Biology of HIV Disease in Women

• Sex differences
  • Greater surface area in women
  • Semen can stay in genital tract for days leading to longer exposure to virus

• Comorbidities
  • Inflammation (i.e. sexually transmitted infections)
  • Hormonal status
  • Altered vaginal flora (i.e. bacterial vaginosis)

• Reproductive aging
  • Differences in mucosal immunology
  • Adolescents have more ectropion
  • Menopausal women have estrogen leading to thinning of vaginal epithelium, altered vaginal flora, increased risk of trauma/abrasions
Co-factors:
- Inflammation (i.e. STIs)
- Bacterial vaginosis
- Trauma
- High seminal viral load
- Hormonal status

Events
- Exposure to HIV at mucosal surface (day 0)
- HIV replicates locally (days 0-2)
- Virus present in lymph nodes
- Virus released into blood and spread to other organs (day 3)
HIV Prevention

- PrEP
- Clean injecting equipment
- Vaccines
- Condoms
- Microbicides
- Treatment of sexually transmitted infections
- PEP
- PMTCT
- Male circumcision
- Voluntary counselling and testing
- Clean injecting equipment

STDs
HIV Prevention Technologies

FIGURE 7: HIV Prevention Technologies Shown to Be Effective in Reducing HIV Incidence in Randomized Clinical Trials

Other: Needle exchange programs, 0.42 (95% CI 0.22, 0.81)

Cohen MS, et al. NEJM 365, 493-505 (2011); Aspinall et al
CONTRACEPTIVES DOUBLE HIV RISK

The most popular contraceptive in Kenya doubles the risk of women becoming infected with HIV, a new study has shown.

"The study is a call to action for HIV prevention in women," said Dr. John Mbachu, a researcher at the University of Nairobi.

The study, which surveyed 1,500 women, found that those using oral contraceptives were twice as likely to become infected with HIV compared to those not using any form of contraception.

"It's a wake-up call for health providers," said Dr. Mbachu. "We need to find new ways to protect women from HIV."
Hormonal Contraception and HIV Acquisition

• Meta-analysis of 12 observational studies

• DMPA associated with a 40% increased risk of HIV acquisition (HR 1.40, 95% CI 1.16-1.69)
  • Risk was lower after excluding high-risk groups (1.31, 1.1-1.57)

• No increased risk of HIV acquisition found in OCPs (1.00, 0.86-1.16) or NET-EN (1.1, 0.88-1.37)
Hormonal Contraception and HIV Acquisition:

• Most studies found no statistically significant association between oral contraception and HIV acquisition

• Evidence on injectable HC varied with some studies showing increases between 48% to 100% and other studies reporting no association

• Evidence rated as low due to inconsistent data and limitations of the studies performed
HIV+ Serodiscordant Couples

- Population based sample of HIV + U.S. patients
  - 50% of couples were in serodiscordant relationships
  - 20% did not know partner’s HIV status

~ 140,000 serodiscordant heterosexual couples in the U.S., about half of whom want children

Conception Options for HIV Serodiscordant Couples

• Antiretroviral therapy is the most important intervention
  • ART Treatment for HIV+ partner as prevention (HPTN 052)
  • PrEP for HIV- partner?

• Screen and treat sexually transmitted infections

• HIV+ woman
  • Artificial insemination or timed condomless sex

• HIV+ man
  • Semen analysis (hypogonadism frequent occurrence in HIV+ men with decreased serum testosterone; abnormal semen analyses)
  • Assisted Reproductive Technology
    • Semen washing with IVF/ICSI (or IUI if outside of U.S.)
Goals of Preconception Counseling and Care

• Assess childbearing plans/desires
  • Patient and provider initiated discussions
    • 57% of pregnant women had not had preconception counseling

• Protection of maternal and fetal health during pregnancy
  • HIV+ women tend to be older and have more co-morbidities

• Prevention of mother-to-child transmission of HIV

• Reduce risk of transmission to uninfected partner
  • 77% of couples in Hopkins cohort were serodiscordant (20% male +)
    • 32% had a detectable viral load

• Prevention of unintended pregnancy
  • Access to safe and effective contraception

Finocchario-Kessler S Discussing childbearing with HIV-infected women of reproductive age in clinical care: *AIDS Behav* 2012
Boelig, Coleman, et al Preconception Counseling and Care in the Setting of HIV. *Infect Dis Ob Gyn* 2015
Elimination of MTCT

• Identifying HIV + women
  • HIV Testing @ intake and repeat in 3rd trimester
    • Patient and provider perception of risk or changing risk during pregnancy

• Initiation or continuation of highly active ART if HIV+
  • Adequate prenatal care
  • Adherence to medications, appointments
    • Only 73.5% (95% CI 71.5-79.7) of pregnant women reported adequate adherence (>80% adherence)
    • Physical, economical, and emotional stressors, depression, alcohol or drug use, and ART dosing frequency or pill burden reported as barriers
  • ART safety in pregnancy
    • Experience with new drugs is limited

• Postpartum linkage and retention in care
  • Higher ART adherence during pregnancy vs. postpartum (75.7% vs. 53%)
  • Breastfeeding debate in developed countries

Nachega JB et al Adherence to ART during and after pregnancy AIDS 2012; Sheth, Coleman, et al Association between depression and non-adherence to ART in pregnant women with perinatally acquired HIV. AIDS Care 2015
Contraception for HIV+ Women

• Benefits
  • Prevents unintended pregnancy
    • Half of all pregnancies in U.S. are unintended
    • Prevents maternal and neonatal mortality
  • Poor uptake of long-acting reversible contraception in HIV+ women
    • 73% relied on condoms as predominant mode of contraception
    • <4% LARC

• Special considerations
  • Potential drug interaction with ART

Cervical Cancer Prevention

• Cervical dysplasia is 4-5 fold higher and cancer 5-8 fold higher in HIV
  • High prevalence of multifocal dysplasia
  • HIV infected women have larger CIN lesions, higher rates of HPV and disease persistence and recurrence (up to 87% recurrence if CD4 count <200)
  • Mixed results regarding impact of ART on CIN and cancer incidence

• Screening
  • Twice in the 1st year after diagnosis and then annually, if normal results
  • Rapidly changing guidelines not applicable to HIV + women (i.e. primary HPV)
  • Low risk HIV+ women (normal pap and negative high risk HPV) risk of precancer at 5 yr is similar to HIV- women: 5% (95% CI 1-8%) vs 5% (95% CI 2-8%)

• Diagnosis and treatment of cervical disease/cancer is same as uninfected women

• HPV vaccination recommended (≤26yo), regardless of pap history

HIV & Aging - Menopause

- Not well studied
- Higher frequency of early menopause in some studies
  - Low CD4+ cell count
  - Methadone or opioids (lower estrogen)
  - Tobacco smoking
- Symptom management might be more difficult
  - Drug-drug interactions with ART and HRT
- Bone health worse
  - Fracture risk 1.9-3.7 times higher in HIV +
- Cardiovascular disease and MI risk higher in HIV +

Ethical Issues

- Barriers to inclusion of women and pregnant women in HIV clinical trials
- Participation in HIV clinical trials during pregnancy
  - Prevention trials exclude pregnant women
  - Management of HIV during pregnancy
- Inclusion of women in the HIV cure agenda

Lyerly and Faden http://www.bioethicsinstitute.org/phases
HIV Research Questions
NIH OAR Women and Girls Research Priorities FY 2015

1. Female genito—anal microenvironment
   How does reproductive aging influence risk of HIV?

2. HIV prevention models that integrate biological, social, and behavioral approaches
   How do we improve uptake of PrEP among providers and women?
   How do women perceive risk of HIV?
   Multipurpose technology
   Partner testing

3. Models of HIV treatment and care
   Adherence – what are the best measures and what strategies can best improve adherence?
   Access – how to expand access to HIV care, safer conception, and family planning?
   How do we improve postpartum linkage into care and retention?
   How to optimize cervical cancer screening without increasing harm in HIV+ women?
   Menopause- are there drug-drug interactions with HRT? Increased fracture risk in HIV+ women?

4. Sex and gender identity differences
   How to increase inclusion of women in clinical trials?
   Are there sex differences in frequency of anal intercourse and HIV risk?
   Does menopause influence the course of HIV?

5. Trauma and violence
   Does trauma alter immune protection in the FRT?
Thank you!
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