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2016 Australasian Sexual Health Conference
2016 Australasian HIV & AIDS Conference

Supporting the HIV, Viral Hepatitis and Sexual Health Workforce

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Senior Project Officer

Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine

ASHM is a signatory to the ACFID Code of Conduct and is committed to the principles of the Ottawa Charter for health promotion and the Jakarta Declaration on health promotion.

2016 Australasian Sexual Health Conference
14-16 November 2016

The National Cervical Screening Program: On the Cusp of Change

A/Prof Marion Saville
VCS Pathology

HPV Vaccination:

- In 2015, 77.4% 15 year old Australian girls were vaccinated, along with 66.4% of boys
- Declines in rates of high grade histologically confirmed cervical abnormalities observed in women <30 years
- Australia is likely to move to a two-dose, nine-valent HPV vaccine

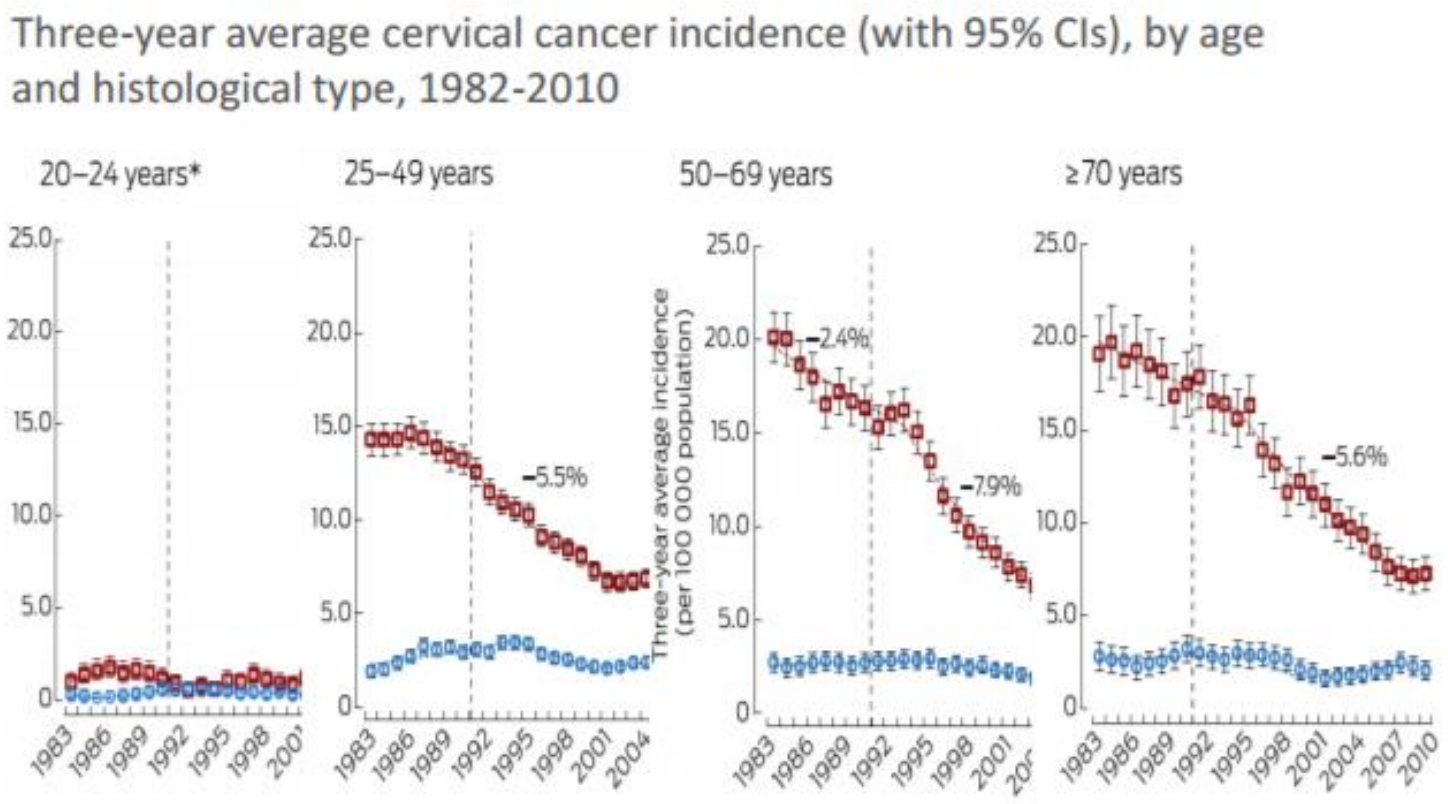
“Renewal” of the National Cervical Cancer Screening Program

From 1 May 2017:

- the Pap smear will be replaced with the Cervical Screening Test
- time between tests will be 5 years
- first age of screening is 25 years
- women aged 70-74 will be invited to have an exit screen
- women will be invited to participate via the National Cancer Screening Register
- vaccinated women still require regular screening

http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/future-changes-cervical

“Renewal” of the National Cervical Cancer Screening Program



Marion Saville

“Renewal” of the National Cervical Cancer Screening Program

- National Cervical Screening Program 2016 Guidelines will be published early 2017
- Management:
  - Low risk

    HPV not detected - Repeat in 5 years
  - Higher risk

    HPV (16/18) detected OR HPV (not 16/18) + abnormalities

    Refer for colposcopy
  - Intermediate risk

    HPV (not 16/18) detected, no abnormalities

    Repeat in 12 months

The likely impact of the renewal of the cervical screening program in Australia on the prevalence of *Trichomonas vaginalis*: a modelling study

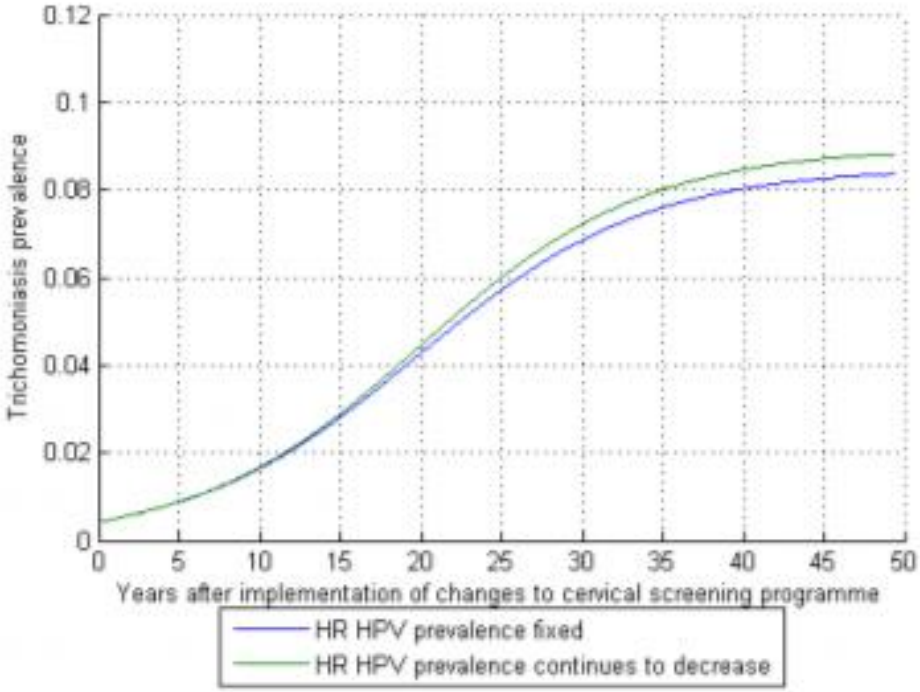
David Regan, Kirby Institute

- Trichomonas vaginalis (TV) prevalence <1% in urban Australia
- Testing not recommended for asymptomatic individuals
- Detected opportunistically through Pap smears
- Hypothesis: In the absence of further changes to guidelines, the renewal of the cervical cancer screening program will lead to an increase in TV prevalence in urban Australia over time

Renewal and TV

Results (3)

- Scenario 3: HPV testing replaces cytology, screening commences at age 25 and screening interval is 5-yearly
- Model predictions at t = 25 yrs
  - HR HPV prevalence remains constant: prevalence of TV infection will increase from 0.4% to 5.7%
  - HR HPV prevalence continues to decrease at current rate: prevalence of TV infection will increase from 0.4% to 6.0%



Ruelin C, Hui BB, Guy RJ, Donovan B, Regan DG, 2016

HIV, viral hepatitis and sexually transmissible infections in Australia Annual Surveillance Report 2016

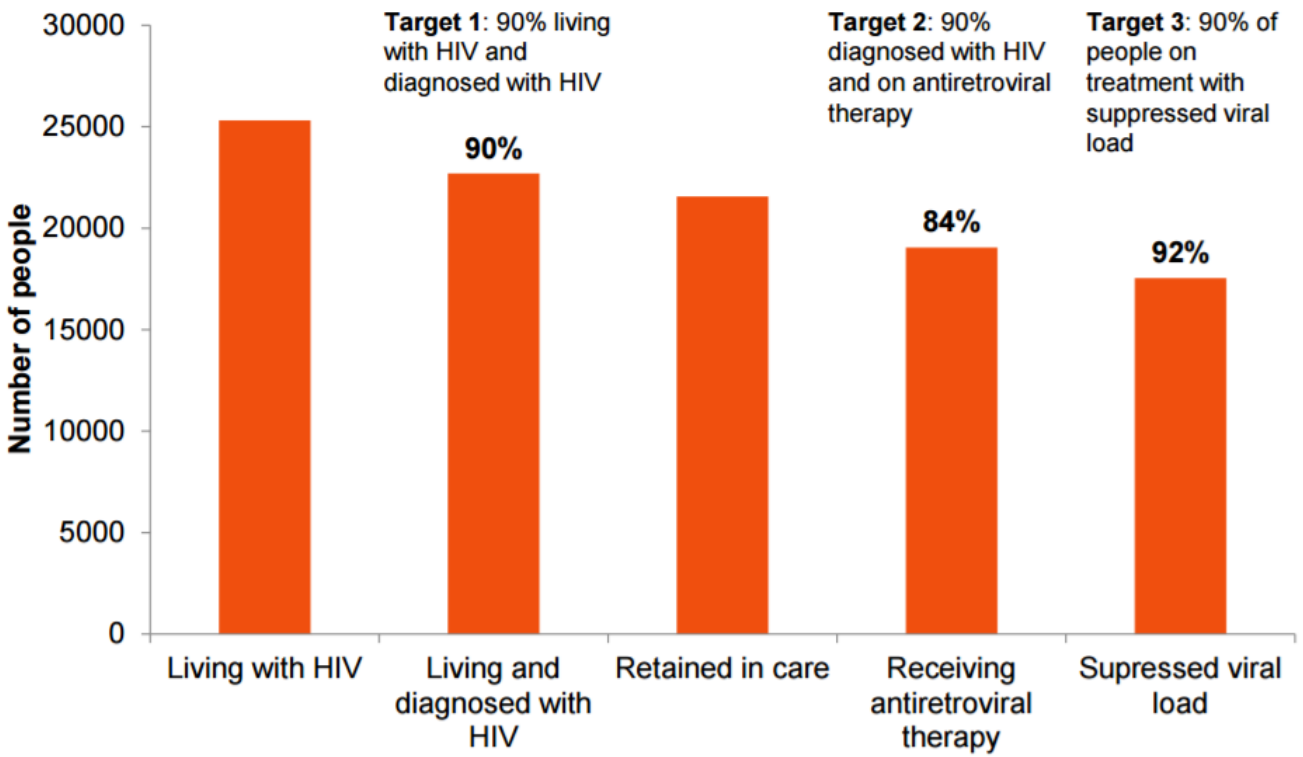
The Kirby Institute

HIV

- Notification rate stable
- 29% of new diagnoses were estimated to have an infection duration of longer than 4 years, based on immune function
- 27% increase in HIV testing in MSM in last 5 years
- 45% increase in treatment in MSM in last 10 years
- Zero mother to child transmissions from 2013 onward

Kirby Annual Surveillance Report 2016

The 2015 HIV diagnosis and care cascade



Kirby Annual Surveillance Report 2016

Hepatitis C

- Notifications stable since 2011
- 57% among those attending NSPs
- 29 070 severe fibrosis, 17 149 cirrhosis, 818 deaths

Hepatitis B

- Declining in Australian-born under 25yrs (due to vaccination)
- 24 months vaccination coverage 95% non-indigenous, 96% Aboriginal and Torres Strait Islander

Kirby Annual Surveillance Report 2016

Sexually transmissible infections

- 19% decline in chlamydia in 15-19yr in last 5 years
- Chlamydia testing rate in general practice has doubled to 16%
- Increasing gonorrhoea notifications, particularly in men
- Infectious syphilis rates increased from 6.5 per 100,000 in 2006 to 21.0 per 100,000 in 2015
- Four notifications of congenital syphilis in 2015 (3 in Qld), down from 11 in 2006 (1 in 2012, 7 in 2013)

Aboriginal and Torres Strait Islander Sexual Health

- HIV rate double the Australian-born non-indigenous population (6.8 vs 3.1 per 100,000)
- Hepatitis C rate 4 times greater, 43% increase in the past five years
- Hepatitis B rate 3 times higher, declining in young people
- Chlamydia rate 3 times higher
- Gonorrhoea 10 times higher, but a 22% reduction in 4 years (compared to a 94% increase in non-indigenous)
- Infectious syphilis 6 times higher

Men's role in childbearing decision making: implications for public education

Prof Robert McLachlan - Monash

- 1:20 men are "subfertile" – 60% with no identifiable cause

Five reasons to asses the male partner:

- Identify **treatable disorders**
- Provide a **diagnosis**
- Diagnose **co-existent disease**
- Consider **genetic issues**
- Counsel re **ART safety** (man & offspring)

Physical examination is essential

https://www.andrologyaustralia.org/

2016 Australasian HIV & AIDS Conference
16-18 November

HIV Cure - Where's the science up to?

Tony Kelleher – Kirby Institute & St Vincents

Latency – virus not transcribing

Mechanisms:

- Integration into silent gene / gene becomes silent
- Viral promoter competition with host gene
- Defective virus – not replication competent
- Epigenetic silencing

Only a small fraction (~0.1%) of total HIV DNA is replication competent and inducible

HIV Cure – Where's the science up to?

Cellular **reservoirs**

- T cells – all CD4+ T cells
    - Naïve, memory, follicular T helper cells
- Monocytes, macrophages and dendritic cells
- Brain
- Gut, genitourinary tract

How to control the reservoir?

- "Kick and kill" – activate virus in presence of ART
- Immunotherapies to enhance anti-HIV immune response ie. monoclonal antibodies

HIV Cure – Where's the science up to?

Kick and kill

- "kick" ie. with histone deacetylase (HDAC) inhibitors
    - HDACi non-specifically activate viral transcription (including defective virus)
- IL-2: massive T cell activation, reduction in viral RNA but no assessment of reservoir
- IL-7: increases the reservoir
- Therapeutic vaccines: best reduced viral load by 1 $\log_{10}$

Reservoir is small, but widely disseminated

Non-specific activation may have unwanted off target effects

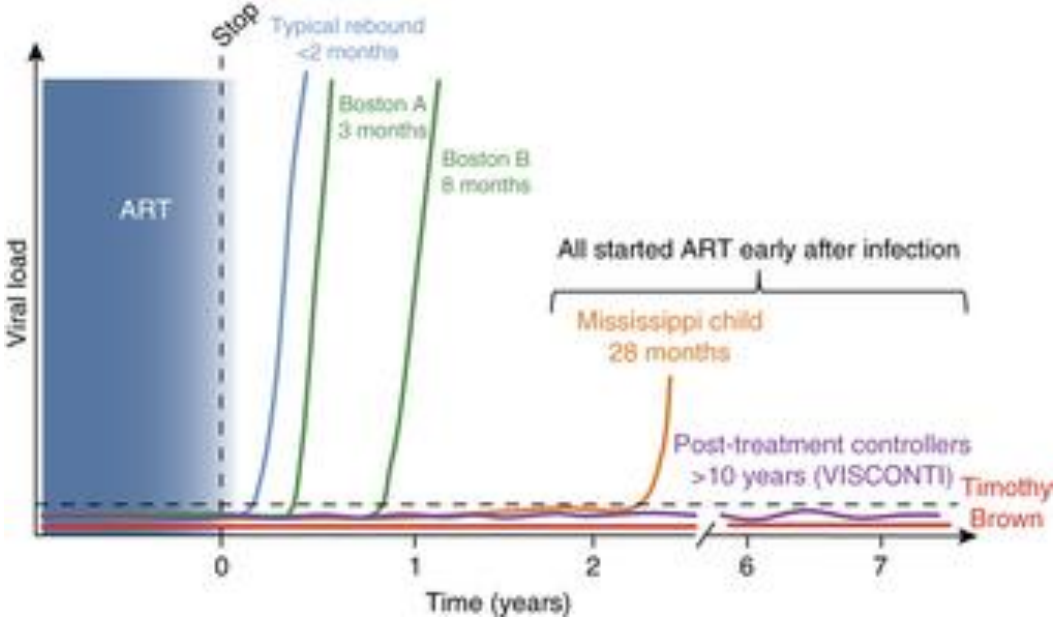
HIV Cure – What do the Clinical trials and cohorts tell us?

James McMahon – Monash & Burnet Institute

Current approaches to cure:

- Reduce the reservoir (kick & kill)
- Boost immunity to HIV
- Develop a HIV resistant immune system
- Early ART

Deeks, Lewin et al Nat Med 2016



HIV Cure – What do the Clinical trials and cohorts tell us?

Reduce the reservoir (kick & kill)

Latency reversing agent	Site of action	HIV latency	US HIV RNA	Plasma RNA	HIV DNA
Vorinostat	HDACi	Single dose[1] Intermittent[2] Continuous[3]	↑	↔	↔
Panobinostat	HDACi	Intermittent[4]	↑	+/-	↔
Romidepsin	HDACi	Weekly[5]	↑↑	↑↑	↔
Disulfiram	AKT activation	High dose[6]	↑	↑	↔
Bryostatin	PKC agonist	Low dose[7]	↔	↔	↔

1 Archin, Nature 2012; **2** Archin, J Infect Dis 2014; **3** Elliot J, PLoS Pathogens 2014; **4** Rasmussen, Lancet HIV 2014; **5** Sogaard PLoS Pathogens 2015; **6** Elliot J, Lancet HIV 2015; **7** Guiterrez, AIDS 2016

HIV Cure – What do the Clinical trials and cohorts tell us?

Boost immunity to HIV – Immune checkpoint blockade

Immune checkpoint blocker	Study design	Patient population	Outcome
Anti-PDL1 (BMS)	Dose escalation phase 1	Healthy	Ceased due to pre-clinical toxicity
Anti-PD1 (Merck)	Multi-dose phase 1B	Malignancy: AIDS defining or non-AIDS	Reservoir substudy
Anti-PD1 + Anti-CTLA4 (BMS)	Phase 1 Dose escalation	Malignancy: HIV-associated tumours including lung, anal, and Kaposi's sarcoma	Reservoir substudy
All immune checkpoint blockers	Observational study	Malignancy: melanoma or small cell lung cancer	Ongoing

HIV Cure – What do the Clinical trials and cohorts tell us?

Develop a HIV resistant immune system

- ART + α4β7 monoclonal antibody in macaques → prolonged virological control and restoration of CD4+ cells (persisted after termination)
- Clinical trial ongoing of Vedolizumab (α4β7) infusions followed by ART interruption
- Gene therapy – CCR5 knockout ie. CRISPR

HIV Cure – What's in it for me? – Balancing hope and scepticism about HIV cure research

Brent Allen – Living Positive Victoria

Australia has an outstanding history of people living with HIV participating in many different kinds of research

How do you prepare yourself or others for a cure? If it's tomorrow, or in ten years time, how do you prepare to change your identity?

Pre-clinical evaluation of a mucosal HIV vaccine strategy

Charani Ranasinghe – ANU

- Mucosal (intranasal) immunisation gives broad protection of the genitorectal mucosa
- In non-human primates, a single dose of a poxviral vector-based HIV/SIV gag/pol/env vaccine induced excellent env-specific antibodies post-challenge (similar to HIV elite controllers)

A Novel Mucosal HIV Vaccination Regimen Involving Live Recombinant Human Rhinovirus and DNA Vaccines to Elicit Protective HIV-Specific Immunity

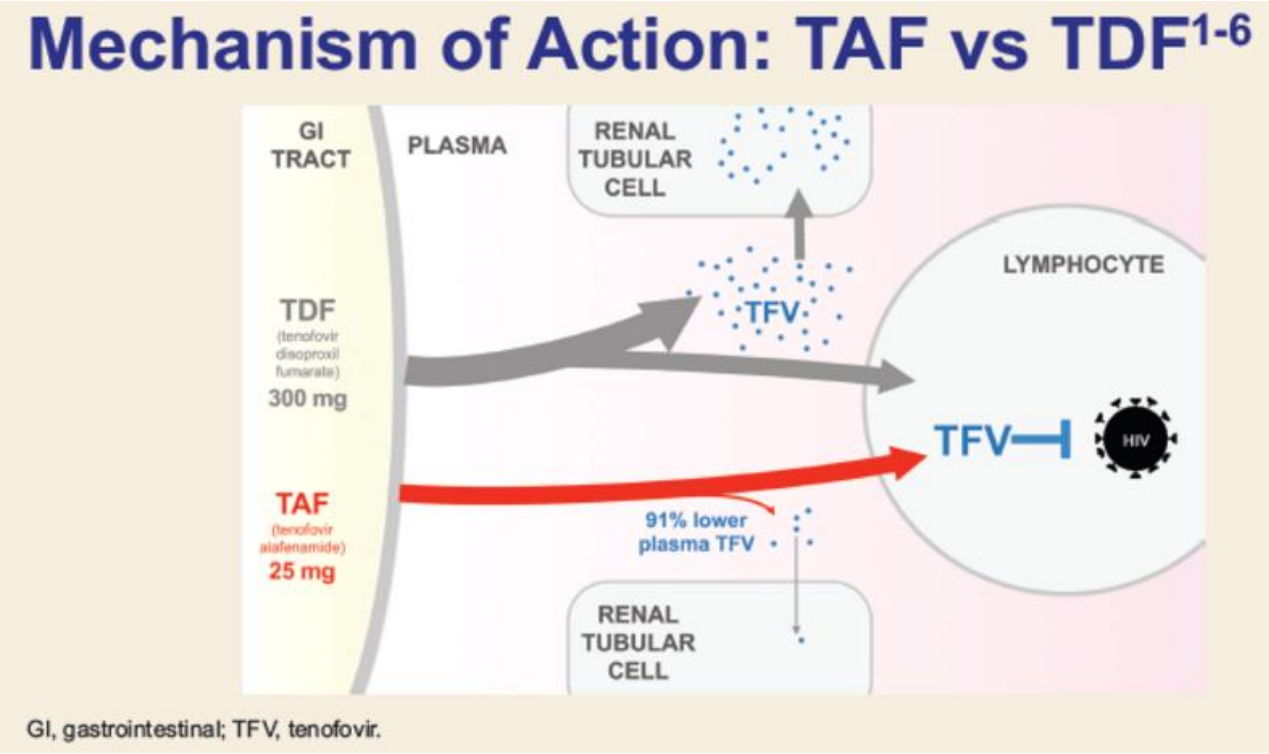
Danushka Wijesundara – The University of Adelaide

- "HIV vaccine research: Adelaide team achieves 'glimpse in right direction'" – ABC News, 21 Nov 2016
- Vaccinated mice had a 10 fold lower viral load compared to unvaccinated after 7 days, with non-classical neutralizing antibodies to Tat (HIV encoded transcription factor)
- First evidence that a rHRV-DNA vaccination can elicit protective HIV-specific immunity

- http://www.abc.net.au/news/2016-11-21/hiv-vaccine-research/8042526

Descovy

- Available on the PBS 1st December 2016
- Emtricitabine 200mg / Tenofovir alafenamide (TAF) 25mg



Levin J, EACS 2015

Pharmacokinetic-pharmacodynamic (PK-PD) of Emtricitabine/Tenofovir alafenamide (F/TAF) demonstrated wide exposure range associated with clinical safety

Paul Slade – Gilead Sciences

- F/TAF compared to F/TDF
- No difference in drug-related serious adverse events or discontinuation due to adverse events
- No difference in hip and spine BMD or fasting lipids after 48 weeks

A Case Study of HIV Detection Following Post-Exposure Prophylaxis

Julian Langton-Lockton – Nepean Sexual Health and HIV Clinic

- 21 yr old MSM university student
- Presented 36 hrs after high risk HIV exposure (involving “Ice” and multiple casual male partners)
- Prescribed Tenofovir/Emtricitabine and Raltegravir

PEP Case Study

	Baseline
HIV Ab/Ag	Negative
Syphilis	**TPPA Positive** FTA Negative VDRL Negative
Chlamydia Gonorrrhoea	Negative by PCR
Liver Function Tests	ALT 103 AST 164 CK 4138
Hepatitis BsAb	>1000
Hepatitis C Ab	Negative

PEP Case Study

- Diagnosed with HIV 3 weeks into PEP
- Viral load undetectable
- Recommended to continue Tenofovir/Emtricitabine and Raltegravir
- Used Single Copy Assay to monitor at 4, 7, 9, 17 and 67 weeks
- At 67 weeks, HIV RNA levels were <0.3-0.5 copies/ml for 4-7ml samples (limit of detection of assay)

- Was this failed PEP? Was 36hrs too late?
- Can treatment in “hyper acute infection” achieve functional cure?

PrEP at age 6

Jared Baeten – University of Washington

What should we expect from a 6 year-old? Developmental milestones?

1. Begin to understand cause-and-effect relationships
   = take it, it works
2. Magical thinking quickly fades
   = only 5 year olds believe in magic bullets
3. Starts to understand the feelings of others
   = PrEP is wanted, and wanted in deep ways
4. Becomes more flexible in their thinking
   = PrEP makes us think differently
5. Understands more about their place in the world
   = Time to think big

HIV Management in Australasia: a guide for clinical care

http://hivmanagement.guidelines.org.au/

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