PEP: INTEREST 2015

Francois Venter
Wits Reproductive Health and HIV Institute (RHI)

GUIDELINES

POST-EXPOSURE PROPHYLAXIS

- http://www.sahivsoc.org/ - or go to http://www.sahivsoc.org/upload/documents/guidelines_nov_2008.pdf
- Sensible!

"Are these just guidelines, or are they actual new policies?"


POST-HIV EXPOSURE PROPHYLAXIS GUIDELINES
The following actions should be taken immediately upon possible exposure to HIV:
1 Treatment of exposure site
Wounds and skin sites:
Wash with soap and water
Mucous membranes:
Flush with water
2 Timing of post-HIV exposure prophylaxis initiation
If therapy is necessary, prophylaxis should be initiated promptly, preferably within 1 to 2 hours post-exposure
3 Assessment of exposure risk
High risk exposure is:
exposure to a large volume of blood or potentially infectious fluids
injury with a hollow bore needle
deep and extensive injury
drug resistance in source patient
4 Post-HIV exposure prophylaxis
Risk category
Low Risk
RETROVIR® 200mg 8-hourly
3TC® 150mg 12-hourly
High Risk
RETROVIR® 200mg 8-hourly
3TC® 150mg 12-hourly
Indinavir 800mg 8-hourly
Duration
28 days
5 Recommended drug toxicity and HIV serology testing after exposure
Time period from exposure
Recommended tests
Baseline
Full blood count
Liver & renal function tests
HIV serology
Two weeks
Full blood count
Liver & renal function tests
Six weeks
HIV serology
Three months
HIV serology
Six months
HIV serology
Your Life May Depend On It
3TC®/Retrovir®
HIV/AIDS Hotline 0800 110 605
GlaxoWellcome

Is it a problem?

- Huge number of traditional occupational exposures – not just side effects, costs, also anxiety, burnout
- Other exposures – bewildering array, as awareness goes up – more request for PEP

Big thorny questions in PEP?

- Should I give antiretrovirals? (and high vs low risk)
- Should I give 2 or 3 drugs?
- Role of pre-exposure prophylaxis?

Big new ideas

- Make peace with limited data – and that we are unlikely to get better ‘pure PEP’ data
- Occupational vs non-occupational
- Safe ‘third’ drugs

Classic division: Occupational vs non-occupational (vs PMTCT)

- Mucosal splashes, needlesticks, bites
- Helping at traffic accidents
- Sharing needles
- Sport injuries
- Sex worker and burst condom
- One night stands, cheating on partner
- Veno-terrorism
- Exposure to sex toys
- Cat-scratch disease
- The clumsy hijacker
- The nursery school and biting

Occupational

- Management's fault!
- Hep B
- Structural alterations: Workplace, times, access to PEP

Type of exposure (HIV)	Risk
Needlestick	**0.3%**
Mucous membrane	**0.1%**
Receptive oral sex	0-0.04%
Insertive vaginal sex	<0.1%
Insertive anal sex	<0.1%
Receptive vaginal sex	0.01-0.15%
Receptive anal sex	<3%
Sharing IDU needle	0.7%
Transfusion	**90-100%**

UNAIDS

Source: UNAIDS

- Anal sex – 33x increase vs vaginal
- Uncircumcised – 8x over circumcised
- Ulcerative – 6x vs no ulcer
- Early infection – 2.5 vs mid-point
- Late – 1.85x vs midpoint

- “Can climb to 1/10-1/3.”

Powers K, Poole C, Pettifor A, Cohen M. Rethinking the heterosexual infectivity of HIV-1: A systematic review and meta-analysis. 3rd International

Workshop on HIV Transmission: Principles of Intervention. July 31-August 2, 2008, Mexico City. Abstract 14.

New CDC risk table

Estimated Per-Act Probability of Acquiring HIV from an Infected Source, by Exposure Act[a]

Type of Exposure	Risk per 10,000 Exposures
Parenteral	
Blood Transfusion	9,000[b]
Needle-sharing during injection drug use	67[c]
Percutaneous (needle-stick)	30[d]
Sexual	
Receptive anal intercourse	50[e, f]
Receptive penile-vaginal intercourse	10[e, f, g]
Insertive anal intercourse	6.5[e, f]
Insertive penile-vaginal intercourse	5[e, f]
Receptive oral intercourse	low[e, i]
Insertive oral intercourse	low[e, i]
Other[h]	
Biting	negligible[j]
Spitting	negligible
Throwing body fluids (including semen or saliva)	negligible
Sharing sex toys	negligible

How effective is PEP?

- IF you take it? Probably>90% (off low baseline in most cases)

Recent data…

- PrEP data suggests ART very effective IF you take it
- 052: Treat the partner; also, implications for needlesticks
- TDF/FTC and AZT most evidence based; CCR-5 blockers and integrase inhibitors interesting

Will we give out PEP for sexual exposure?

- We probably should…
- Same lessons as emergency contraception – but 28 days
- ?opportunity here to make this available over the counter? Like ‘’Plan B””?

Estimated Per-Act Probability of Acquiring HIV from an Infected Source, by Exposure Act[a]

Type of Exposure	Risk per 10,000 Exposures
Parenteral	
Blood Transfusion	9,000[b]
Needle-sharing during injection drug use	67[c]
Percutaneous (needle-stick)	30[d]
Sexual	
Receptive anal intercourse	50[e, f]
Receptive penile-vaginal intercourse	10[e, f, g]
Insertive anal intercourse	6.5[e, f]
Insertive penile-vaginal intercourse	5[e, f]
Receptive oral intercourse	low[e, i]
Insertive oral intercourse	low[e, i]
Other[h]	
Biting	negligible[j]
Spitting	negligible
Throwing body fluids (including semen or saliva)	negligible
Sharing sex toys	negligible

Occupational versus non-occupational

- WHO following Society lead– dumped these categories (some ‘special occupations’ in new guidelines)
- BUT: major medico-legal consequences, hence may justify more monitoring
- “You are more at risk of HIV off duty than on duty”

Who thinks they are risk?

- Surgeons/Obstetricians – NO transmission with a hollow needle; no confident transmission
- Surgery usually very controlled environment – lighting, paralysed patient, often daylight hours in case of cold surgery
- Intake wards/casualty a different story

Who is at risk?

- #1 Lab techs
- #2 Junior nurses
- #3 Junior doctors
- … others

Should we give a third drug?

- Or even a second drug?
- NO data on this – whether adding gives additional protection or any drug being better than the other (and we probably will never know)
- Adds very little to current prevention BUT
- Simpler, less anxiety
- Problem is toxicity and cost

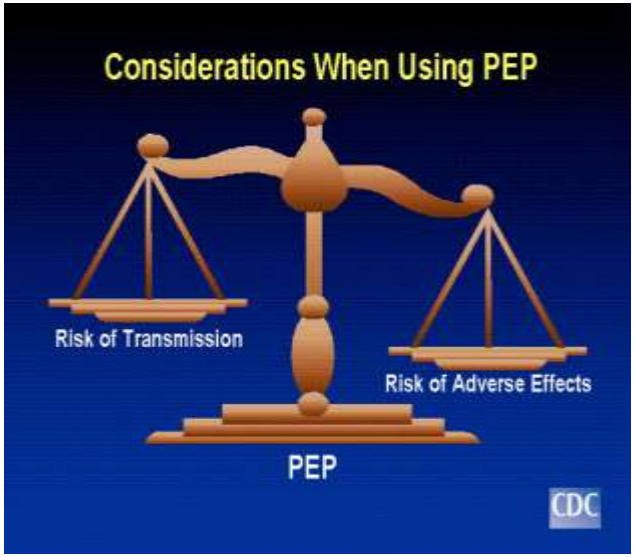

09:58
1
Talk on pep 09:57
Mother f[redacted]side effects are horrible 09:57
Tell them that 09:57
:) 09:57
Alluvia sucks 09:57
Sorry
You
I
And

Which third drug?

- Lop/rit safer than Ataz/rit; Darunavir/rit now an option
- EFV – unpopular
- Integrase inhibitors – decrease price, excellent side effect profile

But…

- Weigh up rare but serious side effect vs very rare transmission event (for a disease that is now easy and cheap to treat)



WHO guidelines

- Almost all low quality evidence (except adherence!)

Big recommendations

A two antiretroviral drug regimen is effective but three drugs are preferred.

Which drug?

Preferred antiretroviral regimen for adults and adolescents

TDF+3TC(or FTC) is recommended as the preferred backbone regimen for HIV PEP in adults and adolescents.

LPV/r or ATV/r are suggested as preferred third drugs for HIV PEP in adults and adolescents.

Where available the following alternatives can be considered: DRV/r, RAL, EFV.

(Conditional recommendation, very low quality of evidence)

Preferred antiretroviral regimen for children ≤10 years

AZT+3TC is recommended as the preferred backbone for HIV PEP in children 10 years and younger. ABC+3TC or TDF+3TC (or FTC) can be considered as alternative regimens.

(Strong recommendation, low quality evidence)

LPV/r is recommended as the preferred third drug for HIV PEP in children less than 10 years.

Prescribing frequency

A full 28 day prescription of antiretrovirals should be provided for HIV PEP following initial risk assessment.

Adherence support

Enhanced adherence counselling is suggested for all individuals initiating HIV PEP.

(Conditional recommendation, moderate quality of evidence)

<72 hours?

- Based on animal models and observational data
- BUT…

NATURE | LETTER

Rapid seeding of the viral reservoir prior to SIV viraemia in rhesus monkeys

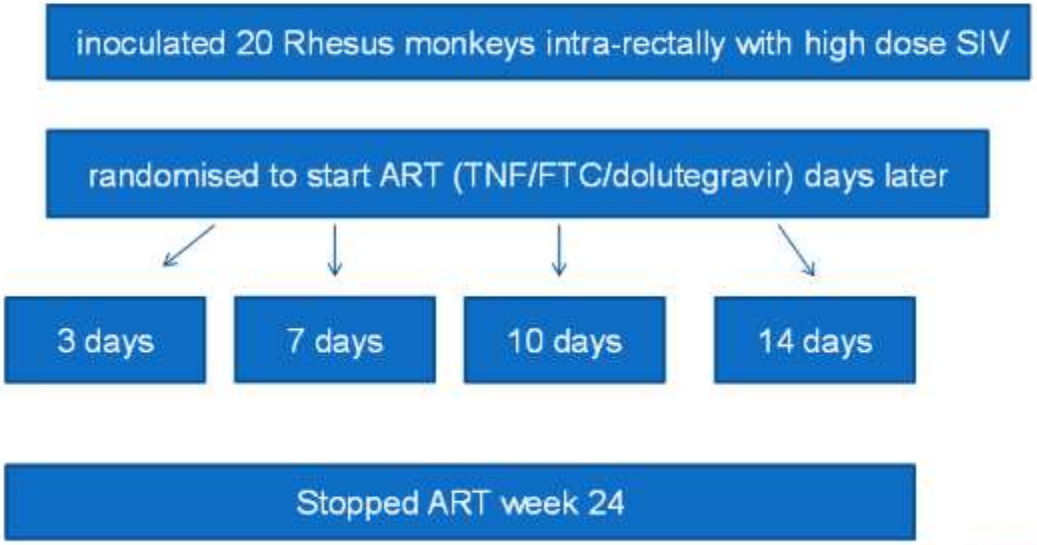
James B. Whitney, Alison L. Hill, Srisowmya Sanisetty, Pablo Penaloza-MacMaster, Jinyan Liu, Mayuri Shetty, Lily Parenteau, Crystal Cabral, Jennifer Shields, Stephen Blackmore, Jeffrey Y. Smith, Amanda L. Brinkman, Lauren E. Peter, Sheeba I. Mathew, Kaitlin M. Smith, Erica N. Borducchi, Daniel I. S. Rosenbloom, Mark G. Lewis, Jillian Hattersley, Bei Li, Joseph Hesselgesser, Romas Geleziunas, Merlin L. Robb, Jerome H. Kim, Nelson L. Michael + *et al.*

Affiliations | Contributions | Corresponding author

Rapid seeding of SIV viral reservoir in rhesus monkeys

Whitney Nature 2014

Investigated how quickly reservoir established after infection



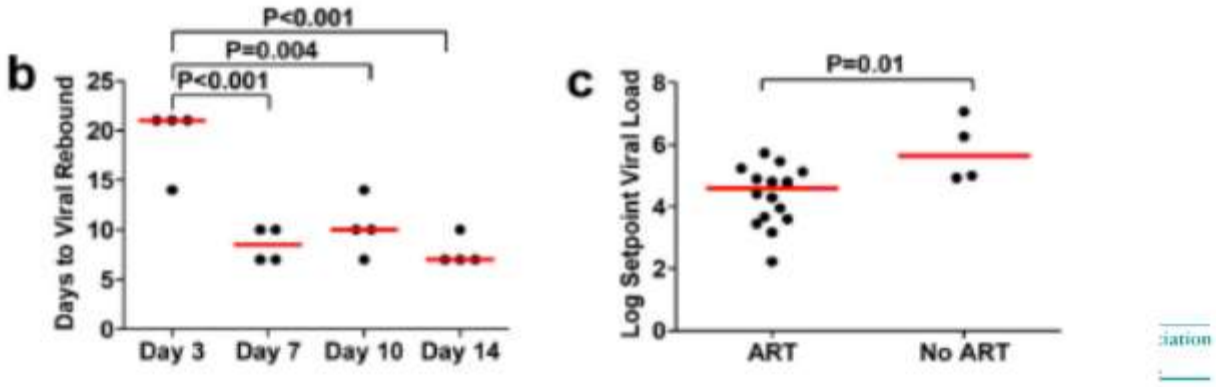
British HIV Association
BHIVA

on ART

	Day 3	Day 7	Day 10	Day 14
Plasma RNA ever	No	Yes	Yes	Yes
Plasma proviral DNA ever	No	Yes	Yes	Yes
Immune responses (cellular and humoral) ever	No	Yes	Yes	Yes
viral evolution	No			
Tissue proviral DNA	+ v.low and ↓ over time (absent in ¼ week 20)	+++ stable after week 12	+++ stable after week 12	+++ stable after week 12

Off ART: All rebounded

- Day 3 ART group had a 3 fold delay in viral rebound viraemia
- Rebound RNA set point was lower in all groups compared to ART naïve controls (with no difference between randomisation groups)



For slightly richer countries?

- WHO guidelines plus…
- Recommend integrase inhibitors as third drug (?rilpivarine, others)
- All usual suggestions around hepatitis B, followup etc etc

The principles for occupational and non-occupational are similar

- Prevention – management structures, hep B vaccines
- Anxiety management critical
- HIV/hep B baseline important
- Discourage unnecessary tests
- Encourage full completion of 28 day course
- Don’t dwell too hard on 2 vs 3 drugs
- ACTIVE side effect management

SAVE THE DATE

3rd Southern African HIV Clinicians Society Conference

13 – 16 April 2016

Sandton Convention Centre
Johannesburg, South Africa

www.sahivsoc2016.co.za