

REVIEW

Mounting anomalies in the epidemiology of HIV in Africa: cry the beloved paradigm

Devon D Brewer PhD¹, Stuart Brody PhD², Ernest Drucker PhD³,
David Gisselquist PhD⁴, Stephen F Minkin BA⁶, John J Potterat BA⁵,
Richard B Rothenberg MD MPH⁷ and François Vachon MD⁸

(Authors are listed alphabetically)

¹University of Washington, Seattle, Washington, USA, ²Institute of Medical Psychology and Behavioral Neurobiology, University of Tübingen, Germany, ³Department of Epidemiology and Social Medicine, Montefiore Medical Center/Albert Einstein College of Medicine, New York City, USA, ⁴Hershey, PA, USA, ⁵Colorado Springs, Colorado, USA, ⁶Network for Infection Prevention, Brattleboro, Vermont 05302, USA, ⁷Department of Family and Preventive Medicine, Emory University School of Medicine, Atlanta, GA, USA, ⁸University of Paris 7, France

Keywords: HIV, Africa, risk factors, epidemiology, heterosexual transmission, medical transmission

Introduction

There is substantial dissonance between much of the epidemiologic evidence and the current orthodoxy that nearly all of the HIV burden in sub-Saharan Africa can be accounted for by heterosexual transmission and the sexual behaviour of Africans. The mounting toll of HIV infection in Africa is paralleled by a mounting number of anomalies in the many studies seeking to account for it. We propose that existing data can no longer be reconciled with the received wisdom about the exceptional role of sex in the African AIDS epidemic.

Anomalies in sub-Saharan Africa

Discontinuity between HIV and STIs

During the 1990s HIV propagated rapidly in Zimbabwe, increasing at an estimated rate of 12% annually. At the same time, the overall sexually transmitted infections (STI) burden declined an estimated 25% and while there was a parallel increase in reported condom use by high-risk persons (prostitutes, lorry drivers, miners, and young people)¹. This example frames the problem: why would a relatively low efficiency sexually transmitted virus like HIV outrun more efficiently transmitted STI²? In the notable four-cities study³, many common sexual risk factors linked to HIV transmission (eg, high rate of partner change, sex

with prostitutes, and low condom use) were not correlated with HIV prevalence—although some risk markers (young age at first coitus or marriage, large age difference between partners) and presumed facilitating factors (lack of circumcision, genital herpes, and trichomoniasis, but not bacterial STI) were. In addition, concurrency of sexual partnerships was not correlated with HIV prevalence, yet was associated with bacterial STI⁴. It is of concern that many key sexual transmission variables are not associated with a large HIV epidemic in Africa, yet do correlate, as expected, with other STIs.

Transmission efficiency

A study of HIV transmission efficiency in Africa, using data from serodiscordant couples⁵, produced estimates remarkably similar to those reported for couples in the developed world⁶. Observed probabilities presumably reflect some of the influence of facilitating factors (eg, unorthodox sexual practices, circumcision status, STI exposure, etc) recruited to explain the 'turbo effect'⁷ noted in Africa's epidemiologic context. Recent empiric research casts doubt that such co-factors can sufficiently amplify the force of infectivity to account for observed trends in the sexual transmission of HIV in Africa⁸. The anomalies regarding transmission efficiency are well illustrated by a recent study in South Africa⁹. The authors recognized that, to explain HIV acquisition by 16–18 year old women in their study, they needed to postulate a per partnership transmission probability of 0.92 (0.49, assuming double the number of reported partnerships per woman). By extension, the per-contact probability of transmission would be 0.34,

Correspondence to: Mr J J Potterat, 301 South Union Blvd, Colorado Springs, Colorado USA 80910
E-mail: jjpotterat@earthlink.net

making heterosexual sex in this context second only to transfusion in HIV transmission efficiency. Similarly, a model developed to assess the impact of STI on transmission of HIV posited an extraordinary 33-fold increase in transmission efficiency of the latter in the presence of the former¹⁰.

Reported sexual activity

Levels of sexual activity reported in a dozen general population surveys in Africa¹¹ are comparable to those reported elsewhere, especially in North America and Europe. Perhaps more importantly, there appears to be little correlation with the level of risky sexual behaviour shown in these surveys and the epidemic trajectories observed in these countries. (Comparison with country-specific data reported by UNAIDS 2000; data not shown.) The four-city study provides similar discordance¹². For example, Yaounde (in Cameroon, a nation with low and stable prevalence) had the highest level of risky behavioural markers. Ndola (in Zambia, a nation that has experienced a rapid rise in HIV) had the smallest proportion of both men and women who reported a non-spousal sex partner in the previous 12 months. Ndola's other markers were similar to those in Dakar, Senegal and Cotonou, Benin, other areas with low, stable prevalence.

Transmission dynamics

Rapid propagation (of at least bacterial STI) has been associated with core groups¹³, which make up a small proportion of the susceptible population and are proposed to be responsible for most community transmission. Such groups appear to be associated with differing forms of sexual network 'geometry'. This geometry demonstrably differs with transmission intensity¹⁴⁻¹⁶. Evidence suggests that endemic and declining HIV/STI burdens are associated with dendritic (many open-ended termini) patterns of sexual partner connections, while epidemicity is associated with cyclic (closed loops, reflecting cohesiveness and density) patterns. There are few data on the architecture of sociosexual networks in Africa, but the available information suggests predominantly dendritic patterns (eg, contact with prostitutes and then contact with stable and usually monogamous consorts who are network termini). We are aware of no study from sub-Saharan Africa suggesting cyclic sexual network architecture. Without evidence of appropriate network configurations on a scale considerably larger than that observed in developed countries, rapid propagation of HIV in Africa would be difficult to sustain.

Studies have associated putative sexual core groups with HIV transmission in Africa. For example, women who work as prostitutes and their partners have frequently been observed to

have high HIV prevalence. Confusion may arise, however, over conflating the terms 'high risk person' and 'core group'. The former have been labelled in some way, but are not necessarily part of an interconnected group of individuals through whom infection percolates (ie, core group). As noted, such persons would have to be part of an interactive, cyclic group, rather than nodes along a dendritic chain.

Other anomalous findings

A higher HIV prevalence has been observed in women seen in prenatal, postpartum, and induced abortion settings than in their community counterparts¹⁷. In a number of studies, there appears to be a discrepancy between the observed prevalence in women undergoing reproductive medical care, and the prevalence that would be observed in such a group from heterosexual transmission alone. Though few in number, there continue to be reports of HIV seropositivity in persons denying coital exposure and in persons claiming a sole lifetime sexual partner who is reportedly HIV negative¹⁷. Similarly, there are persistent reports of HIV in infants with seronegative mothers¹⁷. A recent large survey from South Africa measured an HIV prevalence of 5.6% in children 2-14 years of age¹⁸. Given mortality from HIV among children who acquire it in Africa, there would appear to be a substantial proportion of such a disease burden that is unexplained by maternal and sexual transmission.

Alternatives

A number of these observations raise the question of an alternative route of transmission, for which medical care and the use of injections are prime candidates^{17,19-22}. Prostitutes, for example, are often recruited for studies from STI clinics, where treatment is frequently given by injection, where non-sterile equipment is used with high frequency, and wherein the underlying prevalence of HIV is high⁷. Many studies that have assessed the impact of sexual activity on HIV transmission—notably those in Mwanza and Rakai, whose discordant results are still a subject of debate²³—failed to consider the potential confounding effects of medical care in the propagation of HIV²⁴.

Rapid HIV transmission in Africa has often occurred in countries with good access to medical care, like Botswana, Zimbabwe, and South Africa. For example, high rates in rural South Africa have paralleled aggressive efforts to deliver health care to rural populations. It is difficult to understand how improved access to health care, with its offers of public health messages, free condoms, and preventive services, would be associated with increased HIV transmission. Similarly, HIV prevalence is often higher in cities and among persons

of high socioeconomic attainment than in rural areas or among less fortunate persons. Favourable access to health care is one of the differences that distinguishes between these groups.

Reactions to the anomalies and alternatives

Since early in the African epidemic, when AIDS was demographically associated with sexually active populations²⁵, studies of HIV transmission in Africa have generally failed to control for possible parenteral confounding²⁶. The importance of this route of infection was well known in the West and in Asia but quickly dismissed in Africa²⁷. The risk of parenteral transmission of HIV is based on good estimates of transmission efficiency, which varies depending on type of injection and circumstances that produce reuse of contaminated equipment. For example, needle stick exposure (HIV transmission probability: about one in 300²⁸, medical injection (recently estimated at approximately one in 30²⁰), or illicit-drug injection (about one in 100²⁹), is much more efficient than penile-vaginal exposure (about one in 1000³⁰).

There is the expectation that, were iatrogenic transmission of HIV common, one would notice substantial HIV prevalence in populations of (non-sexually experienced) children. Regrettably, although a large proportion of Africa's population falls in that category, few serosurveys conducted in Africa have included large enough samples from, say, children aged five through 12 to confidently dismiss this possibility. As more information accumulates that addresses this issue, a clearer perspective on the magnitude of non-sexual, non-maternal transmission in children will emerge.

The risk of exposure to HIV via medical injections is likely to vary with background prevalence and with the specific medical practices in different settings. The demand for consistency and coherence that we have placed on the heterosexual hypothesis should be applied to estimating the role of medical transmission. Its role should vary with background (initial) prevalence, and should be related to the degree of medical hygiene exercised. The same biological basis that exists for heterosexual transmission should be established for medical transmission. (As an aside, such a demonstration poses substantial ethical problems. No investigator should knowingly observe the use of a needle that has a high probability of being contaminated with HIV, but at a minimum, the demonstration of HIV RNA in needles that were to have been used on patients would be an important element in establishing a biological base.) The transmission of blood-borne pathogens with differing biological characteristics, notably hepatitis B and C³¹, should be consistent with parenteral transmission of HIV. Finally, the social epidemiology of HIV (male to female ratios,

for example) should be consistent with observations about non-sexual exposure.

Conclusion

In North America, Europe, and many parts of Asia, the ignition of regional epidemics and rapid HIV transmission has been associated principally with the sharing of contaminated injecting equipment and with anal intercourse. Though heterosexual intercourse has been virtually the sole explanation offered for the AIDS epidemic in sub-Saharan Africa, to our knowledge in no other part of the world has penile-vaginal exposure (as opposed to 'heterosexual sex') been demonstrated to initiate or sustain rapid HIV propagation.

HIV is not transmitted by 'sex', but only by specific risky practices. It is not transmitted by 'injections', but only by contaminated implements, which need to be clearly differentiated as to type and frequency of injection and by the conditions of the exposure setting. In virtually all societies affected by HIV to date, both routes seem to play important roles. If we are to understand and intervene in each of these epidemics, well-designed studies at both the population and individual levels are urgently needed. It is vital that these be properly controlled for parenteral exposure, specific sexual practices, and other co-factors^{2,17,24,32} and the complex and specific social patterns and networks that accompany them³³.

Dispassionate assessment of our conclusions admittedly depends on a willing suspension of disbelief, since the current paradigm is deeply embedded. Counter arguments can (and will) be levelled at each of the anomalies noted, but the depth and breadth of concerns deserve fair scrutiny. At issue in a re-evaluation of the heterosexual hypothesis are the profound implications for our interventive approach, and for the kinds of social and financial commitments that must be made. Finally, Africans deserve scientifically sound information on the epidemiologic determinants of their calamitous AIDS epidemic.

References

- Decosas J, Padian N. The profile and context of the epidemics of sexually transmitted infections including HIV in Zimbabwe. *Sex Transm Infect* 2002;78(Suppl 1):140-6
- Potterat JJ, Brody S. HIV epidemicity in context of STI declines: a telling discordance (letter). *Sex Transm Infect* 2002; 78:467
- Buve A, Carael M, Hayes RJ, et al. The multicentre study on factors determining the differential spread of HIV in four African cities: summary and conclusions. *AIDS* 2001;5(Suppl 4):S127-31
- Rothenberg R, Potterat J, Gisselquist D. Concurrency and sexual transmission (letter). *AIDS* 2002;16:678-80
- Gray RH, Wawer MJ, Brookmeyer R, et al. Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1 discordant couples in Rakai, Uganda. *Lancet* 2001;357:1149-53

- 6 Downs AM, De Vicenzi I, European Group on Heterosexual Transmission of HIV: relationship to the number of unprotected sexual contacts. *J Acquir Immune Defic Syndr* 1996;**11**:388–95
- 7 Vachon F, Coulaud JP, Katlama C. Epidémiologie actuelle du syndrome d'immunodéficit acquis en dehors des groupes à risque. *Presse Médicale* 1985;**14**:1949–50
- 8 Gisselquist D, Potterat JJ. Heterosexual transmission of HIV in Africa: an empiric estimate. *Int J STD AIDS* 2003;**14**:162–73
- 9 Auvert B, Ballard R, Campbell C, *et al.* HIV infection among youth in a South African mining town is associated with herpes simplex virus-2 seropositivity and sexual behavior. *AIDS* 2001;**15**:883–98
- 10 Robinson NJ, Mulder DW, Auvert B, Hayes RJ. Modelling the impact of alternative HIV intervention strategies in rural Uganda. *AIDS* 1995;**9**:1263–70
- 11 Carael M, Cleland J, Deheneffe J-C, Ferry B, Ingham R. Sexual behavior in developing countries: implications for HIV control. *AIDS* 1995;**9**:1171–5
- 12 Buve A, Lagarde E, Carael M, *et al.* Interpreting sexual behaviour data: validity issues in the multicentre study on factors determining the differential spread of HIV in four African cities. *AIDS* 2001;**15**(Suppl 4):S1117–26
- 13 Thomas JC, Tucker MJ. The development and use of the concept of a sexually transmitted disease core. *J Infect Dis* 1996;**176**(Suppl 2):S134–43
- 14 Potterat JJ, Muth SQ, Rothenberg RB, *et al.* Network structure as an indicator of epidemic phase. *Sex Transm Infect* 2002;**78**(Suppl 1):i152–8
- 15 Potterat JJ, Phillips-Plummer L, Muth SQ, *et al.* Risk network structure in the early epidemic phase of HIV transmission in Colorado Springs. *Sex Transm Infect* 2002;**78**(Suppl 1):i159–63
- 16 Potterat JJ, Rothenberg RB, Muth SQ. Network structural dynamics and infectious disease propagation. *Int J STD AIDS* 1999;**10**:182–5
- 17 Gisselquist D, Rothenberg R, Potterat J, *et al.* HIV infections in sub-Saharan Africa not explained by sexual or vertical transmission. *Int J STD AIDS* 2002;**13**:657–66
- 18 Shisana O, Simbayi L, Bezuidenhout F, *et al.* Nelson Mandela/HSCR study of HIV/AIDS: South African national HIV prevalence, behavioural risks and mass media: household survey 2002. Cape Town, Human Sciences Research Council 2002. <http://www.hsrc.ac.za/research/npa/SAHA/news/20021205Keynote.html>
- 19 Simonsen L, Kane A, Lloyd J, *et al.* Unsafe injections in the developing world and transmission of bloodborne pathogens: a review. *WHO Bull* 1999;**77**:789–800
- 20 Gisselquist DP. Estimating HIV-1 transmission efficiency through unsafe medical injections. *Int J STD AIDS* 2002;**13**:152–9
- 21 Drucker EM, Alcabes PG, Marx PA. The injection century: consequences of massive unsterile injecting for the emergence of human pathogens. *Lancet* 2001;**358**:1989–92
- 22 Potterat JJ, Brody S. Does sex explain HIV transmission dynamics in developing countries? (Letter) *Sex Transm Dis* 2001;**28**:730
- 23 Grosskurth H, Gray R, Hayes R, *et al.* Control of sexually transmitted diseases for HIV-1 prevention: understanding the implications of the Mwanza and Rakai trials. *Lancet* 2000;**355**:1981–7
- 24 Gisselquist D, Potterat J. Confound it: latent lessons from the Mwanza trial of STD treatment to reduce HIV transmission. *Int J STD AIDS* 2003;**14**:179–84
- 25 Quinn TC, Mann JM, Curran JW, Piot P. AIDS in Africa: an epidemiologic paradigm. *Science* 1986;**234**:955–63
- 26 Gisselquist D, Rothenberg R, Potterat J, Drucker E. Non-sexual transmission of HIV has been overlooked in developing countries (letter). *BMJ* 2002;**324**:235
- 27 Gisselquist D, Potterat J, Brody S, Vachon F. Let it be sexual: how health care transmission of AIDS in Africa was ignored. *Int J STD AIDS* 2003;**14**:148–61
- 28 Tokars JL, Marcus R, Culver DH. Surveillance of HIV infection and zidovudine use among health care workers after occupational exposure to HIV-infected blood. *Ann Intern Med* 1993;**118**:913–19
- 29 Kaplan EH, Heimer R. A model-based estimate of HIV infectivity via needle sharing. *JAIDS* 1992;**5**:1116–18
- 30 Royce RA, Sena A, Cates W Jr, Cohen MS. Sexual transmission of HIV. *N Engl J Med* 1997;**336**:1072–8
- 31 Madhava V, Burgess C, Drucker E. Epidemiology of chronic hepatitis C virus infection in sub-Saharan Africa. *Lancet Infect Dis* 2002;**2**:293–302
- 32 Gisselquist D, Potterat JJ. Uncontrolled HSV-2 as a co-factor in HIV transmission (response to Sutcliffe *et al.*). *JAIDS* (in press)
- 33 Aral SO, Holmes KK. Social and behavioral determinants of the epidemiology of STDs: industrialized and developing countries, in Holmes KK, Sparling PF, Mårdh P-A, *et al.* (eds): *Sexually transmitted diseases* (3rd edn). New York: McGraw-Hill Book Co, Inc., 1999:39–76

(Accepted 15 December 2002)