Published in final edited form as:

AIDS. 2006 April 4; 20(6): 895–900. doi:10.1097/01.aids.0000218554.59531.80.

Lower levels of HIV RNA in semen in HIV-2 compared with HIV-1 infection: implications for differences in transmission

Geoffrey S. Gottlieb^a, Stephen E. Hawes^b, Habibatou D. Agne^c, Joshua E. Stern^d, Cathy W. Critchlow^b, Nancy B. Kiviat^{a,d}, and Papa Salif Sow^c

^aDepartment of Medicine, School of Medicine, the University of Washington, Seattle, Washington

^bDepartment of Epidemiology, School of Public Health and Community Medicine, the University of Washington, Seattle, Washington

^cUniversity of Dakar, Senegal

^dDepartment of Pathology, School of Medicine, the University of Washington, Seattle, Washington

Abstract

Background and objectives—HIV-2 infection, in comparison with HIV-1, is characterized by lower plasma viral loads, slower CD4 cell count decline, decreased AIDS-related mortality, and lower rates of mother-to-child and sexual transmission. To gain further insight into why HIV-1 is more readily transmitted as compared with HIV-2, we analyzed semen and plasma HIV RNA levels in HIV-1 and HIV-2-positive men from Senegal.

Design and methods—Twenty-two HIV-1 and 10 HIV-2-infected subjects from the University of Dakar donated semen and blood samples for this analysis. HIV-1 and HIV-2 viral loads in semen and plasma were quantified using type-specific polymerase chain reaction assays.

Results—The mean age of the subjects was 37 and 40 years; mean CD4 cell count was 222 and 276 cells/ μ l and the mean plasma viral load was 4.7 and 3.0 log₁₀ copies/ml for HIV-1 and HIV-2, respectively ($P = 0.002$). HIV RNA was detected in semen in 21 of 22 (95%) of HIV-1 and seven of 10 (70%) of HIV-2-infected subjects; $P = 0.07$). However, the levels of HIV RNA present in semen were markedly different between those with HIV-1 and HIV-2, with a mean of 4.4 log₁₀ copies/ml among those with HIV-1 and a mean of 2.6 log₁₀ copies/ml among those with HIV-2 ($P < 0.001$). In multivariate analysis, plasma viral load and HIV type, but not CD4 cell count, were independently predictive of semen viral load ($P = 0.03, 0.05, 0.48$, respectively).

Conclusions—These data suggest that differences in semen viral load between HIV-1 and HIV-2 may be in part responsible for the markedly different transmission rates of these two viruses. In addition, risk of male genital tract shedding strongly correlates with plasma viral loads. Interventions that decrease viral load may help decrease transmission of both HIV-1 and HIV-2.

Keywords

HIV-1; HIV-2; virus shedding; semen; male; Africa; Senegal

Introduction

Understanding the correlates of HIV transmission is important to determining effective preventative strategies. The pandemic spread of HIV-1, in contrast to the limited spread of HIV-2, primarily in West Africa, is likely due to different rates of transmission of these two viruses [1–4]. Nonetheless, both HIV-1 and HIV-2 are primarily spread by heterosexual transmission [5,6]. Similar to other sexually transmitted infections (STIs), risk of HIV transmission is in part a function of the quantity of HIV in genital tract secretions [7–17]. A greater understanding of patterns and risk factors associated with genital tract HIV-1 and HIV-2 shedding will permit the development of more efficient strategies to control HIV transmission [18]. Only three studies have compared risk factors for detecting HIV-1 versus HIV-2 in the genital tract; all were performed in women [19–22]. Potential differences in HIV shedding rates among subjects infected with HIV-1 versus HIV-2 have been hypothesized to result from lower HIV plasma loads among HIV-2 infected persons [23–25]. Indeed, HIV-1 plasma viral load has been the only factor directly linked to transmission [26–30]. Factors shown to be associated with shedding in semen have been less well studied but plasma viral load appears to be a strong correlate [13–15] as do concurrent STIs [31–34].

In this study we examined semen shedding in 22 HIV-1 and 10 HIV-2-infected men from Senegal, West Africa. These data may help explain the different transmission rates between HIV-1 and HIV-2 and may provide new insights regarding prevention.

Materials and methods

Study population and study design

Men aged 18 years and older presenting to the University of Dakar, Fann Hospital, Infectious Disease Clinic were offered HIV-1 and HIV-2 serologic testing. Sera were tested using a microwell plate HIV-1/HIV-2 enzyme immunoassay (Genetic Systems, Redmond, Washington, USA), with positive sera confirmed using a rapid synthetic peptide-based membrane immunoassay (Multispot; Sanofi Diagnostic Pasteur, Redmond, Washington, USA) which classifies subjects as HIV-1, HIV-2, or dually seropositive. Semen and blood samples for HIV viral load assays were obtained from 22 men infected with HIV-1 and 10 with HIV-2. All subjects were antiretroviral therapy naive. This study was conducted according to procedures approved by the institutional review boards of the Universities of Washington and Dakar, and the Senegalese National AIDS Committee. All subjects provided informed consent for study participation.

Collection of specimens and clinical assessment

Subjects completed an interview with questions concerning demographic characteristics, and sexual and other behaviors. A routine medical history was taken and recorded on a standardized form by a clinician who also performed a general physical examination and a genital examination and clinical assessment for sexually transmitted infections (STI). Five milliliters of peripheral blood was collected into tubes containing ethylenediamine tetraacetic acid (EDTA) or acid citrate dextrose (ACD) and analyzed using the FACSCount analyzer (Becton Dickinson Biosciences, San Jose, California, USA) to determine the number of CD4, CD8 and CD3 cells/ μ l of blood; 10 ml of peripheral blood was collected for HIV-1 and HIV-2 quantitative RNA viral load assays. Semen was obtained by masturbation into a sterile container.

Quantitative detection of HIV-1 and HIV-2 RNA

Quantitative viral load assays for HIV-1 and HIV-2 plasma and semen RNA were performed using polymerase chain reaction-based assays developed at Roche Molecular Systems (Pleasanton, California, USA) as previously described [25,35].

Statistical methods

Fisher's exact tests were performed to compare detection of semen and plasma HIV RNA among men with HIV-1 versus HIV-2. Continuous variables (e.g., CD4 cell count, log₁₀ plasma/semen RNA) were compared using the Wilcoxon rank-sum test. Undetectable levels of plasma or semen HIV-1 and HIV-2 RNA were set to the lower limit of detection minus one for statistical analyses. To evaluate the sensitivity and robustness of our study findings to samples that had negative results on quantitative assay for HIV RNA we performed a series of analyses, setting the values for those samples to a range of values between 0 and the limit of detection. None of these analyses gave qualitatively different results. The level of statistical significance used in all analyses was $P < 0.05$. Data analyses were conducted using SAS 8.2 for Windows and JMP for Macintosh (SAS Institute, Cary, North Carolina, USA).

Results

The demographic, clinical, immunologic and virologic characteristics of the 22 HIV-1 and 10 HIV-2 infected men in this study are shown in Table 1. The mean age of the HIV-1 and HIV-2 subjects was 37 and 40, respectively. Experiencing greater than 10 life-time sexual partners and having sex with female sex workers was common in these men, whereas consistent condom usage was less frequent. Symptomatic STI were infrequent: none of the men had penile discharge or inguinal lymphadenopathy, genital ulcer disease (GUD) was also uncommon (Table 1). The majority of subjects had WHO stage 3 disease and the mean CD4 cell count was 222 and 276/ μ l for HIV-1 and HIV-2-infected subjects, respectively ($P = 0.8$ for CD4 cell count difference by Wilcoxon rank sum test). The mean plasma viral load was 4.7 and 3.0 log₁₀ copies/ml for HIV-1 and HIV-2, respectively ($P = 0.002$ for difference by Wilcoxon rank sum test). The presence of HIV RNA in semen was marginally higher in those with HIV-1 compared to those with HIV-2, (being detected in 21 of 22 (95%) of HIV-1 and seven of 10 (70%) of HIV-2 infected subjects; $P = 0.07$ by Fisher's exact test). However, the levels of HIV RNA present in semen were markedly different between those with HIV-1 compared to HIV-2, with a mean of 4.4 log₁₀ copies/ml among those with HIV-1 and a mean of 2.6 log₁₀ copies/ml among those with HIV-2 ($P < 0.001$ for difference by Wilcoxon rank sum test). Semen HIV RNA viral load correlated with plasma viral load (adjusted $R^2 = 0.53$, $P < 0.0001$) irrespective of HIV type ($P = 0.007$ for HIV-1 and $P = 0.05$ for HIV-2) (Fig. 1). However, HIV-2 infected subjects had 0.7 log₁₀ lower HIV semen load than those with HIV-1 after adjusting for log₁₀ plasma level ($P = 0.07$). In addition, semen HIV RNA viral load was inversely correlated with CD4 cell count (adjusted $R^2 = 0.16$; $P = 0.02$) irrespective of HIV type ($P = 0.03$ for HIV-1 and $P = 0.18$ for HIV-2) (Fig. 2). However, HIV-2 infection was associated with a 1.5 log₁₀ lower HIV semen load than that in HIV-1 after adjusting for CD4 cell count ($P < 0.001$). In multivariate analysis, plasma viral load and HIV type, but not CD4 cell count, were independently predictive of semen viral load (P -values = 0.03, 0.05, 0.48, respectively).

Discussion

To our knowledge this is the first study to examine levels of HIV-2 in the male genital tract or compare them to those of HIV-1. We examined semen HIV shedding in 22 HIV-1 and 10 HIV-2-infected men from Senegal, West Africa. We found significantly lower levels of HIV

in semen of those with HIV-2 compared to HIV-1, and shedding generally correlated with plasma viral load irrespective of virus type. This study confirms previous reports of a strong correlation between HIV-1 male genital shedding and plasma viral load [13–15] and expands the data on male genital tract HIV-1 levels in individuals from sub-Saharan Africa [36–39]. In addition, we have previously shown that equal plasma viral loads predict a similar rate of CD4+ T cell decline in HIV-1 and HIV-2-infected individuals from our Senegalese cohort and that viral load but not HIV type is the most important factor [25]. Our current data suggest that while levels of semen viral loads were lower in HIV-2 compared to HIV-1, plasma viral load is stronger predictor than HIV type in determining the level of semen shedding. Furthermore, our current study of HIV-1 and HIV-2 in the male genital tract shows similar findings to previous studies comparing HIV-1 and HIV-2 levels in the female genital tract; namely that HIV-2 levels are typically lower than HIV-1 in both plasma and the genital tract [19–22]. Taken together, these data help explain the different transmission rates between HIV-1 and HIV-2 and may provide new insights regarding prevention.

Limitations of this study include the small sample size, especially the number of HIV-2 infected subjects, and the lack of longitudinal follow-up. The lack of longitudinal follow-up leaves unanswered the question of whether the usually low plasma HIV-2 RNA viral load throughout the course of HIV-2 infection [25] leads to persistently reduced seminal shedding. Moreover, the question of whether the similar levels of peripheral blood mononuclear cell HIV DNA found in HIV-1 and HIV-2 infection [25] are also found in HIV-infected seminal cells also remains unanswered. Given the small sample size of HIV-2 subjects, other potential correlates, such as factors previously found to be associated with HIV-1 shedding, could not be assessed. Specifically, it is unclear whether concurrent STI increase HIV-2 seminal shedding as they do in HIV-1 infection. Symptomatic STI in this study were rare. None of the men had penile discharge or inguinal adenopathy suggesting that gonorrhea and/or chlamydia were unlikely and consequently swabs for gonorrhea/chlamydia were not taken in asymptomatic men. GUD was present in 11% of the HIV-1 and 13% of the HIV-2 infected men. It was not further assessed for specific pathogens (e.g. syphilis, herpes simplex virus, chancroid). There was no association between presence of GUD and semen or plasma loads ($P = 0.46$ and 0.23 , respectively) although power to detect an effect was low given the small sample size. However, given the GUD data and the low prevalence of symptomatic STI we believe semen viral loads were unlikely to be differentially biased in the HIV-1 versus HIV-2 groups. Unfortunately this study was prematurely ended due to community concerns regarding semen donation; however, we do not believe this premature termination systematically biased our results. Despite these important constraints, we found a significant correlation of HIV-2 semen viral load with plasma viral load.

Despite the correlation between plasma and semen viral load, evidence suggests that the genital tract can be a persistent reservoir for HIV-1 replication in men and that treatment with antiretroviral drugs only suppresses semen HIV-1 shedding to varying degrees [40–44]. In addition, antiretroviral drug-resistant HIV-1 can be detected in semen of men on antiretroviral therapy [45,46]. Whether these observations will be seen in HIV-2-infected men treated with antiretroviral therapy will require further studies. Ultimately, a thorough understanding of the correlates of HIV shedding in the male genital tract will help in defining strategies to prevent HIV transmission and curtail its epidemic spread.

Acknowledgments

We thank Deana Rich, Elise Reay-Ellers, Macoumba Touré, Dr Mame B. Diouf, Dr Mame A. Faye Niang and Dr Awa M. Coll-Seck for their invaluable co-ordination and supervision of study procedures in Senegal; Dr Aissatou

Diop, Dr Pierre Ndiaye, Marie Pierre Sy and Mame Dieumbe Mbengue-Ly for patient care; and Alison Starling for forms development and data management. In addition, we would like to thank Shirley Kwok, Rich Respass, Kelly Lagassic, Cindy Christopherson and Jane Kuypers for their work in the development of assays and testing of study samples for HIV-1 and HIV-2 RNA and David Nickle and Jim Mullins for helpful discussions. We would like to thank the study participants without whom these studies would not be possible.

Sponsorship: These studies were supported by grants from the NIH/NIAID and the University of Washington CFAR.

References

1. De Cock KM, Adjorlolo G, Ekpini E, Sibailly T, Kouadio J, Maran M, et al. Epidemiology and transmission of HIV-2. Why there is no HIV-2 pandemic [published erratum appears in JAMA 1994; 271:196] [see comments]. JAMA. 1993; 270:2083–2086. [PubMed: 8147962]
2. Donnelly C, Leisenring W, Kanki P, Awerbuch T, Sandberg S. Comparison of transmission rates of HIV-1 and HIV-2 in a cohort of prostitutes in Senegal. Bull Math Biol. 1993; 55:731–743. [PubMed: 8318928]
3. Kanki PJ, Travers KU, MBoup S, Hsieh CC, Marlink RG, Gueye-NDiaye A, et al. Slower heterosexual spread of HIV-2 than HIV-1. Lancet. 1994; 343:943–946. [PubMed: 7909009]
4. Gilbert PB, McKeague IW, Eisen G, Mullins C, Gueye NA, Mboup S, et al. Comparison of HIV-1 and HIV-2 infectivity from a prospective cohort study in Senegal. Stat Med. 2003; 22:573–593. [PubMed: 12590415]
5. Poulsen AG, Aaby P, Gottschau A, Kvinesdal BB, Dias F, Molbak K, et al. HIV-2 infection in Bissau, West Africa, 1987–1989: incidence, prevalences, and routes of transmission. J Acquir Immune Defic Syndr. 1993; 6:941–948. [PubMed: 8315578]
6. UNAIDS. [Accessed on 17 November 2005] Report on the Global HIV/AIDS Epidemic 2004. http://www.unaids.org/bangkok2004/GAR2004_html/GAR2004_00_en.html
7. Clemetson DB, Moss GB, Willerford DM, Hensel M, Emonyi W, Holmes KK, et al. Detection of HIV DNA in cervical and vaginal secretions. Prevalence and correlates among women in Nairobi, Kenya. JAMA. 1993; 269:2860–2864. [PubMed: 8497089]
8. Mostad SB, Overbaugh J, DeVange DM, Welch MJ, Chohan B, Mandaliya K, et al. Hormonal contraception, vitamin A deficiency, and other risk factors for shedding of HIV-1 infected cells from the cervix and vagina. Lancet. 1997; 350:922–927. [PubMed: 9314871]
9. Mostad SB, Jackson S, Overbaugh J, Reilly M, Chohan B, Mandaliya K, et al. Cervical and vaginal shedding of human immunodeficiency virus type 1-infected cells throughout the menstrual cycle. J Infect Dis. 1998; 178:983–991. [PubMed: 9806025]
10. Mostad SB. Prevalence and correlates of HIV type 1 shedding in the female genital tract. AIDS Res Hum Retroviruses. 1998; 14(suppl 1):S11–S15. [PubMed: 9581878]
11. Goulston C, McFarland W, Katzenstein D. Human immunodeficiency virus type 1 RNA shedding in the female genital tract. J Infect Dis. 1998; 177:1100–1103. [PubMed: 9534992]
12. Kovacs A, Wasserman SS, Burns D, Wright DJ, Cohn J, Landay A, et al. Determinants of HIV-1 shedding in the genital tract of women. Lancet. 2001; 358:1593–1601. [PubMed: 11716886]
13. Coombs RW, Speck CE, Hughes JP, Lee W, Sampoleo R, Ross SO, et al. Association between culturable human immunodeficiency virus type 1 (HIV-1) in semen and HIV-1 RNA levels in semen and blood: evidence for compartmentalization of HIV-1 between semen and blood. J Infect Dis. 1998; 177:320–330. [PubMed: 9466517]
14. Vernazza PL, Gilliam BL, Dyer J, Fiscus SA, Eron JJ, Frank AC, et al. Quantification of HIV in semen: correlation with antiviral treatment and immune status. AIDS. 1997; 11:987–993. [PubMed: 9223732]
15. Tachet A, Dulioust E, Salmon D, De Almeida M, Rivalland S, Finkielsztejn L, et al. Detection and quantification of HIV-1 in semen: identification of a subpopulation of men at high potential risk of viral sexual transmission. AIDS. 1999; 13:823–831. [PubMed: 10357382]
16. Chakraborty H, Sen PK, Helms RW, Vernazza PL, Fiscus SA, Eron JJ, et al. Viral burden in genital secretions determines male-to-female sexual transmission of HIV-1: a probabilistic empiric model. AIDS. 2001; 15:621–627. [PubMed: 11317000]

17. Pilcher CD, Tien HC, Eron JJ Jr, Vernazza PL, Leu SY, Stewart PW, et al. Brief but efficient: acute HIV infection and the sexual transmission of HIV. *J Infect Dis.* 2004; 189:1785–1792. [PubMed: 15122514]
18. Critchlow CW, Kiviat NB. Detection of human immunodeficiency virus type 1 and type 2 in the female genital tract: implications for the understanding of virus transmission. *Obstet Gynecol Surv.* 1997; 52:315–324. [PubMed: 9140133]
19. Ghys PD, Fransen K, Diallo MO, Ettiegn-Traore V, Coulibaly IM, Yeboue KM, et al. The associations between cervicovaginal HIV shedding, sexually transmitted diseases and immunosuppression in female sex workers in Abidjan, Cote d'Ivoire. *AIDS.* 1997; 11:F85–F93. [PubMed: 9342059]
20. Seck K, Samb N, Tempesta S, Mulanga-Kabeya C, Henzel D, Sow PS, et al. Prevalence and risk factors of cervicovaginal HIV shedding among HIV-1 and HIV-2 infected women in Dakar, Senegal. *Sex Transm Infect.* 2001; 77:190–193. [PubMed: 11402227]
21. Critchlow, C.; Hawes, S.; Redman, M.; Sow, P.; Kiviat, N. Detection of human immunodeficiency virus (HIV) type 1 and type 2 RNA and DNA in vaginal secretions among women in Senegal, West Africa. Ninth Conference on Retroviruses and Opportunistic Infections; Seattle, WA. 2002. [abstract 19]
22. Hawes, S.; Critchlow, C.; Redman, M.; Sow, P.; Kiviat, N. A longitudinal study of the detection of human immunodeficiency virus (HIV) type-1 and type-2 RNA in vaginal secretions among Senegalese women. Ninth Conference on Retroviruses and Opportunistic Infections; Seattle, WA. 2002. [abstract 785-W]
23. Simon F, Matheron S, Tamalet C, Loussert-Ajaka I, Bartczak S, Pepin JM, et al. Cellular and plasma viral load in patients infected with HIV-2. *AIDS.* 1993; 7:1411–1417. [PubMed: 7904166]
24. Popper SJ, Sarr AD, Travers KU, Gueye-Ndiaye A, Mboup S, Essex ME, et al. Lower human immunodeficiency virus (HIV) type 2 viral load reflects the difference in pathogenicity of HIV-1 and HIV-2. *J Infect Dis.* 1999; 180:1116–1121. [PubMed: 10479138]
25. Gottlieb GS, Sow PS, Hawes SE, Ndoye I, Redman M, Coll-Seck AM, et al. Equal plasma viral loads predict a similar rate of CD4R T cell decline in human immunodeficiency virus (HIV) type 1- and HIV-2-infected individuals from Senegal, West Africa. *J Infect Dis.* 2002; 185:905–914. [PubMed: 11920314]
26. Pedraza MA, del Romero J, Roldan F, Garcia S, Ayerbe MC, Noriega AR, et al. 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.* 1999; 21:120–125. [PubMed: 10360803]
27. Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. *N Engl J Med.* 2000; 342:921–929. [PubMed: 10738050]
28. Fideli US, Allen SA, Musonda R, Trask S, Hahn BH, Weiss H, et al. Virologic and immunologic determinants of heterosexual transmission of human immunodeficiency virus type 1 in Africa. *AIDS Res Hum Retroviruses.* 2001; 17:901–910. [PubMed: 11461676]
29. Gray RH, Wawer MJ, Brookmeyer R, Sewankambo NK, Serwadda D, Wabwire-Mangen F, et al. Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda. *Lancet.* 2001; 357:1149–1153. [PubMed: 11323041]
30. Wawer MJ, Gray RH, Sewankambo NK, Serwadda D, Li X, Laeyendecker O, et al. Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. *J Infect Dis.* 2005; 191:1403–1409. [PubMed: 15809897]
31. Speck CE, Coombs RW, Koutsy LA, Zeh J, Ross SO, Hooton TM, et al. Risk factors for HIV-1 shedding in semen. *Am J Epidemiol.* 1999; 150:622–631. [PubMed: 10490002]
32. Jackson DJ, Rakwar JP, Bwayo JJ, Kreiss JK, Moses S. Urethral *Trichomonas vaginalis* infection and HIV-1 transmission. *Lancet.* 1997; 350:1076. [PubMed: 10213555]
33. Winter AJ, Taylor S, Workman J, White D, Ross JD, Swan AV, et al. Asymptomatic urethritis and detection of HIV-1 RNA in seminal plasma. *Sex Transm Infect.* 1999; 75:261–263. [PubMed: 10615314]
34. Coombs RW, Reichelderfer PS, Landay AL. Recent observations on HIV type-1 infection in the genital tract of men and women. *AIDS.* 2003; 17:455–480. [PubMed: 12598766]

35. Andersson S, Norrgren H, da Silva Z, Biague A, Bamba S, Kwok S, et al. Plasma viral load in HIV-1 and HIV-2 singly and dually infected individuals in Guinea-Bissau, West Africa: significantly lower plasma virus set point in HIV-2 infection than in HIV-1 infection. *Arch Intern Med.* 2000; 160:3286–3293. [PubMed: 11088091]
36. Moss GB, Overbaugh J, Welch M, Reilly M, Bwayo J, Plummer FA, et al. Human immunodeficiency virus DNA in urethral secretions in men: association with gonococcal urethritis and CD4 cell depletion. *J Infect Dis.* 1995; 172:1469–1474. [PubMed: 7594704]
37. Cohen MS, Hoffman IF, Royce RA, Kazembe P, Dyer JR, Daly CC, et al. Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. AIDSCAP Malawi Research Group. *Lancet.* 1997; 349:1868–1873. [PubMed: 9217758]
38. Dyer J, Kazembe P, Vernazza P, Gilliam B, Maida M, Zimba D, et al. High levels of human immunodeficiency virus type 1 in blood and semen of seropositive men in sub-Saharan Africa. *J Infect Dis.* 1998; 177:1742–1746. [PubMed: 9607862]
39. Hobbs MM, Kazembe P, Reed AW, Miller WC, Nkata E, Zimba D, et al. *Trichomonas vaginalis* as a cause of urethritis in Malawian men. *Sex Transm Dis.* 1999; 26:381–387. [PubMed: 10458630]
40. Krieger JN, Coombs RW, Collier AC, Ross SO, Chaloupka K, Cummings DK, et al. Recovery of human immunodeficiency virus type 1 from semen: minimal impact of stage of infection and current antiviral chemotherapy. *J Infect Dis.* 1991; 163:386–388. [PubMed: 1988523]
41. Gupta P, Mellors J, Kingsley L, Riddler S, Singh M, Schreiber S, et al. High viral load in semen of human immunodeficiency virus type 1-infected men at all stages of disease and its reduction by therapy with protease and nonnucleoside reverse transcriptase inhibitors. *J Virol.* 1997; 71:6271–6275. [PubMed: 9223532]
42. Zhang H, Dornadula G, Beumont M, Livornese L Jr, Van Uitert B, Henning K, et al. Human immunodeficiency virus type 1 in the semen of men receiving highly active antiretroviral therapy. *N Engl J Med.* 1998; 339:1803–1809. [PubMed: 9854115]
43. Barroso PF, Schechter M, Gupta P, Melo MF, Vieira M, Murta FC, et al. Effect of antiretroviral therapy on HIV shedding in semen. *Ann Intern Med.* 2000; 133:280–284. [PubMed: 10929169]
44. Leruez-Ville M, Dulioust E, Costabliola D, Salmon D, Tachet A, Finkielsztejn L, et al. Decrease in HIV-1 seminal shedding in men receiving highly active antiretroviral therapy: an 18 month longitudinal study (ANRS EP012). *AIDS.* 2002; 16:486–488. [PubMed: 11834963]
45. Kroodsma KL, Kozal MJ, Hamed KA, Winters MA, Merigan TC. Detection of drug resistance mutations in the human immunodeficiency virus type 1 (HIV-1) pol gene: differences in semen and blood HIV-1 RNA and proviral DNA. *J Infect Dis.* 1994; 170:1292–1295. [PubMed: 7963730]
46. Eron JJ, Vernazza PL, Johnston DM, Seillier-Moiseiwitsch F, Alcorn TM, Fiscus SA, et al. Resistance of HIV-1 to antiretroviral agents in blood and seminal plasma: implications for transmission. *AIDS.* 1998; 12:F181–F189. [PubMed: 9814860]

Fig. 1. HIV plasma and semen RNA viral loads

Quantitative viral load assays for HIV-1 (black diamonds) and HIV-2 (gray squares) plasma and semen RNA were performed using polymerase chain reaction-based assays as described (See Materials and methods). Limit of detection (LOD) was 1.9 and 1.6 log₁₀ copies/ml for HIV-1 and HIV-2 in both plasma and semen, respectively. Undetectable viral loads were arbitrarily set at the LOD minus 1 and then log transformed (See Materials and methods). Linear regression line for all data points shown (adjusted $R^2 = 0.53$, $P < 0.0001$). Semen HIV RNA viral load correlated with plasma viral load irrespective of HIV type ($P = 0.007$ for HIV-1 and $P = 0.05$ for HIV-2). HIV-2-infected subjects had 0.7 log₁₀ lower HIV semen load than those with HIV-1 after adjusting for log₁₀ plasma level ($P = 0.07$).

Fig. 2. HIV semen RNA viral loads versus CD4 cell count

Quantitative viral load assays for HIV-1 (black diamonds) and HIV-2 (gray squares) semen RNA were performed using polymerase chain reaction-based assays as described (See Materials and methods). Limit of detection (LOD) was 1.9 and 1.6 log₁₀ copies/ml for HIV-1 and HIV-2 in semen, respectively. Undetectable viral loads were arbitrarily set at the LOD minus 1 and then log transformed (See Materials and methods). CD4 cell counts (CD4+ T cells/μl) were determined by FACSCount. Linear regression line for all data points shown.

Table 1

Characteristics of men infected with HIV-1 or HIV-2.

Characteristic	HIV serologic status	
	HIV-1 N = 22 (%) ^a	HIV-2 N = 10 (%) ^a
Age (mean)	37.2	40.5
20–29 years	3 (14)	1 (10)
30–39 years	11 (50)	3 (30)
40–49 years	6 (27)	5 (50)
50–59 years	2 (9)	1 (10)
Marital Status		
Married – monogamous	8 (36)	2/9 (22)
Married – polygamous	6 (27)	6/9 (67)
Widowed	2 (9)	0/9 (0)
Divorced	5 (23)	0/9 (0)
Never married	1 (5)	1/9 (11)
Born in Senegal	19 (86)	9 (90)
Lifetime sex partners		
1–10	5 (23)	5 (50)
11–20	5 (23)	2 (20)
21–50	7 (32)	2 (20)
> 50	5 (23)	1 (10)
Regular condom use	5/14 (36)	1/7 (14)
Sex w/commercial sex workers	13 (59)	3 (30)
Male genital-urinary exam		
Penile discharge	0/19 (0)	0/8 (0)
Genital ulcer disease	2/19 (11)	1/8 (13)
Inguinal lymphadenopathy	0/19 (0)	0/8 (0)
WHO stage of disease		
1	2/19 (11)	1/8 (13)
2	2/19 (11)	1/8 (13)
3	15/19 (79)	6/8 (75)
4	0/19 (0)	0/8 (0)
CD4 cell count (mean cells/μl ± SD)	222 ± 159	276 ± 213
Log ₁₀ plasma HIV RNA (mean copies/ml ± SD)	4.7 ± 0.8	3.0 ± 1.2
Log ₁₀ semen HIV RNA (mean copies/ml ± SD)	4.4 ± 1.1	2.6 ± 0.8

^aData not available for all subjects.