly by week 2 whilst there was no significant change in mtDNA copy number and no correlation between baseline or change in mtDNA and changes in mtRNA. No consistent differences were seen between pre and post treatment biopsies with respect to the light- or electron microscopic appearances of adipocytes and mitochondria.

	Baseline	Week 2	p	%change
COX1 mRNA	1.64 [1.2]	0.58 [1.7]	0.002	-72 [77]
COX3 mRNA	10.7 [12.2]	1.67 [9.5]	0.001	-88 [49]
Cyt b mRNA	3.86 [2.8]	1.38 [3.6]	0.005	-60 [63]
mtDNA (ng/cell)	85 [53]	75 [102]	0.1	+16 [94]
Fat cell count (Cells/hpf)	62 [23]	59 [36]	0.6	-

Table 1. Values are median [IQR]. hpf=high powered field.

Independent of HIV-infection, exposure to AZT/3TC or d4T/3TC decreases mtRNA expression in the absence of significant changes in mtDNA copy number or ultrastructure. These data suggest that NRTIs affect mtRNA expression in adipose tissue early after exposure by a means other than through inhibition of DNA polymerase γ-mediated mitochondrial replication and suggest that the earliest changes in adipose tissue occur at the mtRNA level.

P76
CRYOPERSERVATION OF PERIPHERAL BLOOD MONONUCLEAR CELLS (PBMC'S) USING A PROGRAMMABLE CONTROLLED RATE FREEZING UNIT HELPS PRESERVE LYMPHOCYTE IMMUNOPHENOTYPE AND FUNCTION

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Functional T cell assays are usually performed real time, using freshly isolated PBMC's. Real time assay set up is not always possible, and is limited by inter-operator or inter-laboratory variation. Cryopreserved PBMC's with reproducibly preserved immunophenottype and functionality for use in batched assays would result in greater standardisation of results and reduce cost inefficiencies. A major source of variability in cryopreservation of PBMC's is the rate of cooling, which can be controlled by using a "MrFrosty" (MrF) container system or a programmable controlled rate freezer (CRF). Viability, yield, immunophenotype and functionality of PBMC's cryopreserved using the two freezing systems were compared.

Freshly isolated PBMC's were stored in equal cell numbers using a NALGENE MrF or a PLANER "Kryo360-3.3" CRF using a number of different protocols. After cryopreservation the PBMC's were transferred to LN2 storage for a minimum of 7 days, thawed, and assessed for viability and yield using trypan blue exclusion dye. Immunophentoyping, lymphoproliferation and IFNγELISPOT assays were performed.

There was no significant difference between the two freezing systems or the programmes in terms of viability and yield (median viability for –70°C programme CRF: 89.4 and MrF: 87.4, for –180°C programme CRF: 94.8 and MrF: 94.7). There was no significant difference between the two freezing methods for the ELISPOT background (median SFC/mill CRF: 5, MrF: 5) or the mitogen induced response to SEB (median SFC/mill CRF: 4507, MrF: 4075). However, importantly PBMC's that were cryopreserved using the CRF had a significantly higher antigen induced CD4+ response to CMV whole lysate (median SFC/mill CRF: 225, MrF: 80, Wilcoxon signed rank test P=0.04) Preliminary lymphoproliferation results showed a trend of better responses from cells cryopreserved using the CRF however further data will be obtained by processing an increased number of samples. The immunophenotype results showed that the key markers CD38, HLA-DR, CD28, CD27, CD45RA, CD45RO and Ki-67 were retained during cryopreservation using the controlled rate freezer, further data for the MrF is also required.

P77
MOLECULAR AND BIOLOGICAL MECHANISMS IN HIV-1 INFECTION WITH A REPLICATION INCOMPTENT STRAIN IN A NON-PROGRESSIVE INDIVIDUAL

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Non-progressive HIV-1-infected therapy naïve individuals, who have been infected for 20+ years, may harbor clues to biopharmaceuticals and have the potential to explain underlying mechanisms of nonprogressive HIV disease. Viral evolutionary processes play a significant role in disease progression, and they can also serve a guiding tool to the discovery of natural anti-HIV agents from such rare individuals who comprise 0.8% of total HIV-infected population.

Several HIV-1-infected, therapy naïve non-progressing individuals, with below detectable levels of plasma viremia and high CD4+ and CD8+ T cell counts were studied for full-genome sequences over time to derive information of the influence of viral evolutionary processes on HIV disease progression. PCR and sequencing of full-genomes was carried out. In addition, various biological and immunological analyses were performed to derive information of host mechanisms.

Viral evolutionary rate was the single most important determinant of HIV disease progression. Sequencing analysis of a unique HIV-1 infected long-term non-progressor (LTNP) with undetectable viral load and unculturable virus revealed no viral evolution over the past six years, suggesting the absence of viral evolution of HIV-1 strains *in vivo*. Super-infection of the study subject's PBMC with HIV-1 strains showed that each strain could replicate in his isolated CD4+ T cells, but this was without any visible cytopathic effect. This was in sharp contrast to healthy donor PBMC and CD4+T cells. These data are highly unique suggesting that in some non-progressive HIV-infected individuals, there is post-entry protection against cell killing as seen by transmission EM studies. Detailed immunological analyses indicate that several mechanisms, including a strong HIV-specific CD8+ T cell response, vigorous HIV-p24-specific helper T cell proliferative responses, and high-level IFN-gamma release by both CD4 and CD8 T cells, were associated with and may have promoted this antiviral suppressive activity. Understanding the induction of these protective immune responses in other individuals could provide a major step forward in the design of effective immunotherapeutics or vaccines against HIV infection.

P78
ANALYSIS OF *TAT* GENES RECOVERED FROM LONG-TERM NON-PROGRESSERS INFECTED WITH HIV-1

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Both exons (1 and 2) of the tat coding region were analysed for functional attributes from the from an epidemiologically-linked Canadian cohort, which consists of 3 individuals. In this cohort a non-progressor transmitted virus to two individuals and the two recipients developed AIDS. Full tat gene, comprising of exon 1 and 2, was amplified by RT-PCR from patient plasma samples, over time. Analysis of the primary amino acid sequence revealed that many of these tat genes contained amino acid sequences of mixed subtypes. This feature was not common in the first 20 amino acids, but other regions of Tat which contained higher frequencies of unusual amino acid substitutions including the core domain (from aa 39-48), the basic domain (from aa 49-57), and in carboxyl-terminal domain (aa 58-72). Here we report the activity of these Tat genes to induce HIV-1 gene expression in a tissue culture model using an HIV-1 LTR reporter plasmid.

P79
ANALYSIS OF HIV CO-RECEPTOR USE AND QUASISPECIES DIVERSITY IN INDIVIDUALS FAILING PROLONGED ANTIRETROVIRAL THERAPY

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The aim of this study was to determine the relationship between the emergence of X4 viral genotype, HIV quasispecies diversity and immunological outcome in HIV-infected individuals who are persistently viremic on highly active antiretroviral therapy (HAART).

Plasma from HIV-infected individuals who were persistently viremic and were taking at least 3 antiretroviral agents was collected (n=12). All individuals had at least one primary mutation in protease or reverse transcriptase associated with drug resistance. V3 sequence and quasispecies diversity was determined for HIV from plasma taken prior to initiation of and following at least 2 years of HAART. The V3 region from plasma virus was sequenced directly following nested PCR.The predicted tropism was determined based on charge and amino acid at position 11 and 25 of the V3 loop. Length polymorphisms in V1-V2 of the *env* gene was assessed using fluorescently labeled PCR products separated by size on an automated DNA sequencer and analysed by the GeneScan program. Diversity was scored based on the number of peaks and size relative to the maximum peak.

The number of individuals infected with a dominant R5 quasispecies (as determined by genotype) prior to HAART was 10/11 as compared with 8/12 following HAART (median duration 50 months; range 27 – 208 months). In 3 individuals there was a switch from R5 to X4 viral variants during HAART. Using length polymorphisms in the V1-V2 region as a surrogate for quasispecies diversity, there was either no change (n=3), an increase in diversity (n=4) or a decrease in diversity (n=5). There was a trend toward reduced quasispecies diversity in individuals with declining CD4 counts.

X4 variants emerge in individuals receiving HAART. Reduced quasispecies diversity was associated with immunological failure. Confirmation of these findings is required using detailed cloning and sequencing of the C2-V5 region of *env*.

P80
ANALYSIS OF GENETIC DIVERSITY IN KENYAN MOTHERS AND INFANTS

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There is great genetic diversity among circulating HIV-1 strains in sub-Saharan Africa. In Kenya, HIV-1 subtypes A and D are predominant and inter-subtype recombinants between these strains have been reported. HIV recombinants emerge in individuals who carry multiple virus strains. Recombination has been shown to create fitter viral strains and presents a challenge to the development of subtype specific vaccines. We have analyzed the HIV-1 gag and env regions, from the peripheral blood mononuclear cells (PBMC) of vertically transmitting mothers and their infants in Kisumu, Kenya, to examine viral genetic diversity and inter-subtype recombination in this area. PCR and population sequencing analysis of the gag and env genes was performed on 37 patients (16 mother-child pairs, 4 unpaired mothers and one unpaired infant). The program Simplot was used to compare each sequence against background reference sequences for multiple subtypes to define subtype and identify recombinants. Cloning of PCR fragments was then performed using the pGEM-T vector system II, to verify the presence of recombinants and detect any potential dual infections. Phylogenetic analysis of inter-patient relationships was performed using the neighbouring joining method. 17 patients (8 mother-child pairs, and paired one infant) were found to be infected with HIV-1 recombinants and 18 patients (7 paired and 4 unpaired) carried pure HIV-1 strains. In addition 2 patients showed strong evidence of having dual infections. The first dual infection, between a pure A and an A/D recombinant was found in a paired mother and only a single strain (A/D recombinant) was detected in the paired baby. The second dual infection, between subtype A2 and and A2/D recombinant, was found in an unpaired mother. All the strains identified belonged to or were recombinants of HIV-1 subtypes A1, A2 or D. The recombinant strains seen were unique to each individual or mother-child pair, and show that the HIV epidemic in Kenyan is extremely diverse. Such diversity in a small geographical region highlights the need for continual monitoring of the HIV epidemic, particularly in Africa where there are numerous subtypes present. Knowledge of currently circulating HIV-1 subtype and recombinants will be vital to the development of effective HIV vaccines, which may need to be continually improved to keep up with the ever increasing diversity of HIV strains.

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ROLLING CIRCLE AMPLIFICATION (RCA) FOR ULTRASENSITIVE VIRAL GENOME DETECTION

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Recently, the utility of circularizable oligonucleotides, or 'padlock probes', for the detection of target nucleic acid sequences has been demonstrated, with greater sensitivity than conventional PCR. In isothermal conditions, RCA is capable of a 10^9-fold signal amplification and a single target template can be efficiently detected by this method. Here we demonstrate and explain the feasibility of using RCA technology for detection of SARS-CoV. In the near future, we will adopt a similar strategy for detecting <50 copies of HIV-1 genome, which has not been achieved by any of the conventional assays.

SARS-CoV specific circularizable oligonucleotides were designed and synthesised. Upon hybridization to SARS RNA molecule, the two ends of the probe become juxtaposed and can be joined by DNA ligase. The circularized DNA probe then creates an effective template for exponential, or hyperbranching, rolling-circle amplification (RCA) reaction using two primers in isothermal conditions.

Using serially diluted artificial templates, single template can be detected in both 'liquid-phase' and 'solid-phase' RCA. Stronger signal and lower background was observed in solid phase RCA and tests on culture-derived SARS isolates and SARS patient samples, less than 5 SARS RNA copies can be easily detected.

Solid phase RCA offers an inexpensive and accurate alternative for SARS diagnosis with sensitivity comparable to current commercial RT-PCR assays. In addition to ultrasensitive detection with high specificity, the RCA method employs simple reaction conditions, very applicable to laboratories for SARS diagnosis in developing countries where scientific equipment is minimal. The problem of false-positive results, which continues to hinder PCR-based diagnostics is also avoided with RCA-based assays, as signal detection is generated directly from the circularized probe rather than amplification of the target. We expect that, with this rapid diagnostic method, prompt identification of this pathogen will facilitate control of the disease and provision of prompt treatment of patients. RCA has immense future potential in detecting low copy HIV, which will be very useful in predicting disease progression and define therapy strategies for HIV patients.

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DENDRITIC CELLS AND THE HUMAN BRAIN

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Dendritic cells (DCs) play an important role in the capture and transmission of HIV to T cells in primary HIV infection, however little is known about their role in illnesses common in advanced HIV such AIDS Dementia Complex (ADC). DCs are present in meninges and dura of healthy rats/mice and infiltrate the brain and spinal cord in autoimmune and infectious encephalitis. DCs are present in human choroid plexus and cerebrospinal fluid. If DCs migrate into, or are constitutively present in the central nervous system (CNS) their role may be important in inflammatory and viral diseases of the CNS including ADC. We sought to determine the presence, distribution and phenotype of DCs in the CNS of HIV positive and negative patients with and without CNS disease.

Sections of dura and meninges obtained at post-mortem from an HIV-negative patient with multiple sclerosis were cultured for 36 hours. The culture medium was harvested and centrifuged. Nycodenz density centrifugation was performed and retrieved cells were incubated with HLA-DR-FITC following cytospin. Fluorescent microscopy revealed ≈ 20% of cells obtained from meninges and dura had strong expression of HLA-DR and typical DC morphology. In another HIV-negative, neurologically-intact patient similar techniques were used to obtain cells from dura, meninges, cortex and putamen. FACS analysis revealed that meninges and dura contained cell populations with the following phenotypes: HLA-DR^{hi} CD14^{+}, HLA-DR^{hi}CD11b^{++}. A cell population expressing HLA-DR^{hi}CD11b^{lo} was present in dura, but had low expression in meninges. There was no evidence of DCs in the brain parenchyma.

These initial experiments show DCs to be present in dura and meninges, but not in brain parenchyma. Further studies using FACS analysis and immunohistochemistry are ongoing, including studies to determine the distribution of DCs in ADC.

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POTENTIAL ROLE OF ACTIVIN A IN HIV IMMUNE-COMPROMISED PATIENTS

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The growth factor, activin A, was originally isolated as a putative reproductive hormone, but it is now known to participate in many other non-reproductive cellular and tissue functions. One of these is in the setting of inflammatory processes and immune compromise. In experimental animal models, activin is released rapidly into the circulation following challenge with a common inflammatory insult, such as the bacterial cell wall protein, lipopolysaccharide (LPS) or endotoxin. Furthermore, recent studies by us have shown that in human septicemia, activin and follistatin are elevated in the bloodstream of septic patients. A role in viral infections is suggested by perturbation of serum activin levels in viral hepatitis patients, particularly in hepatitis B. We have performed preliminary screening of HIV patients (n=41; mean %CD4=19.04; average VL=226918 copies/ml) for serum levels of activin and its binding protein, follistatin (mean physiological level = 0.15 ng/ml and 9.3 ng/ml respectively). While the mean levels of both activin and follistatin in HIV-infected individuals (activin = 0.14 ng/ml, follistatin = 8.1 ng/ml), was similar to that of HIV-negative individuals, several patients had moderate elevations in both proteins, suggestive of a role in immune status. We are currently investigating the kinetics of activin and follistatin in macaques infected with the SHIV chimeric virus; in patients who are in the initial phases of HIV-1 infection and those that have failed therapy and have progressed to AIDS.

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