

Research to design community based prevention

IAS Satellite – July 17, 2011

**“Controlling the HIV epidemic – The promise
of ARV-based prevention”**



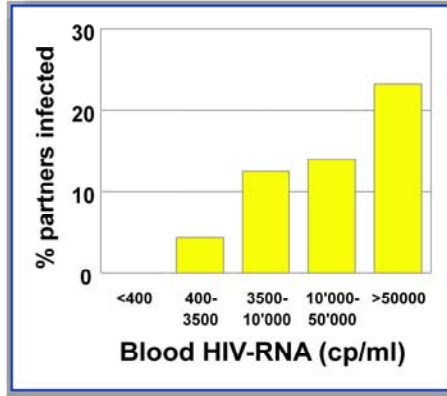
Planning community based interventions

The trivial key questions

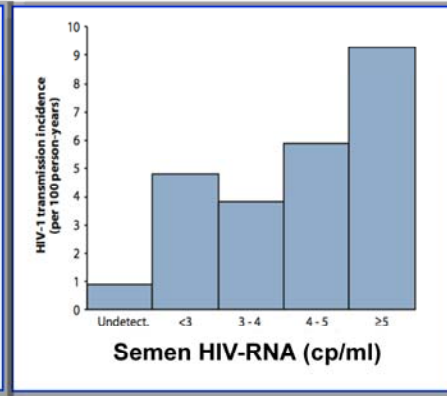
- **When does infection occur**
- **Where does it occur**
- **Who is most likely to transmit HIV**
- **Who is most likely to get infected**
- **What is the impact of behavior**

Who is most likely to transmit HIV

Blood and Genital Viral Load

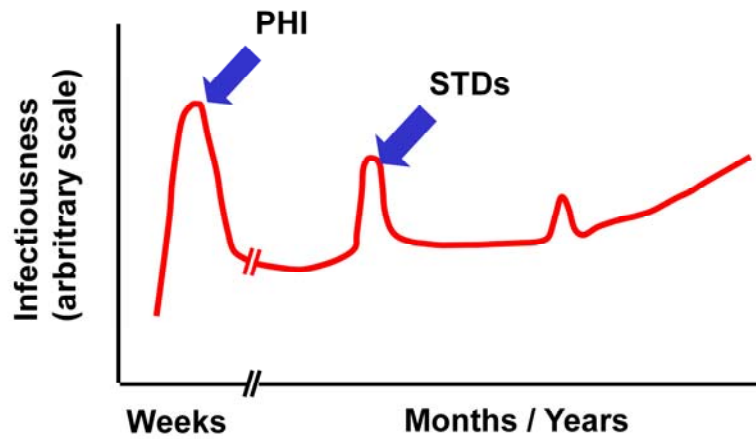


Quinn, NEJM, 2000; 342:921-9



Beaten, Science Trsl Medicine 2011

When does HIV transmission occur?
The role of PHI and STDs



Vernazza et al, AIDS, 1999

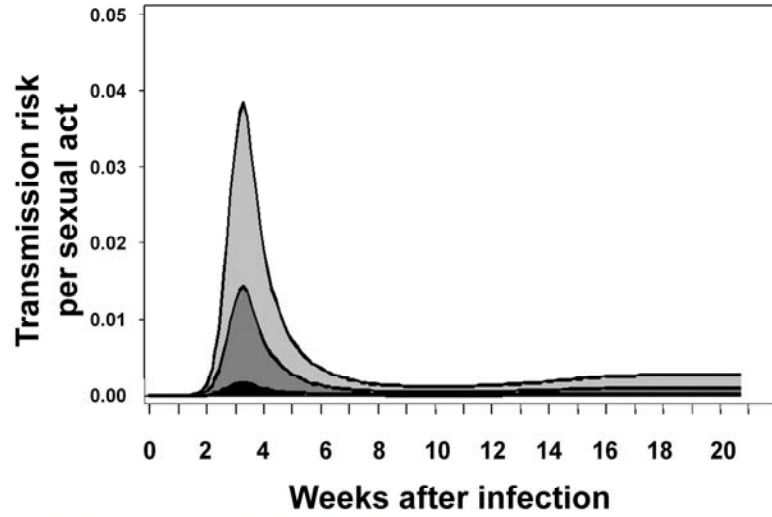
Kantonsspital
St.Gallen **HIV**

FB Infektiologie / Spitalhygiene

Vernazza et al, AIDS, 1999

When does HIV transmission occur?

The role of Primary HIV Infection



Pilcher et al JID 2004; 189:1785–92

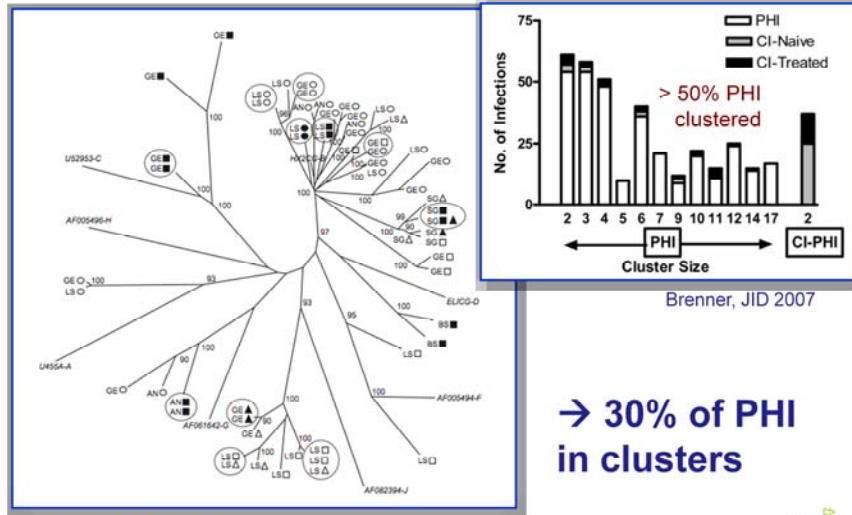
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Pilcher et al JID **2004**; **189**:1785–92

When does HIV transmission occur?

The role of Primary HIV Infection



Yerly, AIDS 2001

Brenner, JID 2007

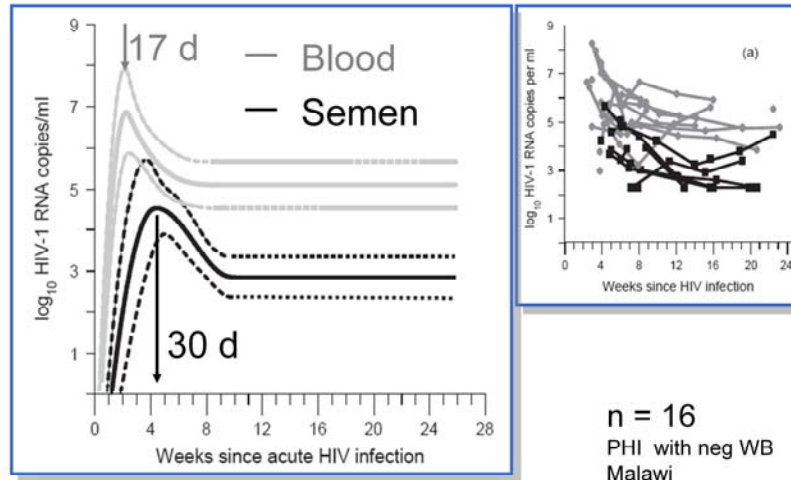
→ 30% of PHI in clusters



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Yerly, AIDS 2001

PHI: Long duration of infectivity



Pilcher et al, AIDS, 20.8.2007; 21:1723–1730

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n = 16
PHI with neg WB
Malawi

Pilcher et al, AIDS, 20.8.2007; 21:1723–1730

Objectives: This study was conducted to compare viral dynamics in blood and semen between subjects with antibody negative, acute HIV-1 infection and other subjects with later stages of infection.

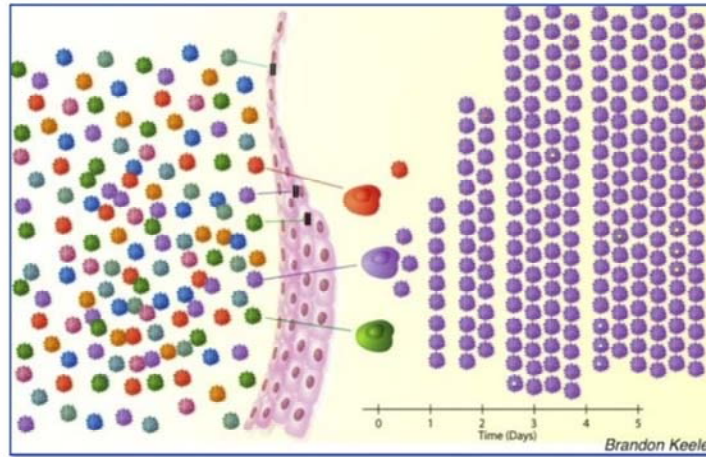
Design: A prospective cohort study was embedded within a cross-sectional study of HIV screening in a Lilongwe, Malawi STD clinic.

Methods: Blood samples from HIV antibody negative or indeterminate volunteers were used to detect HIV RNA in plasma using a pooling strategy. Blood and seminal plasma HIV-1 RNA concentrations were measured over 16 weeks.

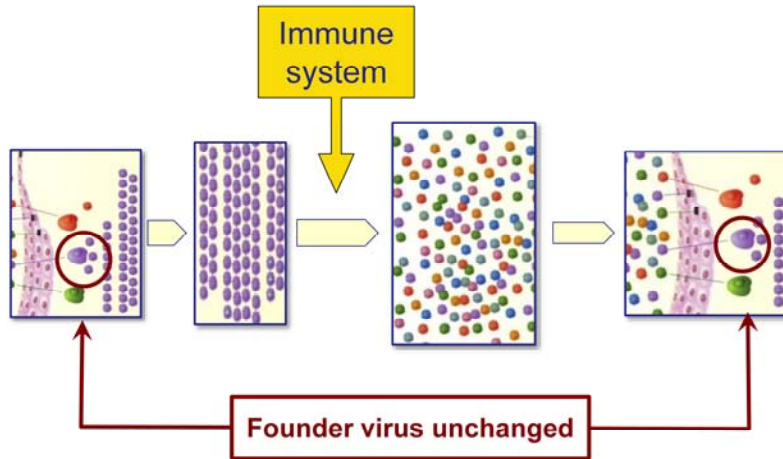
Results: Sixteen men with acute HIV infection and 25 men with chronic HIV infection were studied. Blood viral load in subjects with acute HIV infection was highest about 17 days after infection (meanSE, 6.90.5 \log_{10} copies/ml), while semen viral load peaked about 30 days after infection (4.50.4 \log_{10} copies/ml). Semen viral load declined by 1.7 \log_{10} to a nadir by week 10 of HIV infection. Semen and blood viral loads were more stable in chronically infected subjects over 16 weeks. Higher semen levels of HIV RNA were noted in subjects with low CD4 cell counts.

Conclusions: These results provide a biological explanation for reported increases in HIV transmission during the very early (acute) and late stages of infection. Recognizing temporal differences in HIV shedding in the genital tract is important in the development of effective HIV prevention strategies.

Bottleneck of Transmission



Not all viruses are transmitted equally



Redd, CROI 2011 # 160 / Wilen, J Virol 2011 / Nawaz, PLoS Pathogen 2011

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Redd, CROI 2011 # 160 / Wilen, J Virol 2011 / Nawaz, CROI 2011 #156LB

Who is getting infected ?

HIV infections are clustered (Clade B)

- 5700 Patients, >50% in 60 Clusters
- Define:
 - Swiss clusters: Different from Intl sequ.
 - MSM or IDU/Het-clusters: 80%

Table 2. Distribution of the Patients from the Different Transmission Groups over the Different Cluster Types

Transmission group	MSM cluster	IDU/HET cluster	Ambiguous cluster	No transmission cluster
MSM	903 (36)	86 (3)	83 (3)	1469 (58)
HET	159 (11)	525 (38)	87 (6)	617 (44)
IDU	37 (2)	1113 (63)	125 (7)	490 (28)

Kouyos et al. 2010 JID

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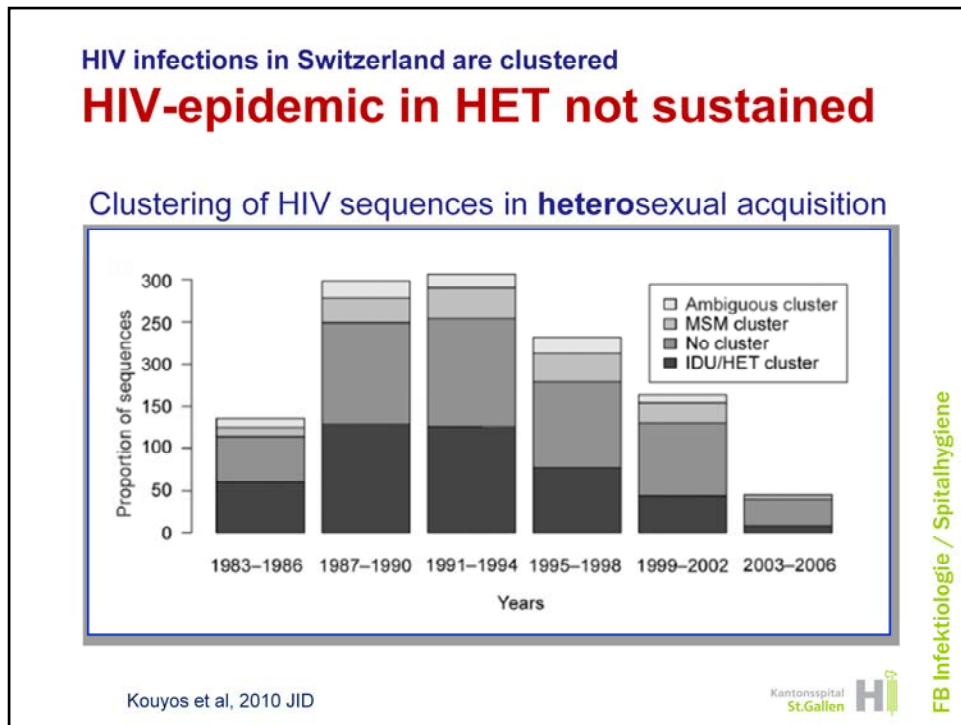
Kouyos et al, 2010 JID

→ In summary, we identify transmission chains as clades dominated by Swiss sequences. In the remainder of the text, we will refer to these as (Swiss) transmission clusters.

Figure

1 highlights the distribution of the Swiss sequences in the phylogeny. It indicates the presence of 2 types of transmission clusters: the “IDU/HET transmission clusters,” which mainly consist of patients who have acquired HIV through heterosexual contact or injection drug use, and the “MSM transmission clusters,” which mainly consist of patients for whom homosexual intercourse between men is the primary route of transmission.

Of these 60 transmission clusters, 50 contain a significant (according to a binomial test) excess of either MSM (38 transmission



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Of these 60 transmission clusters, 50 contain a significant (according to a binomial test) excess of either MSM (38 transmission

Prevalence of Unsafe Sexual Behavior Among HIV-Infected Individuals: The Swiss HIV Cohort Study

*†Katja Wolf, *James Young, ‡Martin Rickenbach, §Pietro Vernazza, ¶Markus Flepp, ¶¶Hansjakob Furrer, #Enos Bernasconi, **Bernard Hirschel, ††Amalio Telenti, ¶¶Rainer Weber, *†Heiner C. Bucher, and the Swiss HIV Cohort Study

TABLE 2. *Sexual behavior in the preceding 6 months for individuals in the Swiss HIV Cohort Study*

Type of partnership	Sexual intercourse, N (%)	Always used condoms, N (%)
Stable partner (n = 2595)	2117 (82)	1602/2117 (76)
Occasional partners (n = 882)	771 (87)	664/771 (86)

FB Infektiologie / Spitalhygiene

Wolf et al, AIDS 2003

Kantonsspital
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Wolf AIDS 2003

Summary: Sexual contact is the major mode of HIV transmission. Increased sexual risk taking has been described in HIV-infected individuals receiving potent antiretroviral therapy. A new questionnaire on sexual behavior was introduced into the Swiss HIV Cohort Study on April 1, 2000. We evaluated sexual behavior in all individuals who completed the questionnaire for the first time within 1 year after its introduction. Our primary hypothesis was that self-reported unsafe sexual behavior would be more prevalent among individuals with optimal viral suppression. On April 1, 2000, 4948 individuals were registered in the study, and 4723 (95%) completed the questionnaire. Of these individuals, 12% reported unsafe sex, 78% received antiretroviral therapy, and 25% had optimal viral suppression (HIV RNA level always <50 copies/mL during the preceding 12 months). During the preceding 6 months, 55% of individuals had stable and 19% had occasional partners, and 6% had both types of partners. Sexual intercourse was reported by 82% of individuals with stable and 87% of individuals with occasional partners, and of those reporting sexual intercourse in each group, 76% and 86%, respectively, said that they always used condoms. After adjustment for covariates, reported unsafe sex was not associated with optimal viral suppression (odds ratio, 1.04; 95% confidence interval, 0.81–1.33) or antiretroviral therapy (odds ratio, 0.83; 95% confidence interval, 0.65–1.07), but it was associated with gender, age, ethnicity, HIV transmission group, HIV status of partner, having occasional partners, and living alone. There is no evidence that self-reported unsafe sexual behavior is more prevalent among HIV-infected individuals with optimal viral suppression. However, unsafe sex is associated with other factors.

Conclusions

- **The first few months of HIV infection may be major driver of the epidemic**
- **In Switzerland, the HIV epidemic is primarily maintained in MSM (at least clade B)**