



Party-Packs

Issues Surrounding the Use of PrEP

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Learning Objectives

- To explain the physiologic basis of PrPEP.
- To describe animal and human clinical trials involving PrEP.
- To describe potential advantages and disadvantages of widespread PrEP use.
- To discuss the potential application(s) of PrEP in clinical practice.

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The Apple



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The Mosquito



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Definitions

- PEP: postexposure prophylaxis
- nPEP: non-occupational postexposure prophylaxis
- PrEP: preexposure prophylaxis
- PEPSE: postexposure prophylaxis following sexual exposure

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PrEP

- Involves chemoprophylaxis before a high risk exposure
- Therapy continues through the anticipated 'at risk' period
- In cases where infection occurs - PrEP is D/C immediately
- Requires more frequent screening

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What We Know -HIV Risk-

- Percutaneous exposure:
0.32% (95% CI 0.18-0.46)
- Mucous membrane:
0.1%
- Skin exposure:
<0.1%

MMWR 1990;RR1:1-14.

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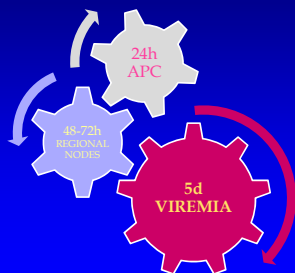
Perinatal Precautions

- Intrauterine - ACTG Protocol 076
- Transmission rate reduction from 26% to 8%
- Correlation with mothers viral burden

MMWR 1994;43:285-7.

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'The Window of HIV Opportunity'



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Impetus

- Millions of worldwide infections
- No significant decreases in overall HIV incidence/prevalence
- 2.7 million new infections in 2008
- No vaccine to date/setbacks
- Anecdotal reports of community use
- Not a novel concept (OIs, influenza)

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Condoms?

- Availability
- Cost
- Preference
- Religious barriers
- Negotiation

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Off-label TF Use

- Circuit party attendees (MTV, Party-Packs)
- Bath houses
- "Club drug" users

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PrEP versus PEPSE

- 'the earlier the better'
- ACTG 076
- Difficulties in access and dosing immediately following time zero (PEPSE)
- *Continual dosing* of PrEP - eliminates access issues and need to self-identify high risk exposures

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Pharmacology

- ARVs consistently ↓ genital tract viral burden
- NRTIs concentrate must efficiently in semen (AZT/3TC achieve concentrations > than those found in the plasma)
- PIs poorly penetrate the genital tract
- Raltegravir: promising initial data

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PrEP Dosing Schemes

- Topical microbicide
- Oral therapy
- Combination

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PrEP Dosing Schemes

- QD*
- Weekly (1-5 doses per week)
- Event-based (disco-dosing, Pocket PEP, T-ing)
- Routine plus event-based (1-3/week base)
- Periodic (around life events)

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PrEP

- Strong non-human primate data
- Challenge: models and agents?

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ANIMAL DATA

CLINICAL FOUNDATIONS

PrEP Macaques - SIV

- 25 animals
- TF 48 h prior, 4 h post, 24 h post IV inoculation x 28 days
- Zero infections
- Extent of protection was 'weakest' when TF was initiated 24h post infection

Tsai CC, Science 72:1998.

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PrEP Macaques - SIV

- 6 animals
- Oral TF delayed infection after repeated exposures and prevented infection in 1/4 animals
- 6 of 6 animals receiving SQ TF-FTC were completely protected
- No significant resistance or toxicity

Tsai CC, Science 72:1998.

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HUMAN DATA

Models? Agents? Regimens?

Antiretrovirals Reduction in 'Infectiveness'

- 415 discordant Ugandan couples
- Infectivity a factor of viral burden (serum/genital tract)
- Risk of infection increased directly with increasing viral burden

QuinnTC, NEJM 342:2000

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Antiretrovirals Reduction in 'Infectiveness'

- No increases in transmission when VL <1,500 copies/ml
- VL >50,000 copies/ml: 12x more likely to transmit compared to <3,500 copies/ml

QuinnTC, NEJM 342:2000

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Antiretrovirals Reduction in 'Infectiveness'

- 436 discordant couples
- All males HIV-infected
- Zidovudine monotherapy
- Overall: 50% risk reduction (80% rr associated with condom use)

Musico M, Arch Intern Med 154:1994

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Antiretrovirals Reduction in 'Infectiveness'

- Closed cohort of homosexual males in SF
- 60% reduction in anticipated cases of HIV when ART was available

Petro T. AIDS 18:2004

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Antiretrovirals Reduction in 'Infectiveness'

On-going trial:

- National Institutes of Health Prevention Trials Network
- 1,750 discordant couples
- Randomized to 'early' or 'delayed ART'
- Powered to detect a 35% decline in transmission risk

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Awareness and Determinants of Use PrEP

Minority Gay Pride Events 2004 Survey

- Use of PrEP among MSM populations
- 397 males; metro areas
 - * 25% (range: 17-29%) 'had heard of PrEP'
 - * 5% (range 0-7%) reported using PrEP
 - * Use of PrEP correlated to
 - # of sexual partners (>10/12 months)
 - OR 2.6 (95% CI 1.1-6.2)

Voetsch A. *J AIDS* 46:2007.

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PrEP Knowledge and Use *California*

- 1,819 HIV-uninfected males in CA
- 16% were aware of PrEP
- 1% of sample had used PrEP
- Awareness of PrEP was correlated with:
 - unprotected anal sex
 - use of recreational drugs

Liu AY. *J AIDS* 47:2008.

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PrEP Knowledge and Use *Boston*

- 227 HIV-uninfected men
- Mean age: 41 years (SD±9.1)
- 54% non-white
- 41% homosexual
- All subjects reported at least one incident of anal sex in past 12 months

Manning M. *J AIDS* 50:2009.

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PrEP Knowledge and Use *Boston*

- 1 participant reported PrEP use
- 19% had previously heard of PrEP
- Sources of information:
 - HIV outreach 44%
 - Media 21%
 - Friends 14%
 - Medical Provider 14%

Mimiaga MJ, *J AIDS* 50:2009.

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PrEP Knowledge and Use *Boston*

- 74%: + PrEP intent-to-use
- Predictors of intent-to-use:
 - 'less education' OR 7.7 (p=0.04)
 - moderate income OR 13 (p=0.04)
 - Perceptions of ↓ SEs OR 3.5 (p=0.01)
 - Cost free access OR 4.2 (0.05)

Mimiaga MJ, *J AIDS* 50:2009.

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PrEP and Outcomes *Mathematical Modeling*

- Cost-effectiveness?
- Assumptions:
 - mean age: 34 years
 - 50% PrEP use
 - tenofovir-emtricitabine @ \$753/month
 - 6 PrEP events/year
 - 50% efficacy rate
 - Local incidence rate: 1.6% (NYC: 1.4-2.0%)

Patel AD, *CID* 48:2009.

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PrEP and Outcomes Mathematical Modeling

- Reduced lifetime HIV risk:
44% → 25%
- Increased life expectancy:
39.9 → 40.7
- Lifetime treatment costs:
\$81,100 → \$232,700

Pattel AD, *CID* 48:2009.

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Current HIV PrEP Trials

STUDY/FUNDER	LOCATION	STRATEGY	POPULATION	STATUS	COMPLETION
U.S. Extended Tenofovir Safety Study/CDC	United States	Oral tenofovir	400 men who have sex with men	Fully enrolled	2009
Bangkok Tenofovir Study/CDC	Thailand	Oral tenofovir	2,400 injection-drug users	95% enrolled (May 2009)	2010
iPREX Study/NIH, BMGF	Brazil, Ecuador, Peru, South Africa, Thailand, United States	Oral Truvada	3,000 men who have sex with men	47% enrolled (January 2009)	2010
CAPRISA 004/USAID, LIFEab	South Africa	Vaginal tenofovir gel	900 sexually active women	Fully enrolled	2010
TDF-2/CDC	Botswana (2 sites)	Oral Truvada	1,800 heterosexual men and women	43% enrolled (May 2009)	2011
Partners PrEP Study/BMGF	Kenya, Uganda	Oral tenofovir, oral Truvada	3,900 serodiscordant heterosexual couples	33% enrolled	2012
FHI FEM-PrEP Study/USAID, BMGF	Kenya, Malawi, South Africa, Tanzania, Zambia	Oral Truvada	3,900 higher-risk women	Started Q2, 2009	2012
MTN VOICE Study/NIH	Malawi, Southern Africa, Uganda, Zambia, Zimbabwe	Oral tenofovir, oral Truvada, vaginal tenofovir gel	4,200 sexually active women	Planning/expected start Q2, 2009	2012

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Issues

- Is PrEP really nPEP?
- Impact on resistance (M184V; K65R)?
- Hepatitis B
- Cost? Cost-effectiveness? Payer?
- STI co-infection ... inflammation

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Concerns/Research

- Ethics/ Activism
- Cost-effectiveness
- Impact on risk behaviors
- Toxicity
- Contributions to resistance pools
- Ability to efficiently treat seroconverts
- Which cohorts? (MSM, IVDU)

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5 Core Factors

1. Fraction of HIV-infected that receive meds
2. Ability to provide meds to sub-populations likely to transmit HIV
3. Extent to which ART reduces genital tract viremia
4. Emergence / transmission of drug resistant strains
5. Impact on high risk behaviors (self-defeating?)

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Future Targets

- Populations (MSM, heterosexuals)
- Antiretroviral agents
- Routes of drug administration
- Dosing regimens
(continuous versus coitally)

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Welcome to PrEP Watch, a comprehensive information source on pre-exposure prophylaxis for HIV prevention.

<http://www.prepwatch.org/>

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BOTTOM LINE
'A Pill A Day To Keep HIV Away'

EFFICACY

TARGETING

PRICING



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