HIV TRANSMISSION DURING HETEROSEXUAL INTERCOURSE

THE EPIDEMIOLOGIST’S PERSPECTIVE
A global view of HIV infection
33.3 million people living with HIV, 2009
HIV prevalence in unmarried women 15 – 19 years old who reported 1 lifetime sex partner vs HIV prevalence in their partners.

<table>
<thead>
<tr>
<th></th>
<th>Kenya (Kisumu)</th>
<th>Zambia (Ndola)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV prevalence in women</td>
<td>20%</td>
<td>15%</td>
</tr>
<tr>
<td>Estimated prevalence in male partners</td>
<td>9 – 11%</td>
<td>12 – 16%</td>
</tr>
</tbody>
</table>

ESTIMATES OF PER SEX ACT TRANSMISSION PROBABILITIES

<table>
<thead>
<tr>
<th></th>
<th>Male to female</th>
<th>Female to male</th>
</tr>
</thead>
<tbody>
<tr>
<td>High income countries</td>
<td>0.08%</td>
<td>0.04%</td>
</tr>
<tr>
<td>Low income countries</td>
<td>0.30%</td>
<td>0.38%</td>
</tr>
</tbody>
</table>

Low income vs high income countries
- Transmission probabilities much higher
- M to F transmission = F to M transmission
- High heterogeneity in estimates

REASONS?

- Differences in disease stage
- Differences in HIV-1 subtypes
- Other sexually transmitted infections
- Male circumcision status
DIFFERENCES IN DISEASE STAGE?

Trial of early ART in HIV discordant couples – all recruited at CD4 count 350-550:

<table>
<thead>
<tr>
<th>Region</th>
<th>Incidence of linked transmissions (per 100 person years - 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>1.6 (1.0 – 2.4)</td>
</tr>
<tr>
<td>Asia</td>
<td>0.2 (0.0 – 0.6)</td>
</tr>
<tr>
<td>Latin America (Brazil)</td>
<td>0.5 (0.1 – 1.5)</td>
</tr>
</tbody>
</table>

• Lower condom use among couples in Africa?

• Plasma viral load higher in Africans?
  – Men in Malawi vs men in US/Switzerland: higher plasma VL for same CD4 count
  
  Dyer et al. High levels of Human Immunodeficiency Virus Type 1 in blood and semen of seropositive men in sub-Saharan Africa. JID 1998; 177: 1742-1746.

• Different subtypes – different transmission probabilities?
  – Subtype C ?
  – Subtype A more transmissible than subtype D?

• Other sexually transmitted infections? HSV-2!
OTHER SEXUALLY TRANSMITTED INFECTIONS

Bacterial STI
- Chancroid
- Syphilis
- Gonorrhoea
- C. Trachomatis
- T. vaginalis
OTHER SEXUALLY TRANSMITTED INFECTIONS

- Bacterial vaginosis
- Bacterial STI
OTHER SEXUALLY TRANSMITTED INFECTIONS

- HSV-2
- Bacterial vaginosis
- Bacterial STI
OTHER SEXUALLY TRANSMITTED INFECTIONS

- HSV-2
- HPV M. genitalium
- Bacterial vaginosis
- Bacterial STI
**THE NEWEST “KIDS ON THE BLOCK”**

**HPV associated with increased risk of HIV acquisition** → HPV vaccination for HIV prevention?

<table>
<thead>
<tr>
<th>Country</th>
<th>HPV prevalence at baseline</th>
<th>Effect on HIV incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men South Africa</td>
<td>14% (HR only)</td>
<td>aIRR = 3.8</td>
</tr>
<tr>
<td>Men Kenya</td>
<td>50%</td>
<td>aHR = 1.8</td>
</tr>
<tr>
<td>Women Zimbabwe</td>
<td>49%</td>
<td>aOR = 2.4</td>
</tr>
</tbody>
</table>
THE NEWEST “KIDS ON THE BLOCK”

*Mycoplasma genitalium* and HIV?

- Strong association between MG and HIV in cross-sectional studies: OR ~ 2
- Increased shedding of HIV in dually infected persons
- Increased risk of HIV acquisition?
  - So far one longitudinal study
  - Women in Kenya and Zimbabwe: OR=2.33
## HERPES SIMPLEX VIRUS 2 INFECTION

### Risk of HIV associated with prevalent HSV-2

<table>
<thead>
<tr>
<th></th>
<th>Summary relative risk</th>
</tr>
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<tbody>
<tr>
<td>Women</td>
<td>3.4</td>
</tr>
<tr>
<td>Men</td>
<td>2.8</td>
</tr>
<tr>
<td>Female sex workers</td>
<td>1.5</td>
</tr>
<tr>
<td>MSM</td>
<td>1.6</td>
</tr>
</tbody>
</table>

+ High prevalence of HSV-2 infection in Africa

25-35% of new HIV infections in Africa due to HSV-2

There is an increased risk of HIV acquisition associated with:
- Bacterial vaginosis (HR 2.12)
- Intermediate Nugent score (HR 2.02)

In women in Uganda and Zimbabwe, 17% of HIV infections are due to BV, and 12% to intermediate Nugent.

Genital shedding of HIV-1 is associated with bacteria associated with BV.

DIFFERENCES IN VAGINAL FLORA BY ETHNIC GROUP IN THE US

- Nearly half: flora dominated by *L. crispatus*
- 10% group IV (high Ph)

*Ravel et al. Vaginal microbiome of reproductive-age women. ww.pnas.org/cgi/doi/10.1073/pnas.1002611107*

- Only 1/5: flora dominated by *L. crispatus*
- 40% in group IV
MALE CIRCUMCISI0N

- Three randomized trials in Africa: MC reduces HIV transmission from women to men by ~ 60%

- Effect of MC larger in Africa than Europe – why? Interaction with genital ulcerations?
MALE CIRCUMCISION

• Effect on transmission from men to women?
  – RCT in Uganda stopped because of futility.
  – Indirect effect? Through effects on other STI and on vaginal flora?

• Effect among MSM? - only observational studies
  – Some protection in MSM who engage predominantly in insertive anal sex


EFFICACY OF HIV PREVENTION STRATEGIES FROM RANDOMIZED CLINICAL TRIALS

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect size (95% CI)</th>
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<tbody>
<tr>
<td>Antiretroviral treatment for prevention</td>
<td>96% (73-99)</td>
</tr>
<tr>
<td>HPTN 052 Africa, Asia, Americas¹</td>
<td></td>
</tr>
<tr>
<td>PrEP for discordant couples</td>
<td>73% (49-85)</td>
</tr>
<tr>
<td>Partners PrEP Uganda, Kenya²</td>
<td></td>
</tr>
<tr>
<td>PrEP for heterosexual men and women</td>
<td>63% (21-84)</td>
</tr>
<tr>
<td>TDF2 Botswana³</td>
<td></td>
</tr>
<tr>
<td>Medical male circumcision</td>
<td>54% (38-66)</td>
</tr>
<tr>
<td>Orange Farm⁶, Rakai², Kisumu⁸</td>
<td></td>
</tr>
<tr>
<td>PrEP for MSMs</td>
<td>44% (15-63)</td>
</tr>
<tr>
<td>iPrEX Americas, Thailand, South Africa⁴</td>
<td></td>
</tr>
<tr>
<td>Sexually transmitted diseases treatment</td>
<td>42% (21-58)</td>
</tr>
<tr>
<td>Mwanza Tanzania⁵</td>
<td></td>
</tr>
<tr>
<td>Microbicide</td>
<td>39% (6-60)</td>
</tr>
<tr>
<td>CAPRISA 004 South Africa³</td>
<td></td>
</tr>
<tr>
<td>HIV vaccine</td>
<td>31% (1-51)</td>
</tr>
<tr>
<td>RV144 Thailand¹</td>
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EFFICACY OF TREATMENT IN PREVENTING HIV TRANSMISSION IN MSM

Same efficacy as found in heterosexual couples?

– Plausible that there will be an effect but…
– Will it as big as in heterosexual couples?

– Lack of empirical data!
Population-level effects of ART depend on
– durable and reliable HIV suppression
– preventing transmitted resistance
– dealing with acute HIV infection

Ms Cohen at ISSTDR 2011
SOME RECENT SOBERING RESULTS

• **Africa**

  Association between duration of ART availability and prevalence of primary drug resistance.


• **Southern India (Avahan project):**

  Annual fraction of new HIV infections in FSW and clients due to primary infection + 20%

  (Boily at ISSTDR 01-S11.01)
TO BE FOLLOWED UP…