Mountain West AIDS Education and Training Center

Non-occupational HIV Post Exposure Prophylaxis (nPEP)

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Updated guidelines to the 2005 DHHS nPEP guidelines providing recommendations on the use of antiretroviral nPEP and other aspects of case management for persons exposed to HIV outside of occupational settings

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https://stacks.cdc.gov/view/cdc/38856

nPEP 2016

- Clinical effectiveness
- Animal studies
- Risk analysis
- Preferred and alternative nPEP regimens
- Laboratory evaluation
- Handling other STIs
- Special populations
- nPEP----> PrEP
- Guideline issues
- Summary

nPEP 2016: Clinical Effectiveness

- Retrospective analysis of HCWs exposed to HIV who were treated with AZT (or not): 81% reduction in transmission
- MSM
  - One nPEP failure with late seroconversion and HCV transmission
  - Six studies of 1535 cases with 48 nPEP failures
    - 40/48 had ongoing risk factors and 35/40 seroconverted > 180 days post nPEP
    - 8/48: one infected with 184V, three provided no information on nPEP timing, regimen choice and adherence and four had delayed seroconversion (days + 91,133,160 and 168)
  - Brazilian study: N=200, given 4 day starter pack and follow up visit for the remaining 28 days
    - 68 took the starter pack: 1 seroconversion
    - 10/132 who did not take the starter pack acquired HIV

Cardo NEJM 1997; Terzi AIDS 2007; Donnell AIDS Behav 2010, Sonder Sex Transmit Dis 2010; Schechter JAIDS 2004; McAllisiter HIV Med 2014; Jain AIDS Pat Care STDs 2015; Foster CID 2015

nPEP 2016: Clinical Effectiveness

- Sexual assault: studies have limited reporting of baseline status, nPEP completion, follow-up:
  - No reports of HIV transmission

- Mixed exposures/other populations (sexual and non-sexual exposures; children, adolescents and adults, international and domestic):
  - 15/19 studies with completed nPEP: 19 transmissions but only 1 nPEP failure (18/19: incomplete nPEP, ongoing risks, etc)

- Perinatal (PMTC): it works – but hard to isolate effect of nPEP to the infant from breast feeding risk, and peri-partum treatment and treatment of mother

nPEP 2016: Animal Studies

Initial study

- Macaques exposed to SIV by *intravenous* injection were given daily subcutaneous TDF starting
  - 48 hours pre (N=15): no transmission
  - 4 hours pre (N=5): no transmission
  - 24 hours post-inoculation (N=5): no transmission
  - No TDF (N=10): all infected

Tsai Science 1995,

nPEP 2016: Animal Studies

Where does the 28 day course come from?

- 24 Macaques were *intravenously* inoculated with SIV and treated with subcutaneous TDF at various times relative to inoculation and for variable durations

Group	Seroconversion	PBMC + DNA
No treatment	4/4	4/4
24 hour post for 28 days	0/4	0/4
48 hour post for 28 days	4/4	4/4
72 hour post for 28 days	4/4	2/4
24 hour post for 10 days	3/4	1/4
24 hour post for 3 days	4/4	2/4

Tsai J Virology 1998

nPEP 2016: Animal Studies

Where does the 72 hour breakpoint come from?

- 16 Macaques were *intravaginally* inoculated with HIV-2 and treated with subcutaneous TDF at various times relative to inoculation

Group	Seroconversion	PBMC + DNA
No treatment	3/4	3/4
12 hour post for 28 days	0/3	0/3
36 hour post for 28 days	0/4	0/4
72 hour post for 28 days	1/3	1/3

Otten J Virology 2000

nPEP 2016: Case Presentation

- A 21 yo gay man was celebrating his birthday and was taken to a local bathhouse after closing two bars. He remembers little but according to “friends” engaged in RAI with several anonymous partners.
- Three days later he notices dysuria, urethral discharge and rectal discomfort.
- He presents to the STD clinic and is diagnosed with urethral and rectal GC
- He is concerned about contracting HIV and asks about PEP
- What do you advise?

nPEP 2016: Risk Analysis

Risk per Act

Increased risk:
STDs, high VL

Decreased risk:
Condoms, ART, PrEP, circumcision

Exposure	Rate/10,000
Parenteral	
Blood transfusion	9250 (93%)
Sharing needles (IDU)	63 (0.6%)
Needle-stick	23 (0.2%)
Sexual	
Receptive anal	138 (1.4%)
Receptive vaginal	8 (0.08%)
Insertive anal	11 (0.1%)
Insertive vaginal	4 (0.04%)
Receptive oral	low
Insertive oral	low
Other	
Biting, spitting, sex toys, etc	negligible

http://www.cdc.gov/hiv/policies/law/risk.html

nPEP 2016: Risk Analysis

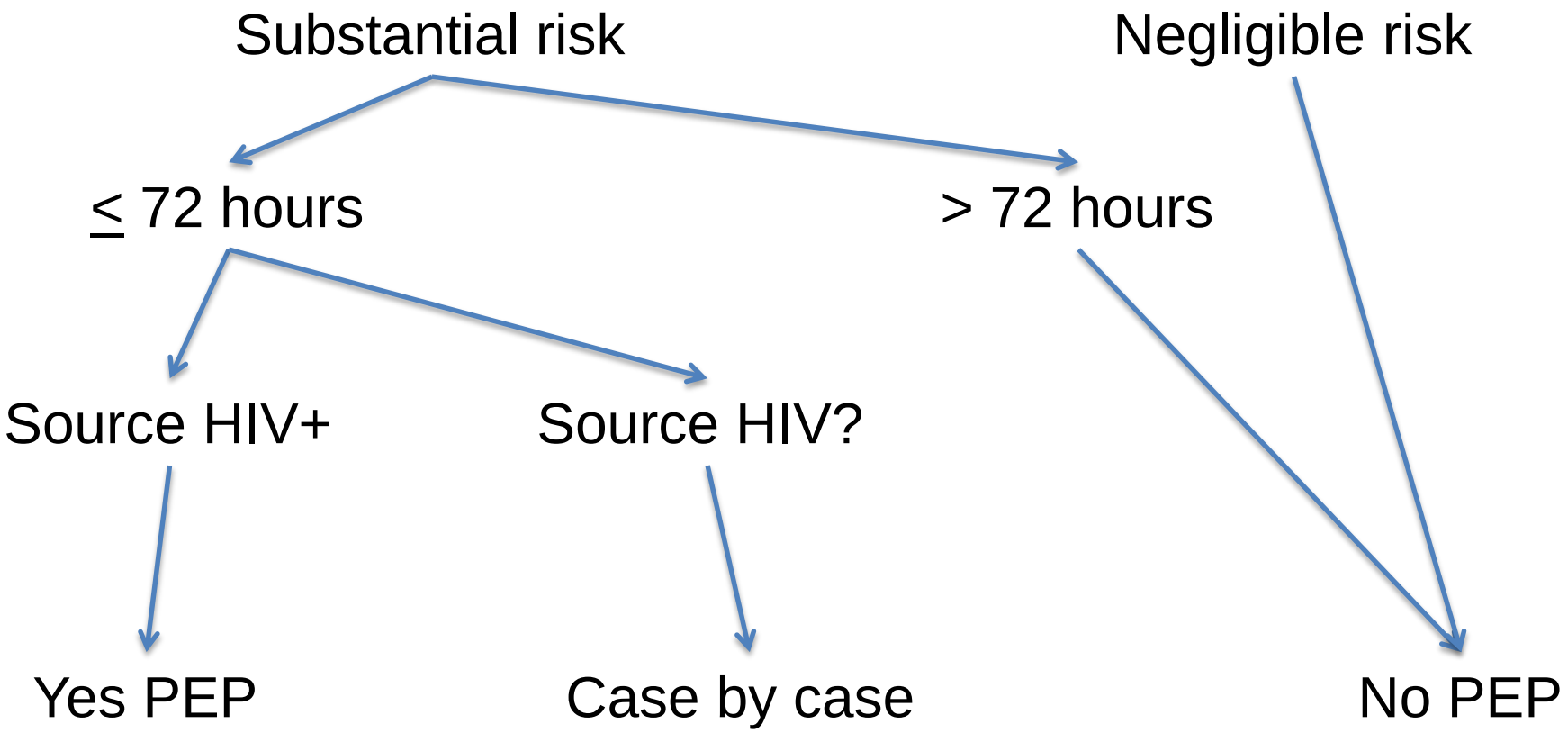
Risk Assessment: The incident

Substantial risk	Negligible risk
Exposure of mucous membranes, non-intact skin or percutaneous route	Exposure of anything: mucous membranes, skin, or percutaneous route
Blood, semen, vaginal secretions, rectal secretions, breast milk or any body fluid with visible blood: from an HIV+ person	Urine, saliva, sweat, tears, nasal secretions – all without visible blood

Risk Assessment: The source

Group	HIV prevalence
Rhode Island	Prisoners 3%, rapists 1%, general population 0.3%
Seattle	MSM 12-17%, IDU < 2%, general population < 1%

nPEP 2016: Risk Analysis



nPEP 2016: ART Regimens

Patient group	Preferred/alternative	Regimen
Adults and adolescents ≥ 13, including pregnant women with CrCl > 60	Preferred	TDF/FTC + RAL or DTG
	Alternative	TDF/FTC + r/DRV
Adults and adolescents ≥ 13, including pregnant women with CrCl ≤ 59	Preferred	AZT/3TC + RAL or DTG
	Alternative	AZT/3TC + r/DRV

nPEP 2016: ART Regimens

Patient group	Preferred/alternative	Regimen (dose adjusted)
Children 2-12	Preferred	TDF/FTC + RAL
	Alternatives	AZT/3TC + RAL or r/LPV TDF/FTC + r/LPV or r/DRV
Children 4 wks – 2 years	Preferred (solutions)	AZT/3TC + RAL or r/LPV
	Alternative (solutions)	AZT/FTC + RAL or r/LPV
Children birth to 4 wks	Call a pediatric HIV specialist	

nPEP 2016: ART Considerations

- Never use!!!
  - Nevirapine (hepatitis and hepatic failure)
  - Abacavir (hypersensitivity reaction and no time for HLA testing)
- Pregnant or potentially pregnant
  - Avoid efavirenz in 1st trimester (teratogenic?)
  - No nevirapine (hepatic failure)
  - No stavudine/didanosine (steatosis, lactic acidosis, pancreatitis)
- Starter packs Vs the whole 28 days
  - Starter packs and return appt in 3-5 days offer the opportunity to check on medication tolerability, original decision to take nPEP, provide additional counseling
  - Just giving the 28 days from the outset is associated with better nPEP adherence and completion
- Counsel to have protected sex until follow up testing negative

nPEP 2016: ART Consideration

- Overall adherence to nPEP is 40-66%.
  - Lower adherence rates for assault victims, those getting starter packs and those in developed countries
  - Lower adherence for regimens with AZT > TDF and PIs > RAL
- Cost effective analyses: with threshold of $60,000/QALY
  - Only nPEP for RAI is cost effective
- PEPline: 888-448-4911
- Financial assistance; pharma assistance
  - http://www.pparx.org/en/prescription_assistance_programs/list_of_participating_programs.

nPEP 2016: Laboratory Evaluation

Test	Source	Exposed person			
	Baseline	Baseline	4-6 wks	12 wks	24 wks
HIV Ag/Ab	X	X	X	X	If HCV acquired
Hep B (sAg, sAb, cAb)	X	X			If HBV susceptible
HCV Ab	X	X			If HCV exposed
Syphilis	X	X	X		X
GC/CT	X	X	If not treated		
β-HCG		X	X		
		If prescribed nPEP			
Creatinine		X	X		
ALT/AST		X	X		

nPEP 2016: Handling STIs

- Consider empiric treatment for GC/CT
- Plan B for women who are sexually assaulted
- STI prophylaxis is not recommended for sexually abused or assaulted children
- Hepatitis B
  - Exposed, unvaccinated: start the Hep B vaccine series
  - Exposed, unvaccinated and source known Hep BsAg+: HBIG and HBV vaccine
  - Exposed, vaccinated but unknown response: HBV vaccine
- HPV: assault victims: women (9-26), men (9-21, MSM to 26) – can start the HPV vaccine series

nPEP 2016: Case Presentation

- A 28 yo woman IDU began sharing injection equipment with a new partner 1 month ago. She just discovered he is HIV infected and her menses is 10 days late.
- A pregnancy test is +, she plans to complete the pregnancy, remains committed to her new partner who has no plans to start anti-retroviral therapy.
- How do you advise her regarding the need for nPEP and PrEP?

nPEP 2016: nPEP→PrEP

- “If patient’s ongoing risk required sequential or near-continuous PEP” consider transitioning to PrEP
- “No evidence that PEP delays seroconversion”: therefore no gap between the completion of PEP and start of PrEP is required.”

nPEP 2016: Guideline Issues

- The 72 hour limit?
  - Based on minimal animal data and what there is suggests still some benefit at 72 hours
  - The oPEP guidelines are softer regarding the 72 hour limit: “The interval after which no benefit is gained from PEP for humans in undefined”
- Oral sex and HIV transmission? Controversial
  - Up to 8% of new HIV infections in SF (Dillon, CROI 2000, #473)
  - 0.04% per act receptive oral sex (Vittinghof, AM J Epidem, 1999, 150:306-11)
  - Population attributable risk of 0.1 to 0.31% (Page-Shafer, AIDS, 2002, 16:2350-52)

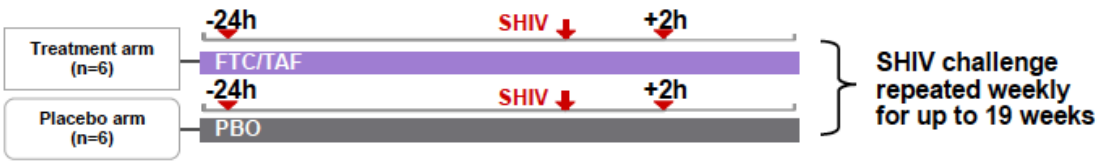
nPEP 2016: Guideline Issues

- Delayed seroconversion due to PEP
  - nPEP guidelines says it can occur with coincident HCV infection
  - Dismissive of other circumstances – but this is probably incorrect
- Aligned with oPEP? There are differences:
  - oPEP guideline has a much softer stop at the 72 hour threshold
  - Recommends follow up HIV testing at 4 months rather than 3
  - Preferred regimen still TRU + RAL but no mention of DTG and alternatives include: Truvada or Combivir + r/DRV or r/ATZ or r/LPV or ETR or RLP
  - Recommends toxicity labs of CBC + CMP at baseline and 2 weeks

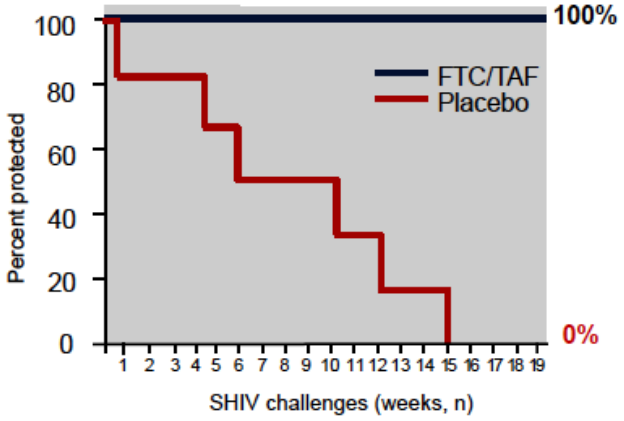
nPEP 2016: Guideline Issues

- What about TAF? Currently NOT recommended.
  - Rectal and vaginal levels of TAF are much lower than TDF
  - But TAF was protective in *PrEP* animal model:

FTC/TAF PrEP Protects Macaques from Rectal SHIV Infection



- FTC/TAF prevents rectal SHIV infection in macaques to a degree similar to that previously found with FTC/TDF but with a substantially reduced TFV dose[1]
  - FTC/TAF protected 100% of macaques (N=6) challenged with SHIV in a similar, pre-clinical trial[2]



FTC/TAF should not be used for PrEP in humans until a planned clinical study is completed

1. Massud I, et al. CROI 2016. Boston, MA. #107
2. Heneine W, et al. CROI 2006. Denver, CO. #32LB

nPEP 2016: Summary

- Evaluate for nPEP ≤ 72 hours post incident
- Use rapid Ag/Ab or Ab testing – if not available – begin nPEP and get testing later
- No nPEP > 72 hours?
- Use TDF/FTC + RAL or DTG
- Alternative is TDF/FTC + r/DRV
- Assess and treat for trauma, GC/CT, syphilis, pregnancy and Hepatitis B and C
- For those with ongoing risks or anyone with ≥ 1 nPEP in the last year consider PrEP