Bundesgesundheitsbl - Gesundheitsforsch - Gesundheitsschutz
2002 · 45:277–285 © Springer-Verlag 2002

P. L. Vernazza[1] · A. D. M. Kashuba[2] · M. S. Cohen[2]
[1] Division of Infectious Diseases, Cantonal Hospital St. Gallen, Switzerland
[2] Division of Infectious Diseases, University of North Carolina at Chapel Hill, N.C. USA

Biological Correlates of Sexual Transmission of HIV

Practical Consequences and Potential Targets for Public Health

Abstract

The probability of sexual transmission of HIV depends on the infectiousness of the index case and the susceptibility of the sexual contact. The risk of HIV transmission is heterogeneous and may be greatest during the initial sexual contacts in a steady partnership. Several factors, including systemic and mucosal acquired protective immune-response might be responsible for the apparent decrease of per-sex-act risk of transmission in a given partnership over time. Biological studies can be used to better understand the complex information obtained by epidemiological surveys. The infectiousness of HIV depends on the inoculum, and virologic factors. The genital tract viral load of the index case is likely the most important determinant of transmission. At the population level, interventions that reduce the genital shedding of HIV by reducing systemic blood viral load and/or local inflammatory processes are likely to have a beneficial impact on HIV incidence. Antiretroviral drugs are likely to reduce sexual transmission of HIV. However, these drugs may not all prove equally. Compartmentalized HIV replication in the male and female genital tract have been observed. Treatment with antiretroviral drugs that poorly penetrate the genital tract harbour the risk of local production and spread of resistant viruses. In addition, increased risk taking behaviour could offset the benefits of reduced probability of transmission at the population level. Biological data about HIV transmission must be used to inform public health policies and optimize HIV prevention strategies.

Keywords

HIV · Sexual Transmission · HIV Prevention Strategies · Susceptibility · Infectiousness

Worldwide, the predominant mode of HIV transmission is clearly heterosexual contact. However, the biological correlates for HIV transmission are less clear because of the heterogeneity of sexual transmission. This heterogeneity is best illustrated by individual case reports where transmission occurs in some partners after limited sexual contact, while other partners of the same individual remain uninfected [1]. The heterogeneity of sexual transmission makes the risk of a single contact much less predictable than for other modes of transmission.

The probability of sexual transmission of HIV is a function of the infectiousness of the index case, the mode of the sexual contact, and the susceptibility of the person exposed to the virus. We have recently reviewed factors contributing to the infectiousness of the infected individual [2] and a review of the susceptibility factors has been published by Buchacz [3]. Here we summarize recent findings about susceptibility and infectiousness, with a focus on infectiousness factors that can be influenced by public health prevention strategies.

Estimating the transmission risk: Where biology meets epidemiology

Estimates for the risk of sexual transmission of HIV have been generated from epidemiological surveys. In most instances, partner studies have been used to calculate the per-partnership transmission risk or the per-sexual-contact risk of transmission. The calculation of the per-sex-act risk is based on the assumption that the risk remains stable over a long period (stage) of the disease [4, 5]. However, studies that report a high transmission risk after a single exposure to an HIV-infected prostitute question the validity of this assumption [6, 7]. The data from partner studies is best predicted by mathematical models that account for a large heterogeneity in HIV infectiousness [8]. Increasing evidence is evolving that indicates a more complex temporal performance for both HIV infectiousness and susceptibility to HIV. Biological studies have therefore been used to complement the information obtained from epidemiological studies; the two combined ap-

First published in "Reviews in Medical Microbiology", 2001. Credit given to Lippincott Williams & Wilkins for the permission to reprint this review.

Pietro Vernazza
M.D., Infectious Diseases,
Department of Medicine, Cantonal Hospital,
9007 St. Gallen, Switzerland
E-Mail: Pietro.Vernazza@kssg.ch

Bundesgesundheitsbl -
Gesundheitsforsch - Gesundheitsschutz
2002 · 45:277–285 © Springer-Verlag 2002

P. L. Vernazza · A. D. M. Kashuba · M. S. Cohen

Biologische Korrelate der sexuellen Transmission von HIV

Zusammenfassung

Die Wahrscheinlichkeit einer Übertragung von HIV auf sexuellem Wege hängt ab von der Infektiosität der Index-Person und der Suszeptibilität der Person, mit der die Index-Person sexuellen Kontakt hat. Das Risiko einer HIV-Übertragung ist sehr heterogen und dürfte während der ersten sexuellen Kontakte in einer sich entwickelnden Beziehung am größten sein. Verschiedene Faktoren, u.a. auch erworbene schützende systemische und Schleimhaut-assoziierte Immunantworten, dürften für den offensichtlichen Rückgang der Übertragungswahrscheinlichkeit pro Kontakt in einer gegebenen Partnerschaft im Zeitverlauf verantwortlich sein. Biologische Untersuchungen können weiteres Licht auf die komplexen Informationen werfen, die aus epidemiologischen Erhebungen resultieren. Die Infektiosität von HIV hängt von der inokulierten Menge und von virologischen Faktoren ab. Die Viruslast im Genitaltrakt der Index-Person ist vermutlich die wichtigste Determinante für eine Übertragung. In einer gesamten Population führen Interventionen, die die Viruskonzentration im Genitaltrakt senken, sei es durch Verminderung der Viruslast im Blut oder durch Behandlung entzündlicher Prozesse im Genitaltrakt, zu einer Senkung der HIV-Inzidenz. Antiretrovirale Substanzen vermindern wahrscheinlich die sexuelle Übertragungsrate von HIV. Allerdings dürfte dies nicht für alle Substanzen im selben Ausmaß gelten. Sowohl der männliche als auch der weibliche Genitaltrakt bilden ein Kompartiment, in welchem sich HIV unabhängig vom lymphatischen System vermehrt. Die Behandlung mit antiretroviralen Medikamenten, die schlecht in den Genitaltrakt penetrieren, birgt die Gefahr einer lokalen Produktion und Ausbreitung resistenter Viren. Zusätzlich könnte eine Zunahme von Risikoverhalten die Verminderung der Übertragungswahrscheinlichkeit durch Reduktion der Viruslast wieder zunichte machen. Die biologischen Erkenntnisse über die HIV-Übertragung müssen als Grundlage für Public-Health-Strategien und zur Optimierung der Präventionsstrategien genutzt werden.

Schlüsselwörter

HIV · Sexuelle Übertragung · Infektiosität · Empfänglichkeit · Präventionsstrategien

proaches will undoubtedly improve our understanding of HIV transmission and facilitate interventions to reduce it.

Heterogeneity of the HIV transmission risk

Three major factors that determine HIV transmission risk contribute to the heterogeneity observed: differences in the susceptibility to HIV, variable infectiousness of infected individuals, and a wide spectrum of sexual behavior in a given population. Heterogeneity of sexual behavior has led to the concept of core groups in which rates of partner change and sexual activity are substantially higher than in the general population [9]. Behavioral issues which affect transmission have recently been reviewed [10].

Susceptibility to HIV

The susceptibility to HIV-infection depends on host immunological and genetic factors. A homozygous CCR5 (Chemokine Receptor 5) coreceptor deletion mutant has been shown to protect against HIV infection [11]. Genetic factors, such as CCR5 and SDF (Stromal Cell-Derived Factor) variants as well as certain HLA types, are also strongly associated with non-progression in HIV-infected individuals [12]. It is conceivable that these factors could also influence the susceptibility to HIV. At least one third of individuals exposed to HIV develop a cell-mediated immune response without overt seroconversion [13, 14]. Some animal models show a protective immune response after sub-infectious exposure to HIV; by analogy, one might expect that some of the HIV-sensitized exposed partners also have a reduced susceptibility to HIV [15]. Some exposed individuals also develop an HIV-specific mucosal and systemic IgA response and these antibodies neutralize primary HIV strains [16]. These data are further supported by several reports of decreased susceptibility to HIV in multiply exposed commercial sex workers (CSW) with continued high-risk behavior [17, 18]. Existence of a (partly) protective immune response after sexual exposure to HIV might explain the decrease of HIV transmission risk after a few sexual contacts in a given heterosexual partnership, as reported in the study that is discussed below.

Local genital factors are also likely to influence the susceptibility to HIV. Up-regulation of the CCR5 co-receptor and increased activation of T-lymphocytes present in the normal cervix have been documented [19]. This finding supports the vulnerability of the female genital tract for HIV and suggest a mechanism for the observed predominance of sexual transmission of HIV variants with CCR5 co-receptor usage [20].

Sexually transmitted diseases (STDs) have long been shown to influence not only infectiousness (see below) but also susceptibility to infection. Local inflammatory reactions in response to STDs are likely to attract CD4+ lymphocytes and release of cytokines that enhance transmission of HIV. Changes in vaginal flora appear to affect susceptibility to HIV as well. Bacterial vaginosis (BV) is associated with a high concentration of vaginal anaerobes, reduced lactobacilli, and an increase in vaginal pH [21]. Sturm-Ramirez and colleagues found in vitro evidence for increased levels of pro-inflammatory cytokines (TNF-α and IL-1) in patients with BV, which could in part explain the association of BV with increased susceptibility to HIV [22].

"The susceptibility to HIV-infection depends on host immunological and genetic factors."

Other local factors also potentially modulate HIV susceptibility: hormones that alter the vaginal epithelium have been investigated for their influence on vaginal HIV shedding. Recently, estrogens were shown to inhibit HIV transmission in the macaque model; this effect was associated by thickening of the vaginal epithelial wall [23].

The effect of circumcision on HIV transmission is highly debated. The estimates for the odds against transmission in circumcised men are in the range of 1.5. Several mechanisms have been proposed to explain this effect, including the reduced surface area for mucosal contact [24]. However, most studies investigating the role of circumcision on HIV transmission are confounded by religion and are therefore difficult to interpret. In a mathematical analysis of per-sex-act male-to-female transmission probabilities, Duerr et al. found similar per-act transmission

risk in otherwise comparable US (mostly circumcised) and Italian (mostly uncircumcised) HIV-discordant couples [25]. This argues against a marked effect of circumcision status on HIV transmission. The role of circumcision on susceptibility to HIV needs to be further examined before recommendations for large-scale circumcision interventions are issued as recently proposed [26].

In summary, a combination of local genital factors, immune response mechanism, and genetic predisposition are all influencing the risk of transmission by affecting susceptibility to HIV. However, based on epidemiological partner studies discussed below, infectiousness of the infected partner is likely to influence transmission probability even more than susceptibility.

Infectiousness of the HIV infected partner

Viral clade, quasispecies and transmission

Based on differences in the replication kinetics in dendritic cells between HIV subtype E and B, Essex and coworkers suggested that the subtype might play a role in transmission efficacy [27]. However, these results have not been confirmed by others [28] and it has been very difficult to document any effect of subtype differences on transmission risk. Miller and coworkers could not find a difference in transmissibility based on HIV macrophage tropism but found in vivo replication capacity to be predictive for the outcome of intravaginal inoculation in the macaque model [29]. Another animal study found that some HIV quasispecies were better adapted for vaginal transmission than others, but the significance of this finding for the case of HIV transmission is not known [30]. Ping and coworkers have argued that clade C expresses biological characteristics which favor sexual transmission [31]. A careful review of the debate has been published by Hu et al. [32]. In summary, systemic and local host factors remain the most important determinants for HIV infectiousness.

Systemic factors influencing HIV infectiousness

Epidemiological studies (mostly partner studies) have previously demonstrated an increased HIV transmission from patients with low CD4 count, advanced stages of disease, p24 antigenemia and the presence of STDs (reviewed in [2]). Subsequently, time variation of HIV infectiousness was proposed by Jacquez et al., based on mathematical models of monogamous partner studies [5]. The authors argue that HIV infectiousness is increased during primary infection (which is consistent with an increase of blood viral load during this phase). However, a key assumption of this model, a stable per-contact transmission rate, was challenged by Downs et al. [33] and further discussed by Shiboski and Padian [34]. Several factors that might explain the observed decline in transmission risk after primary infection need to be considered. Firstly, the large heterogeneity of transmission itself may explain the finding, also termed "frailty selection" [35]. Secondly, the assumption of constant transmission rates during a given partnership might influence the results. Thirdly, key variables on infectiousness and susceptibility that might influence the curve are usually missing in these partner studies. Shiboski and Padian conclude that the nature of variation in infectiousness cannot be confirmed, but that the findings indicate a declining tendency of transmission risk in monogamous heterosexual couples with increasing length of exposure [34]. It is just as likely that the declining risk of transmission in a given partnership results from an acquired protective immune response in the non-infected partner. This would also explain the substantially higher risk estimates (3–8%) for single sexual exposures to commercial sex workers [6, 7].

In general, transmission of a pathogen is concentration-dependent. Vertical transmission of HIV and occupational transmission through needle-stick injuries increase in situations with high viral load in the index person [36, 37]. Several partner studies have demonstrated the association of blood viral load with sexual transmission of HIV [38, 39, 40]. In these studies, neither CD4 count or the number of sexual contacts affected the risk of transmission. In a recently published sub-analysis of discordant couples included in a large STD-intervention study in Rakai, viral load was the most powerful predictor of HIV transmission [41]. Of note, none of the 53 HIV-infected individuals with a viral load below 1500 copies/ml transmitted the virus to their partner despite the negligible use of condoms. In all of the earlier epidemiological studies on transmission risk mentioned above, measurement of HIV-RNA concentration in blood was not available. It is likely that these studies were confounded by blood viral load. Low CD4 count, advanced stage of disease, p24 antigenemia and primary HIV infection are all associated with higher levels of HIV-RNA in blood. While an independent role of all those factors on infectiousness cannot be excluded, it is apparent that blood viral load is by far the most important cofactor.

HIV load in the genital tract as a measure of infectiousness

The strong predictive power of blood viral load for HIV transmission risk is biologically plausible. In general, transmission of a pathogen is concentration-dependent. Likewise, vertical transmission of HIV and occupational transmission through needle-stick injuries increase in situations with high viral load in the index person [42]. We and others have therefore studied the concentration of HIV in genital secretions and postulated that the measurement of HIV in semen can be used to estimate an individual's infectiousness (reviewed in [2, 43]). Similar results have accumulated for female genital secretions, but the variability of the assays for the detection of HIV-RNA or DNA in female secretions is considerably higher than for semen [44, 45, 46, 47, 48]. The menstrual cycle further increases the biological variability of the virus shedding in the female genital tract [49].

The combined information on HIV viral load and tropism in semen and the CCR5 receptor density on target cells in the female genital tract has been used to predict the transmission probability of HIV in the genital tract [50]. In a mathematical model we have developed, HIV transmission was unlikely (1 in 10'000 episodes of intercourse) when HIV-RNA in semen was low (i.e. <5000 copies/ml) but rose to 3 per 100 episodes of intercourse if HIV-RNA in semen was high (10^6 copies/ml). Such high seminal RNA values have been found in semen from HIV-positive men with STDs in Malawi. Thus, seminal viral load can serve as a surrogate marker to determine infectiousness.

Local genital factors influencing HIV infectiousness

Semen studies have revealed a weak but significant correlation (r = 0.55–0.60) of blood viral load and seminal HIV-RNA concentrations. The correlation was considerably higher (r = 0.80) in a recent study of patients with primary infection when a more sensitive HIV-RNA detection assay was used [51]. Thus, in agreement with the epidemiological studies, the biological studies indicate that a major determinant of the viral inoculum size in semen is blood viral load; approximately 60% of the seminal viral load can be predicted by blood viral load alone.

"Seminal viral load can serve as a surrogate marker to determine infectiousness."

Factors that explain the discordance between blood and semen viral load must be investigated. HIV-RNA concentration in semen is approximately one log lower than the respective level in blood. However, some patients have significantly higher levels of HIV in semen than in blood and have therefore been termed as hypersecretors [52, 53]. In one study, hypersecretor status has been associated with positive cell culture from the cellular semen compartment [54], supporting the potential effect of hypersecretor status on sexual transmission risk. Hypersecretor status has been associated with asymptomatic urethritis [55] and was an independent risk factor for the shedding of HIV-RNA in semen.

Symptomatic STDs have long been shown to increase the risk of sexual transmission of HIV [56, 57]. Similarly to the studies of blood viral load described above, biological studies have been performed to demonstrate the influence of STDs on the viral load in genital secretions. Cohen and colleagues studied STD patients in Malawi and found an almost ten-fold increased level of HIV-RNA secretion in semen in patients with gonorrhea as compared to control patients without urethritis [58]. This increase in genital viral load was not associated with an increased HIV-RNA concentration in blood. In the same study, genital ulcer disease was also associated with an increased HIV shedding in semen, indicating the existence of an indirect mechanism by which genital inflammatory diseases stimulate the replication kinetics of HIV in semen [59]. Further analysis of the viral quasispecies in semen and blood samples from this study by heteroduplex mobility assay revealed a discordance of the two compartments in 40% of these individuals [31]. A number of other studies have documented similar associations between genital inflammatory diseases and HIV detection in both semen and cervical secretions [22, 60, 61, 62]. In a recently published study conducted in Nairobi, treatment of women with cervicitis (N.gonorrhea, C.trachomatis or unspecific cervicitis) was associated with a six-fold reduction in the shedding of HIV-1 RNA in cervical secretions [63]. Taken together, the biological findings support the significance of STDs for HIV transmission and identify genital inflammatory diseases as another major determinant of genital shedding of HIV and HIV infectiousness.

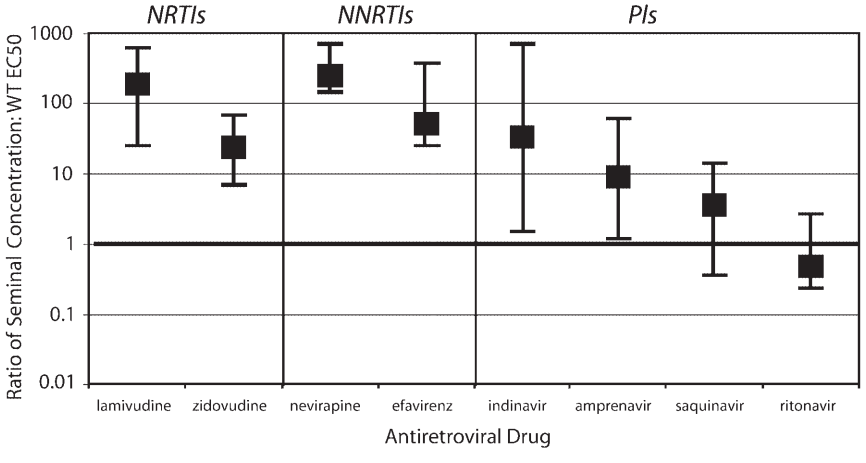

Figure 1 ▲ **Ratio of Seminal Plasma Concentrations to HIV-1 Wild-Type EC50. Ratios were calculated based on median, minimum, and maximum reported seminal drug concentrations. EC_{50} values were obtained from Molla et al [67]**

Reducing HIV infectiousness as a preventive strategy

Efforts to reduce the spread of HIV can target sexual behavior, or the susceptibility of uninfected individuals, or the infectiousness of the HIV-infected population. Reducing HIV susceptibility by the induction of a protective immune response is the central aim of HIV vaccine development. Until a protective vaccine is developed, other strategies– such as the application of vaginal microbicides or syndromic management of STDs in high-incidence areas–are currently under development to help protect individuals from being infected.

HIV prevention efforts have only recently shifted to the infected person, who can now benefit from early detection of infection. Index cases can be encouraged to engage only in safe sex behaviors, with 100% condom usage. In addition, efforts to reduce HIV viral burden in the genital tract can be undertaken

Treatment of STDs and HIV infectiousness

STDs increase the HIV load in the genital tract. The effects of treatment of STDs on genital HIV shedding has been well-documented in men and women [58, 60, 63]. In addition, the benefits of STD treatment on the HIV epidemic have been translated to some, but not all populations. In a community-randomized trial in Mwanza, Tanzania, improved management of STDs resulted in a 40 reduction of HIV incidence [64]. However, in a randomized study in the Rakai district of rural Uganda, mass STD-treatment did not result in a significant reduction of HIV incidence [65]. In that study, absence of a detectable effect on HIV incidence was probably a result of the mature stage of the HIV epidemic in rural Uganda [66]. In such mature, generalized, epidemic settings, a saturating effect is observed in core groups with high-risk behavior; therefore HIV incidence occurs at a lower level in the low-risk population and is less likely to be driven by STDs. Mass treatment of STDs cannot

target individuals with the highest risk of transmitting HIV. On an individual level, however, treatment of STDs is unquestionably an important intervention to reduce HIV infectiousness.

Reduction of viral load by HIV treatment

HIV-RNA concentration in maternal blood is associated with transmission risk [67, 68, 69, 70] and antiretroviral treatment of mothers prepartum results in reduction in maternal viral loads and vertical transmission rates [71]. Both systemic and local genital effects of short-course AZT treatment have been shown to be independently associated with reduced vertical transmission rates [72] Reduction of systemic and genital viral load is also likely to reduce the risk of sexual transmission.

A number of studies have demonstrated that highly active antiretroviral therapy (HAART) suppresses HIV replication, not only in the blood/lymphoid compartment, but also in the male and female genital tract [51, 52, 54, 73, 74, 75, 76, 77, 78, 79, 80, 81]. While some of the earlier studies were conducted among patients on suboptimal antiviral therapy, later studies have included patients with effective HAART. In our series of 114 patients with suppressed blood viral load below 400 copies/ml, only two patients had a seminal viral load slightly above the detection limit of the assay [82]. Although measurement of cell-free virus (HIV-RNA) in semen is usually suppressed in HAART-treated patients, a significant number of treated individuals harbor HIV provirus (HIV-DNA) in CD4 positive cells in their semen. In our recent study, the detection rate of HIV-DNA in semen was 17% in treated individuals compared to 38% in a drug-na control population. Zhang and colleagues have demonstrated that infectious virus can still be recovered in vitro from seminal lymphocytes after more than six months of suppressive HAART [76]. However, in a recent study on quadruple combination therapy in primary HIV infection, only 2 out of 22 patients had more than 50 HIV-DNA copies-per-ejaculate after one year of HAART [51].

In an analysis of Swiss patients with primary infection, Yerly and colleges demonstrated a significant reduction in the transmission of drug-resistant viruses after 1997 [83]. This reduction was paralleled by a gradual improvement of HAART effectiveness in the Swiss HIV Cohort Study. Currently, more than 60% of all treated patients in the Swiss HIV cohort study have HIV-RNA levels below the detection limit of 50 copies/ml in blood.

It is not known how low the blood or genital viral load must be to completely suppress the HIV-transmission risk (threshold level). In Quinn's study (cited above), a threshold level was defined at 1500 copies of HIV-RNA per ml of blood [41]. A similar observation was made for the case of vertical transmission [68]. However, any significant reduction in blood viral load is likely to result in reducing (but not eliminating) the risk of transmission.

Compartmentalization and antiretroviral drug concentrations in the male genital tract

Not all drug combinations for HAART appear to be equally effective in the genital and systemic compartment. Compartmentalization of HIV in semen has been clearly shown by the detection of different quasispecies in semen and blood in treated and untreated individuals [31, 84, 85, 86]. Recent findings of a distinct mutation pattern in virus isolates from blood and cervical samples indicate a similar compartmentalization in the case of the female genital tract [87, 88]. By mathematical modeling, Kepler and Perelson have demonstrated that limited drug penetration into a small compartment is an important risk factor for the development of resistant HIV during treatment [89]. Thus, differential penetration of antiretroviral drugs into the genital tract is an important consideration if these drugs are intended to reduce the likelihood of sexual transmission of HIV-1 [90].

Theoretical factors that may influence antiretroviral drug distribution into the male genital tract, such as protein binding, drug transporters, and drug ionization have been reviewed in detail elsewhere [91]. Seminal concentration data are available for all three classes of antiretroviral agents currently marketed and semen to blood ratio of antiviral drug concentrations (S: B ratio) vary from undetectable to greater than one. In Figure 1, median semen concentration are shown in relation to the wild-type, protein corrected IC_{50} of the drugs [92]. Of the nucleoside analogues, seminal concentration data are available for zidovudine (AZT), lamivudine (3TC), and stavudine (d4 T) [93, 94, 95, 96, 97]. All three appear to achieve seminal plasma concentrations greater than blood plasma [98, 99, 100]. However, data on intracellular drug phosphorylation in seminal lymphocytes is lacking.

Nonnucleoside reverse transcriptase inhibitor semen concentration data have been collected for efavirenz and nevirapine. Nevirapine concentration in semen reaches 60–100% of blood plasma levels [95], while seminal efavirenz exposure was 2.5–10% of that in blood [101]. The protease inhibitors generally achieve the lowest concentrations in the male genital tract, although S:B ratios vary for each compound (nelfinavir<saquinavir=ritonavir<amprenavir<indinavir). Detection of nelfinavir in semen was unsuccessful in one study [96] and both saquinavir and ritonavir reached less than 5% of blood plasma levels in semen during coadminstration of the two [102]. Amprenavir penetration into the seminal compartment was better than for saquinavir (S:B ratio: 0.2, 95% CI 0.05–3.0) [103]. Two groups have demonstrated high levels of indinavir in semen (median S:B ratio 0.4 and 1.2) [104] and further improvement of indinavir penetration by co-administration with low-dose ritonavir [105, 106].

Blood plasma protein binding, p-glycoprotein affinity, and ionizing pH all influence drug penetration into and activity within the genital tract but protein binding appears to be a major determinant of drug concentrations in semen (Figure 2). Additionally, compounds with lower p-glycoprotein affinity (amprenavir and efavirenz) appear to achieve greater genital tract penetration than compounds with greater p-glycoprotein affinity (ritonavir and saquinavir) [107]. To date, no investigation has fully evaluated and compared combination antiretroviral therapy in the context of genital tract pharmacology and virology to determine the most potent and durable regimen for suppressing viral replication in this compartment.

Sexual behavior changes in response to HAART

The increased public awareness of the effects of HAART are likely to change

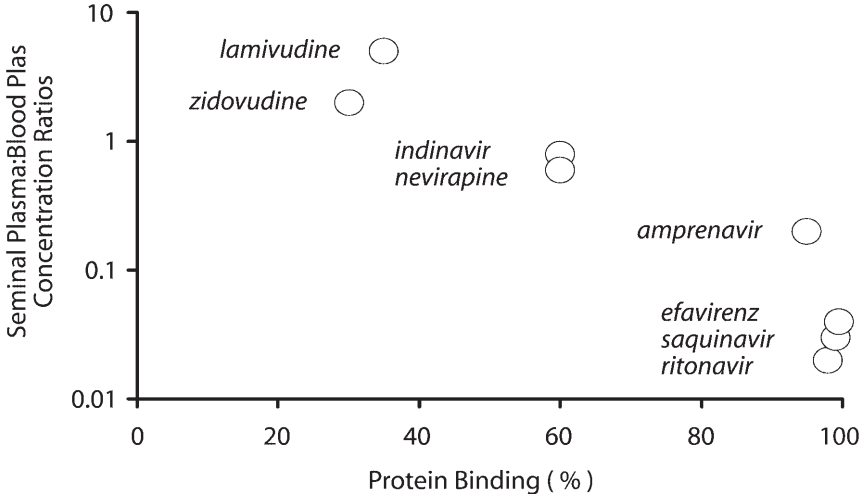

Figure 2 ▲ **Protein Binding Versus Antiretroviral SP:BP Concentration Ratios. Protein binding predicts antiretroviral exposure in the male genital tract; r=0.8 and p=0.017 by nonlinear regression analyses (see text for references)**

concerns about HIV transmission in the population at risk. The first study examining changes in perceived transmission risk associated with HAART was presented by Kravcik et al. in 1998 [108]. The authors described that 20% of HIV-infected individuals attending an HIV clinic thought that the risk of transmission was reduced during HAART and 19% believed that the need for safer sex practices was reduced under HAART. Increased-risk sexual behavior was also documented in a survey of serodiscordant couples [109] from California.

"The effects of HAART are likely to change concerns about HIV transmission in the population at risk."

One third of uninfected partners mentioned that they had already taken a chance with unprotected sex because of improved HIV treatment options and 40% responded that HAART had changed their transmission concerns. HIV-positive gay men studied in London in 1998 also perceived a decreased infectiousness associated with HAART, but this perception was not associated with an increased risk behavior [110]. A marked increase in risk-taking behavior (unprotected anal intercourse) – from 37% to 50% – was reported among gay men in the San Francisco Young Men's Health Study; this increase was also associated with increased rates of rectal gonorrhea in STD clinics [111]. In a survey from the French SEROCO study group, gay or bisexual men were three times more likely to report unprotected sex with a seronegative partner after six months of HAART than they were prior to treatment initiation [112]. No increase in risk-taking behavior was noted among heterosexual individuals; however, the sample size was small. A decrease in sexual risk-taking behavior was documented in French IV-drug users who started HAART [113].

The increased sexual risk-taking behavior in homosexual individuals is alarming. Reduced likelihood of HIV transmission due to the widespread use of HAART could be offset by an increase in risk-taking behavior.

What happens next?

HIV prevention activities were developed in 1980 s the absence of reliable knowledge about HIV transmission. These prevention activities virtually excluded the infected index cases who would have been stigmatized with little benefit by learning their infection status. The situation in 2001 is completely different, and prevention strategies must be informed by ongoing scientific discoveries. First, vaccine and microbicide development directed at preventing infection must take advantage of our knowledge of mucosal exposure and mucosal immunity. Second, STD and behavioral interventions must embrace both HIV infected and uninfected people, and the optimal usage for STD interventions demand intensive and emergent study. The failure of mass STD therapy to prevent incident HIV infection in a population in no way reduces the importance of treatment of STDs. Last, focus on HIV infected subjects is a strategy whose time has come. Early recognition of infection allows improved care for the infected subject as well as critical prevention opportunities. Indeed, the US Centers for Disease Prevention and Control has dedicated substantial prevention resources to this goal (Project SAFE). In addition, ART (Antiretroviral Therapy) may help to prevent transmission, and this issue has the highest global research priority. In the absence of a successful vaccine, strategies to reduce infectiousness – including use of therapy – are likely to develop in the coming years.

References

1. Clumeck N, Teilman H, Hermans P (1989) A cluster of HIV Infection among heterosexual people without apparent risk factors. NEJM 321:1460–1462
2. Vernazza PL, Eron JJ, Fiscus SA, Cohen MS (1999) Sexual transmission of HIV: infectiousness and prevention. AIDS 13:155–166
3. Buchacz KA, Wilkinson DA, Krowka JF, Koup RA, Padian NS (1998) Genetic and immunological host factors associated with susceptibility to HIV-1 infection. AIDS 12 [Suppl A]:S87-S94
4. Devincenzi I (1994) Longitudinal study of human immunodeficiency virus transmission by heterosexual partners. N Engl J Med 331:341–346
5. Jacquez JA, Koopman JS, Simon CP, Longini IM (1994) Role of the primary infection in epidemics of HIV infection in gay cohorts. J Acq Immun Defic Synd 7:1169–1184
6. Mastro TD, Satten GA, Nopkesorn T, Sangkharomya S, Longini IM Jr (1994) Probability of female-to-male transmission of HIV-1 in Thailand. Lancet 343:204–207
7. Cameron DW, D'Costa LJ, Maitra RK et al. (1989) Female to male transmission of human immunodeficiency virus type 1: Risk factors for seroconversion in men. Lancet ii:403–407
8. Hyman JM, Li J, Stanley EA (1999) The differential infectivity and staged progression models for the transmission of HIV. Math Biosci 155:77–109
9. Stigum H, Falck W, Magnus P (1994) The core group revisited: the effect of partner mixing and migration on the spread of gonorrhea, Chlamydia, and HIV. Math Biosci 120:1–23
10. Schiltz MA, Sandfort TG (2000) HIV-positive people, risk and sexual behaviour. Soc Sci Med 50:1571–1588

11. Liu R, Paxton WA, Choe S et al. (1996) Homozygous defect in HIV-1 coreceptor accounts for resistance of some multiply-exposed individuals to HIV-1 infection. Cell 86:367–377
12. Magierowska M, Theodorou I, Debre P et al. (1999) Combined genotypes of CCR5, CCR2, SDF1, and HLA genes can predict the long-term nonprogressor status in human immunodeficiency virus-1- infected individuals. Blood 93:936–941
13. Bernard NF, Yannakis CM, Lee JS, Tsoukas CM (1999) Human immunodeficiency virus (HIV)-specific cytotoxic T lymphocyte activity in HIV-exposed seronegative persons. J Infect Dis 179:538–547
14. Mazzoli S, Trabattoni D, Lo CS et al. (1997) HIV-specific mucosal and cellular immunity in HIV-seronegative partners of HIV-seropositive individuals. Nat Med 3:1250–1257
15. Clerici M, Clark EA, Polacino P et al. (199) T-cell proliferation to subinfectious SIV correlates with lack of infection after challenge of macaques. AIDS 8:1391–1395
16. Mazzoli S, Lopalco L, Salvi A et al. (1999) Human immunodeficiency virus (HIV)-specific IgA and HIV neutralizing activity in the serum of exposed seronegative partners of HIV-seropositive persons. J Infect Dis 180:871–875
17. Fowke KR, Nagelkerke NJD, Kimani J et al. (1996) Resistance to HIV-1 infection among persistently seronegative prostitutes in Nairobi, Kenya. Lancet 348:1347–1351
18. Beyrer C, Brookmeyer R, Natpratan C et al. (1996) Measuring HIV-1 incidence in northern Thailand: Prospective cohort results and estimates based on early diagnostic tests. J Acq Immun Defic Synd Hum R 12:495–499
19. Prakash M, Kapembwa MS, Gotch F, Patterson ST (2001) Lymphocytes in the cervix of normal women show high levels of activation markers and increased levels of CCR5 receptor expression in women taking the combined oral contraceptive. 8th Conference on Retroviruses and Opportunistic Infections Chicago 4.–8. Feb. 2001, Abstract 76.01
20. Hladik F, Lentz G, Delpit E, McElroy A, Mcelrath MJ (1999) Coexpression of CCR5 and IL-2 in human genital but not blood T cells: implications for the ontogeny of the CCR5+ Th1 phenotype. J Immunol 163:2306–2313
21. Sewankambo N, Gray RH, Wawer MJ et al. (1997) HIV-1 infection associated with abnormal vaginal flora morphology and bacterial vaginosis. Lancet 350:546–550
22. Sturm-Ramirez K, Gaye-Diallo A, Mboup S, Kanki P (2000) Bacterial vaginosis is associated with increased levels of proinflammatory cytokines in cervical secretions. 13th International Conference on AIDS, Durban, Abstract 1369.00
23. Marx P, Smith S, Baskin GB (2000) Estrogen protects against vaginal transmission of simian immunodeficiency virus. 13. International Congress on AIDS, 2000, Durban, Abstract 227
24. Szabo R, Short RV (2000) How does male circumcision protect against HIV infection? BMJ 320:1592–1594
25. Duerr A, Hsia J, Nicolosi A, Musicco M, Bowens S, Suriyanon V, Nelson K (2000) Probability of male-to-female HIV transmission among couples with HIV subtype E and B. 13. International Congress on AIDS, Durban, Abstract 1319
26. O'Farrell N, Egger M (2000) Circumcision in men and the prevention of HIV infection: a "meta- analysis" revisited [comment]. Int J STD AIDS 11:137–142
27. Soto Ramirez LE, Renjifo B, McLane MF et al. (1996) HIV-1 Langerhans' cell tropism associated with heterosexual transmission of HIV. Science 271:1291–1293
28. Pope M, Frankel SS, Mascola JR et al. (1997) Human immunodeficiency virus type 1 strains of subtypes B and E replicate in cutaneous dendritic cell-T-cell mixtures without displaying subtype-specific tropism. J Virol 71:8001–8007
29. Miller CJ, Marthas M, Greenier J, Lu D, Dailey PJ, Lu YC (1998) In vivo replication capacity rather than in vitro macrophage tropism predicts efficiency of vaginal transmission of simian immunodeficiency virus or simian/human immunodeficiency virus in rhesus macaques. J Virol 72:3248–3258
30. Neildez O, Le Grand R, Caufour P et al. (1998) Selective quasispecies transmission after systemic or mucosal exposure of macaques to simian immunodeficiency virus. Virology 243:12–20
31. Ping LH, Cohen MS, Hoffman I et al. (2000) Effects of genital tract inflammation on human immunodeficiency virus type 1 V3 populations in blood and semen. J Virol 74:8946–8952
32. Hu DJ, Buve A, Baggs J, van Der GG, Dondero TJ (1999) What role does HIV-1 subtype play in transmission and pathogenesis? An epidemiological perspective [editorial]. AIDS 13:873–881
33. Downs AM, Devincenzi I, Costigliola P et al. (1996) Probability of heterosexual transmission of HIV: relationship to the number of unprotected sexual contacts. J Acq Immun Defic Synd Hum R 11:388–395
34. Shiboski SC, Padian NS (1998) Epidemiologic evidence for time variation in HIV infectivity. J Acquir Immune Defic Syndr Hum Retrovirol 19:527–535
35. Lang W (1989) Frailty selection and HIV [letter]. Lancet 1:1397
36. Gerberding JL (1996) Prophylaxis for occupational exposure to HIV. Ann Intern Med 125:497–501
37. O'Shea S, Newell ML, Dunn DT et al. (1998) Maternal viral load, CD4 cell count and vertical transmission of HIV-1. J Med Virol 54:113–117
38. Operskalski EA, Stram DO, Busch MP et al. (1997) Role of viral load in heterosexual transmission of human immunodeficiency virus type 1 by blood transfusion recipients. Transfusion Safety Study Group. Am J Epidemiol 146:655–661
39. Ragni MV, Faruki H, Kingsley LA (1998) Heterosexual HIV-1 transmission and viral load in hemophilic patients. J Acq Immun Defic Synd Hum R 17:42–45
40. Pedraza MA, del Romero J, Roldan F et al. (1999) Heterosexual transmission of HIV-1 is associated with high plasma viral load levels and a positive viral isolation in the infected partner. J Acquir Immune Defic Syndr 21:120–125
41. Quinn TC, Wawer MJ, Sewankambo N et al. (2000) Viral load and risk of heterosexual transmission of HIV-1 among sexual partners. 7. Conference on Retroviruses and Opportunistic Infections, p 193
42. Araneta MRG, Mascola L, Eller A et al. (1995) HIV transmission through donor artificial insemination. JAMA 273:854–858
43. Taylor S, Drake S (2000) HIV in semen: clinical implications. J HIV Therapy 5:18–25
44. Kovacs A, Reichelderfer P, Datri 009 Study Team (1998) HIV is readily detectable in the female genital tract of HIV+ women. 5th Conf Retro and Opportun Infect, p 711
45. Sherlock CH, Money D, Craib KJP, Merrick L, Arikan Y, Remple V, Birch P, Burdge D (2001) Are measurements of genital HIV-1 viral load in women reproducible? 8th Conference on Retroviruses and Opportunistic Infections, Chicago, 4.–8. Feb. Abstract 241
46. Hart CE, Lennox JL, Pratt-Palmore M et al. (1999) Correlation of human immunodeficiency virus type 1 RNA levels in blood and the female genital tract. J Infect Dis 179:871–882
47. Shaheen F, Sison AV, McIntosh L, Mukhtar M, Pomerantz RJ (1999) Analysis of HIV-1 in the cervicovaginal secretions and blood of pregnant and nonpregnant women. J Hum Virol 2:154–166
48. Kozlowski PA, Lynch RM, Patterson RR, Cu-Uvin S, Flanigan TP, Neutra MR (2000) Modified wick method using Weck-Cel sponges for collection of human rectal secretions and analysis of mucosal HIV antibody. J Acquir Immune Defic Syndr 24:297–309
49. Money D, Arikan Y, Remple V et al. (2001) Genital tract and plasma HIV viral load throughout the menstrual cycle. 8th Conference on Retroviruses and Opportunistic Infections, Chicago, 4.–8. Feb. Abstract 716
50. Chakraborty H, Sen PK, Helms W et al. (2001) Viral burden in genital secretions determines male-to-female sexual transmission of HIV-1: A probabilistic empiric model. AIDS 15:621–627
51. Vernazza PL, Perrin L, Vora S et al. (2000) Increased seminal shedding of HIV during primary infection augments the need for earlier diagnosis and prevention. 7th Conf Retro and Opportun Infections, San Francisco, 30. Jan–2. Feb. Abstract 564

52. Eron JJ, Smeaton L, Degruttola V et al. (1999) The effects of amprenavir (APV) alone or in combination with ZDV/3TC, on HIV-1 levels in semen: a substudy of ACTG 347. 6th Retrovirus Conference, Chicago, Feb. 1.–4, Abstract 222
53. Tachet A, Dulioust E, Salmon D et al. (1999) Detection and quantification of HIV-1 in semen: identification of a subpopulation of men at high potential risk of viral sexual transmission. AIDS 13:823–831
54. Barroso PF, Schechter M, Gupta P et al. (2000) Effect of antiretroviral therapy on HIV shedding in semen. Ann Intern Med 133:280–284
55. Winter AJ, Taylor S, Workman J et al. (1999) Asymptomatic urethritis and detection of HIV-1 RNA in seminal plasma. Sex Transm Infect 75:261–263
56. Wasserheit JN (1992) Epidemiological synergy. Interrelationships between human immunodeficiency virus infection and other sexually transmitted diseases. Sex Transm Dis 19:61–77
57. Fleming DT, Wasserheit JN (1999) From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. Sex Transm Infect 75:3–17
58. Cohen MS, Hoffman IF, Royce RA et al. (1997) Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. Lancet 349:1868–1873
59. Dyer JR, Eron JJ, Hoffman IF et al. (1998) Association of CD4 cell depletion and elevated blood and seminal plasma human immunodeficiency virus type 1 (HIV-1) RNA concentrations with genital ulcer disease in HIV-1-infected men in Malawi. J Infect Dis 177:224–227
60. Ghys PD, Fransen K, Diallo MO et al. (1997) The associations between cervicovaginal HIV shedding, sexually transmitted diseases and immunosuppression in female sex workers in Abidjan, Cote d 'Ivoire. AIDS 11:F85–F93
61. Gadkari DA, Quinn TC, Gangakhedkar RR et al. (1998) HIV-1 DNA shedding in genital ulcers and its associated risk factors in Pune, India. J Acquir Immune Defic Syndr Hum Retrovirol, 18:277–281
62. Levine WC, Pope V, Bhoomkar A et al. (1998) Increase in endocervical CD4 lymphocytes among women with nonulcerative sexually transmitted diseases. J Infect Dis 177:167–174
63. McClelland RS, Wang CC, Mandaliya K et al. (2001) Treatment of cervicitis is associated with decreased cervical shedding of HIV-1. AIDS 15:105–110
64. Gilson L, Mkanje R, Grosskurth H et al. (1997) Cost-effectiveness of improved treatment services for sexually transmitted diseases in preventing HIV-1 infection in Mwanza Region, Tanzania. Lancet 350:1805–1809
65. Wawer MJ, Sewankambo NK, Serwadda D et al. (1999) Control of sexually transmitted diseases for AIDS prevention in Uganda: a randomised community trial. Lancet 353:525–535
66. Grosskurth H, Gray R, Hayes R, Mabey D, Wawer M (2000) Control of sexually transmitted diseases for HIV-1 prevention: understanding the implications of the Mwanza and Rakai trials. Lancet 355:1981–1987
67. The European Collaborative Study (1999) Maternal viral load and vertical transmission of HIV-1: an important factor but not the only one. AIDS 13:1377–1385
68. Cao Y, Krogstad P, Korber BT et al. (1997) Maternal HIV-1 viral load and vertical transmission of infection: the Ariel Project for the prevention of HIV transmission from mother to infant. Nat Med 3:549–552
69. O'Shea S, Newell ML, Dunn DT et al. (1998) Maternal viral load, CD4 cell count and vertical transmission of HIV-1. J Med Virol 54:113–117
70. Mayaux MJ, Dussaix E, Isopet J et al. (1997) Maternal virus load during pregnancy and mother-to-child transmission of human immunodeficiency virus type 1: the French perinatal cohort studies. SEROGEST Cohort Group. J Infect Dis 175:172–175
71. The International Perinatal HIV Group (1999) The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1 – a meta-analysis of 15 prospective cohort studies. N Engl J Med 340:977–987
72. Chuachoowong R, Shaffer N, Siriwasin W et al. (2000) Short-course antenatal zidovudine reduces both cervicovaginal human immunodeficiency virus type 1 RNA levels and risk of perinatal transmission. Bangkok Collaborative Perinatal HIV Transmission Study Group. J Infect Dis 181:99–106
73. Vernazza PL, Gilliam BL, Flepp M et al. (1998) Effect of antiviral treatment on the shedding of HIV-1 in semen. AIDS 11:1249–1254
74. Gilliam BL, Dyer J, Fiscus SA et al. (1997) Effects of reverse transcriptase inhibitor therapy on HIV-1 viral burden in semen. J Acq Immun Defic Synd Hum R 15:54–60
75. Evans JS, Dolan MJ, Walter EA, Anderson SA, Merritt T, Wegner S (1998) Correlates of HIV-1 detection by viral load and culture in semen. 5th Conf Retro and Opportun Infect, Abstract 189
76. Zhang H, Dornadula G, Beumont M, Livornese L, Van Uitert B, Henning K, Pomerantz RJ (1998) Human immunodeficiency virus type-1 in the semen of men receiving highly active antiretroviral therapy. N Engl J Med 339:1803–1809
77. Cu-Uvin S, Caliendo AM, Reinert SE, Mayer KH, Flanigan TP, Carpenter CC (1998) HIV-1 in the female genital tract and the effect of antiretroviral therapy [letter; comment]. AIDS 12:826–827
78. Liuzzi G, Chirianni A, Bagnarelli P, Clementi M, Piazza M (1999) A combination of nucleoside analogues and a protease inhibitor reduces HIV-1 RNA levels in semen: implications for sexual transmission of HIV infection. Antivir Ther 4:95–99
79. Speck CE, Coombs RW, Koutsky LA et al. (1999) Risk factors for HIV-1 shedding in semen [in Process Citation]. Am J Epidemiol 150:622–631
80. Kovacs A, Chan LS, Chen ZC et al. (1999) HIV-1 RNA in plasma and genital tract secretions in women infected with HIV-1. J Acquir Immune Defic Syndr 22:124–131
81. Cu-Uvin S, Caliendo AM, Reinert S et al. (2000) Effect of highly active antiretroviral therapy on cervicovaginal HIV-1 RNA. AIDS 14:415–421
82. Vernazza PL, Troiani L, Flepp MJ et al. (2000) Potent antiretroviral treatment of HIV-infection results in suppression of the seminal shedding of HIV. AIDS 2:122
83. Yerly S, Race E, Vora S et al. (2001) HIV drug resistance and molecular epidemiology in patients with primary HIV infection. 8th Conference on Retroviruses and Opportunistic Infections, Chicago, 4.–8. Feb, Abstract 754
84. Byrn RA, Zhang DZ, Eyre R, McGowan K, Kiessling AA (1997) HIV-1 in semen: an isolated virus reservoir. Lancet 350:1141
85. Eron JJ, Vernazza PL, Johnston DM, Seillier-Moiseiwitsch F, Alcorn TM, Fiscus SA, Cohen MS (1998) Resistance to HIV-1 to antiretroviral agents in blood and seminal plasma: implications for transmission. AIDS 12:[F181], F189
86. Eyre RC, Zheng G, Kiessling AA (2000) Multiple drug resistance mutations in human immunodeficiency virus in semen but not blood of a man on antiretroviral therapy. Urology (Online) 55:591
87. Yamamura Y, Tirado G, Soto A, Sepulveda G, Zorrilla C (2001) Resident HIV of vaginal compartment are distinct from plasma HIV in both drug resistance mutation patterns and viral evolution. 8th Conference on Retroviruses and Opportunistic Infections, Chicago, 4.–8. Feb. Abstract 719
88. De Pasquale MP, Allega J, Sutton L, D'Aquila RT, Caliendo A, Donahue SM, Cu-Uvin S (2001) Drug-selected HIV-1 mutations can differ in cervico-vaginal and blood plasma RNA. 8th Conference on Retroviruses and Opportunistic Infections, Chicago, 4.–8. Feb. Abstract 446
89. Kepler TB, Perelson AS (1998) Drug concentration heterogeneity facilitates the evolution of drug resistance. Proc Natl Acad Sci USA 95:11514–11519
90. Taylor S, Pereira AS (2001) Antiretroviral drug concentrations in semen of HIV-1 infected men. Sex Transm Infect 77:4–11
91. Kashuba AD, Dyer JR, Kramer LM, Raasch RH, Eron JJ, Cohen MS (1999) Antiretroviral-drug concentrations in semen: implications for sexual transmission of human immunodeficiency virus type 1. Antimicrob Agents Chemother 43:1817–1826
92. Molla A, Vasavanonda S, Kumar G et al. (1998) Human serum attenuates the activity of protease inhibitors toward wild- type and mutant human immunodeficiency virus. Virology 250:255–262
93. Pereira AS, Kashuba AD, Fiscus SA et al. (1999) Nucleoside analogues achieve high concentrations in seminal plasma: relationship between drug concentration and virus burden. J Infect Dis 180:2039–2043

94. Henry K, Chinnock BJ, Quinn RP, Fletcher CV, de Miranda P, Balfour HH (1988) Concurrent zidovudine levels in semen and serum determined by radioimmunoassay in patients with AIDS or AIDS-related complex. JAMA 259:3023–3026
95. Taylor S, van Heeswijk RP, Hoetelmans RM et al. (2000) Concentrations of nevirapine, lamivudine and stavudine in semen of HIV-1-infected men [in Process Citation]. AIDS 14:1979–1984
96. Reijers MH, van Heeswijk RP, Jurriaans S, Schuitemaker H, Portegies P, Weverling GJ, Lange J (2000) The concentrations of D4T, 3TC, nelfinavir (NFV), and saquinavir (SQV) in plasma, cerebrospinal fluid (CSF) and semen. 7th Conf Retro and Opportun Infections, San Francisco, Jan. 30–Feb. 2, Abstract 316
97. Liuzzi G, Chirianni A, Casazza R, Tallarino A, Piazza M (2000) Concentration of stavudine in blood an semen from HIV-1 infected patients. AIDS 14 [Suppl 4]:S96-S97
98. Anderson PL, Noormohamed SE, Henry K, Brundage RC, Balfour HH Jr, Fletcher CV (2000) Semen and serum pharmacokinetics of zidovudine and zidovudine- glucuronide in men with HIV-1 infection [in Process Citation]. Pharmacotherapy 20:917–922
99. Fletcher CV, Acosta EP, Henry K et al. (1998) Concentration-controlled zidovudine therapy. Clin Pharmacol Ther 64:331–338
100. Moore KH, Barrett JE, Shaw S et al. (1999) The pharmacokinetics of lamivudine phosphorylation in peripheral blood mononuclear cells from patients infected with HIV-1. AIDS 13:2239–2250
101. Reddy S, Kim JD, Eron JJ et al. (2001) Efavirenz (EFV) – containing antiretroviral (ARV) therapy (T) effectively reduces HIV RNA in the seminal plasma (SP) of HIV-1-infected men (M). 8th Conference on Retroviruses and Opportunistic Infections, Chicago, 4.–8. Feb. Abstract 750
102. Taylor S, Back DJ, Workman J et al. (1999) Poor penetration of the male genital tract by HIV-1 protease inhibitors [letter]. AIDS 13:859–860
103. Pereira AS, Gerber JG, Smeaton L, Acosta EP, Gulick R, Murphy R, Eron JJ (2001) The pharmacokinetics of amprenavir, lamivudine, and zidovudine in the male genital tract of HIV-1-infected men. 8th Conference on Retroviruses and Opportunistic Infections, Chicago, 4.–8. Feb. Abstract 749
104. Taylor S, Back D, Drake S, Gibbons S, Reynolds H, White D, Pillay D (2000) Antiretroviral drug concentration in semen of HIV-infected men: Differential penetration of indinavir, ritonavir, and saquinavir. 7th Conf Retro and Opportun Infections, San Francisco, Jan. 30–Feb. 2, Abstract 318
105. Taylor S, Raynolds H, Drake SM, Stradling C, White DJ, Gibbons SE, Back DJ (2000) A pharmacokinetic study of indinavir (IDV) 600 mg bd and ritonavir (RTV) 200 mg bd in plasma and semen of HIV-1 infected men. AIDS 14 [Suppl 4]:S96
106. van Praag RM, Weverling GJ, Portegies P et al. (2000) Enhanced penetration of indinavir in cerebrospinal fluid and semen after the addition of low-dose ritonavir. AIDS 14:1187–1194
107. Kim R (2001) Role of P-glycoprotein in CNS and genital tract penetration. 8th Conference on Retroviruses and Opportunistic Infections, Chicago, 4.–8. Feb. Abstract S1
108. Kravcik S, Victor G, Houston S et al. (1998) Effect of antiretroviral therapy and viral load on the perceived risk of HIV transmission and the need for safer sexual practices. J Acquir Immune Defic Syndr Hum Retrovirol 19:124–129
109. van der SA, Gomez CA, Saul J, Quan J, Padian N (2000) Sexual risk behaviors among heterosexual HIV serodiscordant couples in the era of post-exposure prevention and viral suppressive therapy. AIDS 14:F47–F54
110. Elford J, Bolding G, Maguire M, Sherr L (2000) Do gay men discuss HIV risk reduction with their GP? AIDS Care 12:287–290
111. Ekstrand ML, Stall RD, Paul JP, Osmond DH, Coates TJ (1999) Gay men report high rates of unprotected anal sex with partners of unknown or discordant HIV status. AIDS 13:1525–1533
112. Miller M, Meyer L, Boufassa F et al. (2000) Sexual behavior changes and protease inhibitor therapy. SEROCO Study Group. AIDS 14:F33–F39
113. Bouhnik AB, Moatti JP, Vlahov D, Gallais H, Dellamonica P, Obadia Y, and the MANIF 2000 study (2000) Impact of HAART on sexual risk behaviors among HIV-infected French injecting drug users. 13. Int. Congress on AIDS, Durban, Abstract 330

Fachnachricht

Ist eine Bluttransfusion noch sicher?

Die BSE-Krise hat eine verstärkte Diskussion über die Sicherheit von Blutprodukten ausgelöst. Experten von Robert Koch- und Paul-Ehrlich-Institut haben angesichts der sich in Europa ausbreitenden Variante der Creutzfeldt-Jakob-Krankheit eine Gesamtstrategie zur Blutversorgung entwickelt. Bislang sei noch kein Fall einer vCJK-Übertragung durch Blut oder Blutprodukte bekannt geworden.

Nach „Worst-case-Szenarien" werden für Deutschland bis 2004 etwa 300-600 vCJK-Fälle erwartet, die auf Primärinfektionen über Nahrungsmittel zurückgeführt werden. Für eine Übertragung von Mensch zu Mensch gibt es bisher keine Hinweise, jedoch kann nicht ausgeschlossen werden, dass vCJK durch chirurgische Instrumente oder durch Blut oder Blutprodukte übertragbar ist. Noch gibt es keine geeigneten Nachweistests zur Erkennung der vCJK im Blut von Blutspendern. Bis ein geeigneter Test entwickelt wird, könnten als Risikovorsorge Personen von der Blutspende ausgeschlossen werden, die früher selbst Empfänger von Bluttransfusionen waren. Problem ist allerdings, dass mit dieser Maßnahme ca. 4% der Blutspender in Deutschland wegfallen würden. Bevor also Transfusionsempfänger von der Blutspende ausgeschlossen werden, sollten z.B. durch Werbe- und Motivationskampagnen neue Spender gefunden werden.

Quelle: Pressestelle RKI
(http://www.rki.de),

Pressestelle PEI
(http://www.pei.de)