

Critical linkages in prevention: HIV and STIs

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Critical linkages in prevention: HIV and STIs

Compare STI and HIV prevention

- Terms: HIV vs STI
- Biomedical perspective

Do STIs get lost in the discussion on HIV prevention?

- If so, why?
- What should be done?

HIV and STIs: Overview

- Brief comparison of pathophysiology and epidemiology of STIs and HIV
- Approaches to prevention: efficacy data
 - Condoms—male and female
 - Male circumcision
 - STI treatment
 - Topical microbicides
 - PrEP, ART
- How to re-focus on STI prevention

HIV and STIs: comparison of pathophysiology

HIV

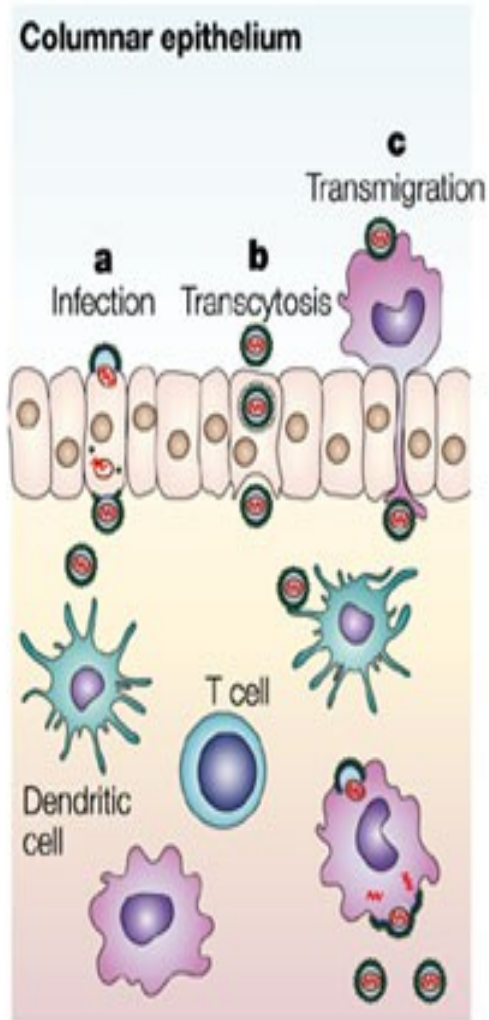
- Intraepithelial CD4 and LC as primary targets
- Mucosal breaks
- Innate immune system builds clusters of infected cells
- OIs and death

N. gonorrhoea

- Columnar epithelial cells as primary target
- Submucosal infection 24-48 hrs later
- Purulent cervicitis, rarely systemic
- Resolution in most

Cervical mucosa

- disruptable single layer



HIV and STIs: Comparison of epidemiologic features

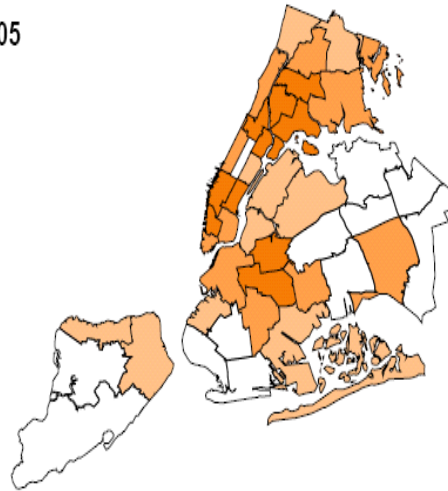
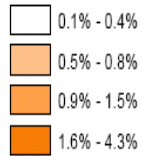
Similar

- Populations
 - Sub Saharan Africa
- Risk factors
 - Freq unprot intercourse
 - Different partners
- Geographic locations
 - Hotspots based on sexual networks

Similar Geographic Hotspots: NYC

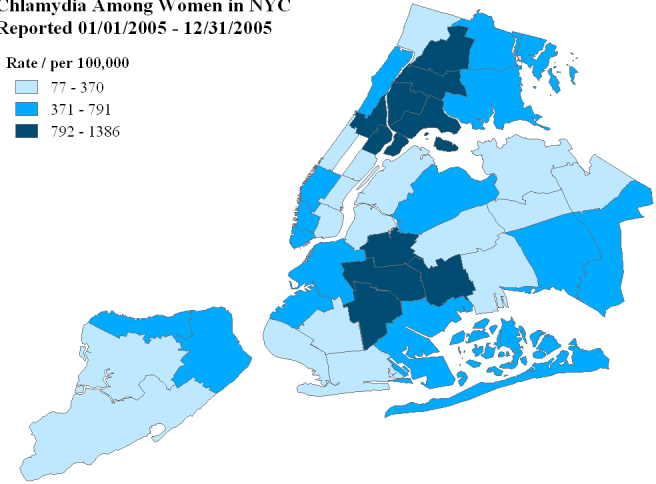
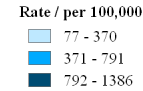
PLWA as % of Population

PWHA as a percent of population in 2005



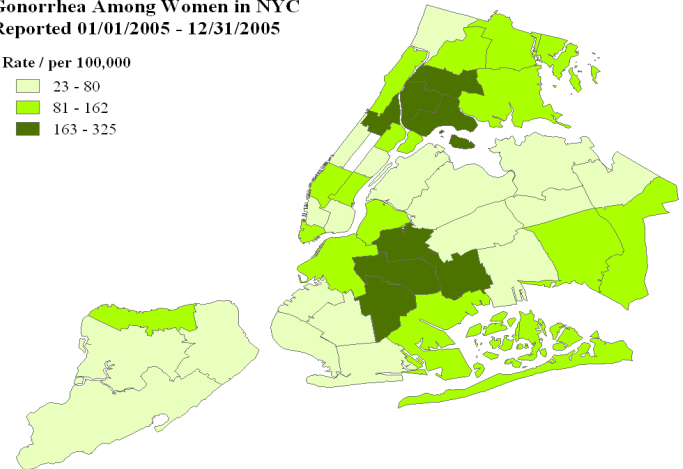
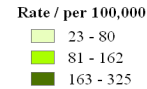
Chlamydia in Women

Chlamydia Among Women in NYC Reported 01/01/2005 - 12/31/2005



Gonorrhea in Women

Gonorrhea Among Women in NYC Reported 01/01/2005 - 12/31/2005



HIV and STIs: Comparison of epidemiologic features

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- Populations
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Different

- Rates of new infections per year (global)
 - HIV: 2.5 million
 - STIs: 340 million
- Associated mortality rates per year
 - HIV: 2 million
 - STIs: HPV: 274,000 per year, (WHO 2007) , others?
- Transmission efficiency per coital act
 - HIV: 0.0082 in acute infection
 - STIs: CT, NG: >0.4

Morbidity and mortality comparison

HIV

- OIs
- Metabolic complications of ART
- Co-morbidities
- Increased mortality

Morbidity and mortality comparison

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STIs

- Curable: syphilis, NG, CT, BV, TV, chancroid
- Non-curable: HSV, HPV
- Morbidities: neonatal infections, infertility, ectopic pregnancy
- Mortality: HPV and cervical cancer

Approaches to HIV and STI prevention: brief summary of available efficacy data

Condoms—male and female

Male condoms

- M & F acquisition: HSV-2, CT, syphilis (Holmes, 2004)
- F acquisition: NG, ?TV, not HPV (Holmes, 2004)
- HIV acquisition reduced by 80% (Weller 2002)

Female condoms

- Trichomoniasis, CT, GC: mixed results but probably as effective as male condoms



Male circumcision

HIV incidence

- Men:
 - Female-to-male HIV transmission reduced by 50-76 percent
 - Male-to-female HIV transmission: ?not

Male circumcision

HIV incidence

- Men:
 - Female-to-male HIV transmission reduced by **50-76 percent**
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STI incidence

- Men
 - ITT: no protection from NG, CT, TV;
 - as-treated: TV protection (Sobngwi-Tambekou J, 2008)
 - MSM: no final word
- Women
 - Observational: No protection NG, CT, TV (Turner AN 2008)

HPV, syphilis and chancroid > NG, CT

Efficacy of STI interventions: 3 Community-level RCTs

- Mwanza (Grosskurth 1995): (12,000)
 - Improved STI case management for symptomatic STIs vs routine care; evolving HIV epidemic
- Rakai (Wawer 1999): (14,000)
 - Intensive STI control w/mass antibiotics vs MVI asympt. STIs q 10 mo x 3; HIV epidemic stable
- Masaka (Kamali 2003): (20,000)
 - Information/education (I/E) alone vs I/E + STI interventions vs routine services; HIV epidemic stable

Efficacy of STI Interventions

Impact on HIV rates

- Mwanza trial
 - 38% reduction
- Rakai trial
 - No impact
- Masaka trial
 - No impact

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Impact on STI rates

- Mwanza trial
 - Syphilis rel risk 0.7
 - [GC, CT, urethritis: NS]
- Rakai trial
 - Syphilis 20% ↓ prev ratio
 - TV 40% ↓ prev ratio
 - [GC, CT, urethritis: NS]
- Masaka trial
 - GC rate ratio 0.29
 - Syphilis rate ratio 0.53
 - [CT: NS]

Microbicide Strategies

Initial Strategies

- Physical disruption of virus: Surfactants
- Boost normal microflora: Acidifying Agents
- Prevent viral entry: Sulfated Polyanions

Recent Strategies

- Prevent replication cycle: Antiretroviral agents (NRTIs, NNRTIs)
- Prevent viral entry: Entry inhibitors (CCR5 inhibitors)



Specificity

Microbicides: Surfactants

HIV activity

- Nonoxynol-9
 - Not protective
- C31G/Savvy
 - 2 trials stopped for futility
 - Nigerian data: no efficacy at 12 months
- Sodium laurel sulfate (Invisible Condom)
 - Phase II/III planned

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STI activity

- Nonoxynol-9
 - Not protective in 12 RCTS against GC, CT, TV
- C31G/Savvy
 - *in vitro* CT, HSV
 - Ph III: no protection from CT, BV, Trich, candida
- Sodium laurel sulfate (Invisible Condom)
 - Theoretical protection

Microbicides: Acidifying Agents

HIV

- BufferGel
 - no protection (HPTN 035)
- Acidform/Amphora
 - ?

Microbicides: Acidifying Agents

HIV

- BufferGel
 - no protection (HPTN 035)
- Acidform/Amphora
 - ?

STIs

- BufferGel
 - HSV2, CT, HPV in animal models
 - BV no protection HPTN 035
- Acidform/Amphora
 - NG, CT in vitro
 - NG and CT efficacy trial planned

Microbicides: Viral Entry Inhibitors

Sulfated Polyanions

HIV

- PRO2000 0.5%
 - 30% efficacy trend
(HPTN 035)
- Carraguard
 - no protection
(3.3 vs 3.8/100PY)
- Cellulose Sulfate
 - No protection
5.29 vs 3.33/100 PY, HR
1.61 [0.86-3.01]

Microbicides: Viral Entry Inhibitors

Sulfated Polyanions

HIV

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- Carraguard
 - no protection (3.3 vs 3.8/100PY)
- Cellulose Sulfate
 - No protection (5.29 vs 3.33/100 PY, HR 1.61 [0.86-3.01])

STIs

- PRO2000 0.5%
 - in vitro NG, CT, HSV
- Carraguard
 - In vitro HSV2, NG, HPV
 - In Ph III, no protection against NG, CT, syphilis, BV, trich, cand]; **low adherence**
- Cellulose Sulfate
 - In vitro NG, CT, HPV, G. vaginalis
 - In Ph III, no protection against NG, CT; ?adherence

Microbicides: Viral Entry Inhibitors

CCR5 Inhibitors

HIV

- PSC-RANTES
 - SHIV activity
- CMPD167
 - SHIV activity with addition of two other peptides

STIs

- No activity expected

Microbicides: Reverse transcriptase inhibitors

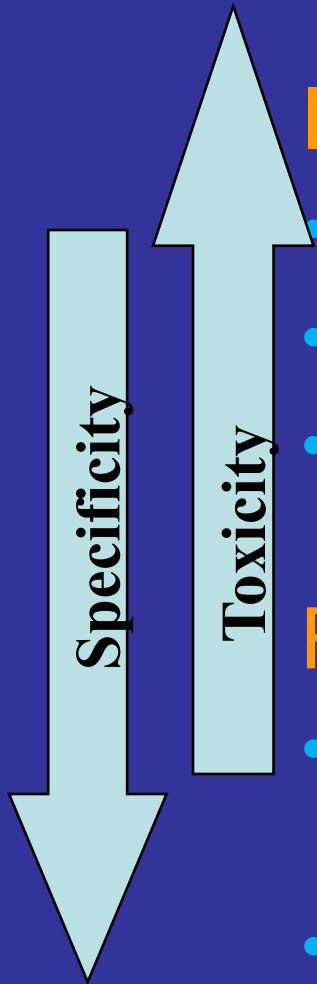
HIV

- Tenofovir
 - CAPRISA 004 Ph lib ongoing
 - VOICE Ph III planned
- TMC120
 - Ph III planned
- UC781
 - Ph I trials ongoing

STIs

- No activity expected

Microbicide Strategies



Initial Strategies

- Physical disruption: Surfactants
- Boost normal microflora: Acidifying Agents
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Recent Strategies

- Prevent replication cycle: Antiretroviral agents (NRTIs, NNRTIs)
- Prevent viral entry: Entry inhibitors (CCR5 inhibitors)

PrEP: TDF vs TDF + FTC

No or limited STI activity expected

ART for HIV prevention

- Observational studies
 - ART reduced HIV transmission risk and high risk sex among 2993 discordant couples in Rwanda and Zambia: HR for HIV if ART used 0.21 [0.09-0.52] (P. Sullivan, CROI 2009)
- RCT: HPTN 052 *Enrolling now*
 - HIV incidence as 1^o endpoint, STI rates as 2^o

Conclusions

Why do STIs get lost in the discussion on HIV prevention?

- STI intervention trial results (Mwanza, Rakai, Masaka)
- Microbicides: lack of STI efficacy and increasingly HIV-specific agents

Best reasons to prevent STIs

- prevent STI morbidity (infertility)
- minimize STI mortality (e.g., cervical cancer)

How to focus on STI prevention?



Condoms, STI services, HPV vaccine