HIV: Focus on Women and Children
3/19/13

Women: We Are Not Little Men
Monica Gandhi, MD, MPH

BIOGRAPHY:

Monica Gandhi MD, MPH is an Associate Professor of Medicine in the Division of HIV/AIDS. She completed her M.D. at Harvard Medical School and then came to UCSF in 1996 for residency training in Internal Medicine. After her residency, Dr. Gandhi completed a fellowship in Infectious Diseases and a postdoctoral fellowship at the Center for AIDS Prevention Studies, both at UCSF. She also obtained a Masters in Public Health from Berkeley in 2001 with a focus on Epidemiology and Biostatistics.

Dr. Gandhi’s clinical and research career has been focused exclusively in HIV-infected women. Besides directing the AIDS Consult Service at San Francisco General Hospital and attending on the Infectious Diseases consult service, she serves as an HIV and primary care provider in the Women’s HIV Clinic at the Positive Health Practice, a multidisciplinary specialty clinic for HIV-infected women. Her research efforts have focused on HIV/AIDS in U.S. women through the Women’s Interagency HIV Study (WIHS), a multisite, prospective cohort study established in 1994 to study the natural history, clinical and laboratory findings of HIV in women. Her particular research is on finding low-cost solutions to measuring antiretroviral levels in resource-poor settings, such as determining drug levels in hair samples. Dr. Gandhi has also participated in research efforts involving the impact of HIV/AIDS in women in India.

Dr. Gandhi also has an interest at UCSF in HIV education and mentorship. Dr. Gandhi co-directs the public health section of the Immunity, Inflammation and Infection (I-3) course for the UCSF medical students, co-directs the “Communicable Diseases of Global Health Importance” course in the Global Health Sciences Masters program, and serves as the Education Director of the HIV/AIDS Division. She also serves as the program director of the UCSF Building Interdisciplinary Research Careers in Women’s Health (BIRCWH) K12 scholarship and the principal investigator on an R24 grant from NIMH/NIH on mentoring early career investigators of diversity in HIV research.
Conceiving (or Not) in the 21st Century
Deborah Cohan, MD, MPH

BIOGRAPHY:

Deborah Cohan, MD, MPH is Associate Professor in the Department of Obstetrics, Gynecology and Reproductive Sciences at University of California, San Francisco. She is Medical Director of Bay Area Perinatal AIDS Center (BAPAC) and provides preconception, prenatal and gynecologic care for HIV-infected women and HIV-uninfected women in serodifferent relationships. She is also the Clinical Director of the National HIV Perinatal Hotline and Clinician’s Network and Associate Director of the UCSF Fellowship in Reproductive Infectious Diseases. Dr. Cohan is a member of the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents and the DHHS Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. She is also a co-author of the DHHS Guidelines on the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents. Dr. Cohan’s research interests include prenatal HIV testing strategies, the use of combined antiretroviral therapy during pregnancy and lactation in resource-limited settings, as well as safer conception options for HIV-affected couples.

BIBLIOGRAPHY:


Heffron R, Donnell D, Rees H, Celum C, Mugo N, Were E, de Bruyn G,


HIV and Children
Theodore Ruel, MD

BIOGRAPHY:

Dr. Ted Ruel is an Assistant Professor in pediatric infectious specialist at the UCSF-Benioff Children's Hospital. After undergraduate work at Dartmouth College, he received his MD from Yale University and completed his training in pediatrics and infectious disease at UCSF. Dr. Ruel has a longstanding interest in global health and HIV in children. In 2002, he co-founded a nonprofit organization, the International Pediatric Outreach Project (now called Global Strategies), that aims to improve maternal and child health primarily through partnerships and training of local providers in Africa and India. For his academic research, Dr. Ruel studies HIV in African children, seeking to understand disease progression how to improve the outcomes of children receiving antiretroviral therapy. Dr. Ruel also serves on the NIH/DHHS guidelines committee that develops the nation’s pediatric HIV Treatment guidelines.

BIBLIOGRAPHY:


HIV in women: We are not Little Men

Monica Gandhi MD, MPH
HIV: Past, Present and Future
Mini-medical school
March 19, 2013

Massive impact in women

- Women and health: today’s evidence tomorrow’s agenda released by the World Health Organization (WHO) on November 9, 2009
- “Globally, the leading cause of death and disease among women of reproductive age (between the ages of 15 and 44) is HIV/AIDS. . .”


What about HIV infections among women in the U.S.?
High HIV Incidence Among At-Risk Women in US

- Recruited at-risk women from "geographic hotspots" around the country and performed acute HIV testing
- HIV incidence (NEW INFECTIONS) was actually 0.24% (2.4/1000) in black women - 5x higher than CDC's 0.05% (5/10,000) estimate for black women
  - Comparable to adult incidence rates in Sub-Saharan Africa (0.28% for Congo and 0.53% for Kenya)

3. UNAIDS Report on the Global AIDS Epidemic; 2010

**Question: What percentage of the HIV population in U.S. is not aware of their HIV infection?**

1. 10%
2. 20%
3. 25%
4. 30%
5. 50%


**CDC guidelines for testing**

- HIV screening in all health-care settings ages 13-64 after patient notified (unless patient declines)¹
- HIV testing for those at high risk at least yearly
- Separate written consent not required
- Screen in 1st trimester pregnancy and repeat in 3rd trimester if risk factors
- BUT, routine testing most limited where infections cluster in women¹


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**Risks in U.S. women cluster with poverty, disempowerment**

- HIV in women clusters with poverty¹-³; interpersonal violence³; incarceration¹⁻⁷; self-esteem, alcohol/drugs⁸


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**Why don’t women know their risk?**

- 83% heterosexual¹
- Economic disempowerment—access to health care, condom negotiation²
- 11% men concomitant relationships³
- Underestimate of bisexual behavior⁴
- 1 in 9 black men incarcerated⁵,⁶
- Poor knowledge about HIV/AIDS⁵

**Bold new guideline from IOM committee**

- Institute of Medicine (IOM) report  July 19, 2011
- **Recommendation 5.4:** Counseling and screening for human immunodeficiency virus infection on an annual basis for sexually active women
- Gestational DM, HPV, counseling on STDs, contraception, lactation, DV, yearly visits

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**HIV prevention in women - any differences from men?**

- **Circumcision**
  - Women having sex with circumcised men – no advantage
- **Microbicides**
  - No clearly effective microbicide yet – conflicting studies
- **Pre-exposure prophylaxis**
  - VOICE, FEMPrEP – didn’t work, but did for women in stable serodiscordant couples (Partners PrEP)
- **Diaphragms**
  - No advantage

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**A case of assumption?**

- **HPI:** 58 yo Caucasian woman with 4-5 years cognitive decline – from employed as printer to sporadic homelessness, all thought from depression. Admitted to UCSF inpatient psychiatric unit. Had non-Hodgkin’s lymphoma 8 yrs ago, treated.
- Pt on multiple psychiatric meds; no smoking or alcohol; uses marijuana; male sexual partners in past 20 yrs
- Patient had low oxygen in her blood on exam; sleepy; not very responsive; only able to follow one-step commands

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**Prevention only works if you know you’re at risk**

“Women at risk for HIV acquisition frequently do not appreciate their risk. The HIV epidemic among US women is, in many ways, hidden from effective dialogue, both among the populations at risk and within the broader scientific community”

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**Treatment works as prevention for both sexes**

HPTN 052: 1763 “serodiscordant” couples; 50:50)

- Total HIV-1 Transmission Events: 39
- Linked Transmissions: 28
- Delayed Arm: 27
- Immediate Arm: 1
- Unlinked or TBD Transmissions: 11

- 96% reduction

- 10/28 (36%) transmissions from male to female partners
- 238 pregnancies

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What about treatment and outcomes in women?

What are the barriers for women?

MSM versus women – updated surveillance in U.S

- Antiretroviral (ARV) therapy
  - Use of effective antiretroviral therapy (HAART) is the single most important predictor of mortality among patients with advanced HIV infection BUT... Sex differences rampant

Palella. Declining morbidity and mortality among patients with advanced HIV. NEJM '98

HIV infected women versus men

- Poorer
- Lower education levels
- Lower rates of having health insurance
- More food insecurity
- More competing priorities (childcare, etc.)
- More depression
- More substance use
- More domestic violence
- Reduced rates of treatment, later presentation

CDC “vital statistics” (Cascade)

- Medical Monitoring Project (MMP)
- Differences by sex in access and adherence
  - Men:
    - 90% prescribed ARVs
    - 79% suppressed
  - Women
    - 86% prescribed
    - 71% suppressed

Trauma associated with risk and failure, possibly mortality

- 30% of American women with HIV/AIDS suffer PTSD (5x times national rate)
- 55.3% of American women with HIV/AIDS suffer intimate partner violence (> 2x the national rate)
- Recent trauma – Four times as likely to have antiretroviral failure
- Domestic violence doubles risk of death from HIV

If women get on medications, they probably do better than men

Differential use of ARVs
Later presentation to care
Unknown infection date
Differential access to care
Differential provider treatment
Social factors
Higher rates of KDU
Better outcomes in women
Worse outcomes in women

Europe and Africa

Pharmacokinetics or “drug levels”: One explanation of sex differences?

- If women have higher ARV levels than men, could explain
  - Why they have more side effects
  - Improved outcomes when can tolerate
  - Most studies show higher levels in women
  - Dosing is one size fits all

Community beliefs about HIV

500 African Americans surveyed by phone
(51% high school and 49% some college or more; 53.4% <$35,000 and 46.6% >$35,000 annual income; 326 or 65.2% female)

- Institutions are trying to stop HIV 75.4%
- AIDS is a form of genocide 15.2%
- AIDS was produced in a government lab 26.6%
- People who take new meds are guinea pigs 43.6%
- Cure for AIDS exists, but withheld from poor 53.4%
- Information about AIDS is being withheld 58.8%

How do women feel about their providers?

Reasons for not getting into care differ by race

- African-American women
  - Mistrust
  - Tuskegee Study: untreated syphilis in the black male
  - Conspiracy theories
- Latina women
  - Decisions made by husband/boyfriends or families
  - Spanish speaking
- Both
  - Provider does not look like the patient or understand her culture (cultural competence)

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Women-living positive survey

- 43% black; 29% white; 29% Latina
- >50% said their providers never discussed women-specific issues
- 1/3 had switched providers due to dissatisfaction – providers not listening
- >75%- Living with HIV has caused them to struggle “somewhat” or “a great deal”
- Limited comfort discussing struggles or feelings of depression with their providers
Conceiving (or Not) in the 21st Century

Deborah Cohan, MD, MPH
Bay Area Perinatal AIDS Center
National Perinatal HIV Hotline and Clinicians’ Network

I have no financial conflicts of interest.

What are reproductive rights?

The basic right of all couples and individuals to decide freely and responsibly the number, spacing and timing of their children and to have the information and means to do so, and the right to attain the highest standard of sexual and reproductive health.

World Health Organization

HIV+ women internalize stigma around conception

Women Living Positive Survey
• n=700 HIV+ women on ARVs for 3+ yrs
• 59-61% believed could have children if appropriate care
• 59% believed society strongly urges not to have children

Squires et al. AIDS PATIENT CARE and STDs 2011

Email survey of 4831 US adults

Fertility desires among HIV+

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>US reproductive-aged women</td>
<td>35%</td>
</tr>
</tbody>
</table>
| HCSUS study, n=1421  | 29% women
| HIV+ men/women in care | 28% men  |

"Being infected with HIV dampens but does not come close to eliminating individuals’ desires and intentions to have children."

Chen et al. Family Planning Perspectives, 2001

Unintended pregnancy

<table>
<thead>
<tr>
<th>US general population</th>
<th>49% pregnancies unintended</th>
</tr>
</thead>
<tbody>
<tr>
<td>US, WIHS</td>
<td>232 adults 77% pregnancies while using contraception (vs. 60% HIV-)</td>
</tr>
<tr>
<td>US</td>
<td>1090 adolescents 83.3% unplanned 49-52% HIV status known</td>
</tr>
</tbody>
</table>

Finer/Henshaw Perspec Sex Reprod Health 2006; Massad AIDS 2004; Koenig AJOG 2007; Florida Antivir Ther 2006

Estimated number of births to women living with HIV, 2000-06

Steps to Reducing Perinatal HIV Transmission

- Primary HIV prevention in women
- Comprehensive preconception/interconception care
- Prevention of unintended pregnancy in HIV+ women
- Accessible, affordable, welcoming prenatal care
- Universal prenatal HIV testing
- Offer ARV treatment/prophylaxis to all HIV-infected women
- Adherence support for ARVs
- Rapid test for women with undocumented HIV status in labor
- ARV prophylaxis for women identified in labor
- ARV prophylaxis of all HIV-exposed newborns
- Comprehensive services for mother and infant

FXB Center UMDNJ, 2002, 2009

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FXB Center UMDNJ, 2002, 2009
Trends in Perinatal HIV Transmission and Maternal Antiretroviral Therapy, Women and Infants Transmission Study: 1990-2004

GLOBAL MONITORING FRAMEWORK AND STRATEGY
for the Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive (EMTCT)

APRIL 2012

Perinatal HIV Transmission: US
# new cases of HIV+ infants

Public health victory!

What about serodifferent couples who want to conceive?
* HIV+ man/HIV- woman

Options for safe conception?
COST=yes
EFFECTIVENESS=??

HIV Heterosexual Serodifference

On HIV Cost and Services Utilization Study (1996)
On=1421 (35k♀, 53k♂)
O Currently married or with heterosexual partner
ODesire future fertility
O29% HIV+ women
O28% HIV+ men

Chen et al. Family Planning Perspectives, 2001
Antiretrovirals = Enough?
- HPTN: trial of immediate vs. delayed initiation of antiretrovirals
- 96% reduction of HIV transmission to negative partner
- ONE DOCUMENTED CASE of sexual HIV transmission
  - HIV+ man with undetectable viral load ➔ male partner
- NO DOCUMENTED CASES of sexual HIV transmission
  - HIV+ man with undetectable viral load ➔ female partner

“Do we have to fill our patients’ lives with years or those years with life?”
Augusto Enrico Semprini

Video:
- HIV+ Men: Having a Healthy Sex Life and Healthy Family
- Coming soon....
- Adherence
- Disclosure

Clinical algorithms: integrating reproductive health into primary HIV care
Educational brochures: safer conception, contraception
http://hiv.ucsf.edu/care/perinatal.html
Children and HIV in 2013
Theodore Ruel MD
March 19, 2013

The “beginning” of pediatric HIV...

• 1982: – 4 infants with immunodeficiency in New York, New Jersey, and San Francisco
• 1983: – recognizing blood transfusion as means of infection (at UCSF)

*Young children and infants got HIV-infection from blood transfusions and from mother-to-child transmission*

(1) MMWR 1982; 31(49): 665-7.

Treat pregnant women and reduce HIV transmission to infants


Perinatal HIV Transmission: US

Taylor, CROI 2012

Outline

• The HIV epidemic in children
• Treating HIV-infected children
• The prospect for a cure
Young adults …

Diagnoses of HIV Infection among Adolescent and Young Adult Males, by Age Group and Transmission Category, 2010—46 States and 5 U.S. Dependent Areas

<table>
<thead>
<tr>
<th>Transmission category</th>
<th>13–19 years</th>
<th>20–24 years</th>
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<tbody>
<tr>
<td>Male-to-male sexual contact</td>
<td>1,634</td>
<td>5,898</td>
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<tr>
<td>Injection drug use (IDU)</td>
<td>23</td>
<td>143</td>
</tr>
<tr>
<td>Male-to-male sexual contact and IDU</td>
<td>51</td>
<td>235</td>
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<tr>
<td>Heterosexual contact</td>
<td>84</td>
<td>289</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Total: 1,792  100  6,565  100

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Estimated number of children (<15 years) newly infected with HIV  | 2011

Total: 330,000 [280,000 – 390,000]
HIV+ women need access to medications

![Graph showing the percentage of women with HIV among children and the coverage of antiretroviral treatment for preventing mother-to-child transmission.](Image)

**Summary**

- We can eliminate mother-to-child transmission
- We need to prevent infections in young adults in the USA and abroad
- We need to get treatment to women and children in Africa

**Current Issues**

- When do you start treatment of infected children with antiretroviral medicines?

**When to start treatment of HIV?**

**Wait**
- Few drugs
- Risk of resistance
- Toxic drugs
- Clinical benefit?

**Start**
- Many drugs
- Fewer side effects
- "Treatment as prevention"
- Non-AIDS morbidity and mortality

**Death before the age of 2 years**

![Graph showing survival probability for different scenarios.](Image)

**Marinda et al., PIDJ, 2007**

**Koyangi et al., PIDJ 2011**
### Approved Medications by age

<table>
<thead>
<tr>
<th>Medications</th>
<th>Newborns</th>
<th>&gt; 3 month</th>
<th>&gt; 2 years</th>
<th>&gt; 6 years</th>
<th>&gt; 13 years</th>
<th>Adults</th>
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<tbody>
<tr>
<td>Lamivudine</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Stavudine</td>
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<td>Zidovudine</td>
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<td>Didanosine</td>
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<tr>
<td>Emtricitabine</td>
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<td>Darunavir</td>
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<td>Indinavir</td>
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<tr>
<td>Maraviroc</td>
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<td>Raltegravir</td>
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<td>Fuzeon</td>
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### HIV - infection

HIV fuses and dumps RNA into cell. RNA turned into DNA and incorporated into host cells. "Latency" (CD4 receptor).

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### Implications of latent reservoir

- You can treat for many years, but still find HIV DNA in cells
- When you stop treatment, HIV comes roaring back...

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### The Mississippi Kid

- "Resting" white blood cells that express CD4
- In blood and tissue
  - gastrointestinal tract
- "pharmacologic reservoirs"
  - where drugs don't penetrate ... e.g. the brain

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### The case

- Baby born to mother without prenatal care
- Rapid HIV test while in labor was +, but no time to give mother treatment before delivery
- Baby transferred to Univ. Mississippi Med Ctr. at 30 hours of life
The case

- 2 tests of infant (separate blood samples) drawn
- Started three HIV medicines (AZT/3tc/NVP) as prophylaxis
  - But used treatment dose of NVP
- Both tests of baby came back HIV +

The case, continued ...

- Mother was lost to care, but returned to at 23 months of age ...
- Reported to have stopped giving infant HIV medicine 5 months
- No virus detected in blood of infant using standard clinical tests!

The case, continued ...

- Since studies using more sensitive tests for virus – no evidence of HIV RNA or DNA
- Is this a “cure” or just effective prophylaxis before “real” infection was established?

Implications for HIV+ children

- A lot to gain …
  - long lives ahead and large numbers
- The best candidates for cure?
  - You know when exposed/infected to can diagnose / treat early
  - Good immune systems
- Change in prophylaxis recommendations?
  - Treat hard, treat early!