

Lad

D5

N (Br W9

LVLAKH "3qu K00 SfIX/N

THE IMPORTANCE OF CORE GROUPS IN THE EPIDEMIOLOGY  
AND CONTROL OF HIV-1 INFECTION

Francis A. Plummer MD, FRCPC, Nico J.D. Nagelkerke, PhD  
Stephen Moses MD, MPH, Jacksoniah o. Ndinya-Achola MBChB,  
Job Bwayo MBChB, Elizabeth Ngugi, RN, PhD.

Departments of Medical Microbiology and Community Health,  
University of Nairobi, Nairobi, Kenya

Departments of Medical Microbiology, Medicine and Community  
Health Sciences, University of Manitoba, Winnipeg, Canada

Dr. Plummer is the recipient of a scholarship from the Medical  
Research Council of Canada. This work was supported in part by  
grants from the Medical Research Council of Canada (Ottawa), the  
International Development Research Centre (Ottawa), the National  
Health Research Development Program (Ottawa) and the Rockefeller  
Foundation.

**Abstract**

A sustained epidemic of a sexually transmitted infection is dependent on the heterogeneity of the sexual behaviour of the population. Within the overall population small sub groups of men and women with rapid rates of partner change are instrumental in the transmission of the infectious agent to the population a large. These groups have been termed " high frequency transmitter core groups". Recognizing the importance of core groups in the epidemiology of HIV-1 infection, programmes for HIV-1 control need to develop strategies for interventions in . these groups .

In the first decade since the recognition of AIDS and the human immunodeficiency virus, HIV-1 has rapidly spread to infect a substantial proportion of the adult population of sub-Saharan Africa. Available data indicate that the rate of growth of the epidemic in newly infected populations is very rapid and that equilibrium infection rates are very high. Even in a country such as Kenya, with low rates of infection, the prevalence of HIV-1 in an unselected population of pregnant women has grown from 2.5% in 1986 to 5.6% in 1990 (table 1, J0 Ndinya-Achola, FA Plummer, P Datta et al, unpublished). In Africa, transmission of the virus takes place principally through heterosexual intercourse. Although all of the factors affecting transmission of the are not understood, behavioral factors are clearly crucial. In order to understand the epidemic spread of the virus and to design appropriate interventions, patterns of sexual behaviour and their epidemiologic significance need to be understood.

The core groups concept and the sexual transmission of infection Infections which are spread solely or principally by sexual relations - the sexually transmitted diseases (STD) - have a unique epidemiology, which is considerably different from the epidemiology of many other diseases spread by human to human contact.

One fundamental theoretical tenet of STD epidemiology, that of "core groups", was developed in work by Yorke, Hethcote and NoldP on the epidemiology of gonococcal infection. It is based on the observation that this infection is "endemic" among a small subpopulation of highly sexually active individuals, from where it spreads in mini-epidemics to the population at large. Thus, the epidemic behaviour of sexually transmitted infections is related to the heterogeneity of the sexual behaviour of the population. This concept can be applied to all STD, including HIV-1.

As with all STD, there is no non human reservoir of HIV-1 and infection can only be acquired from a person infected with the virus. Transmission (including transmission from mother to infant) occurs when a susceptible individual comes into contact with the blood or bodily secretions of an HIV-1 infected person. HIV-1 infection is probably eventually fatal in all cases, so that if no new infections occur, the disease would eventually disappear as infected people become ill and die. For the number of HIV-1 infected individuals to increase (the epidemic situation that the world is in at the moment), each infected individual must infect, on average, more than one other person<sup>4</sup>. The overall transmission frequency of HIV-1 during one episode of sexual intercourse, in the absence of facilitating factors, is probably quite low, between 0.01% and 1.0% on average. This means that in order to produce one new infection, assuming that f

the risk of transmission for each episode of sexual intercourse is independent and equal, an infected person must have sex with between 100 and 10,000 new partners or have sex with one partner 100 to 10,000 times. To infect more than one person would require proportionately more sex with more partners. Of course, very few people have anywhere near these numbers of partners. Within most populations, the majority of individuals are essentially monogamous (polygamous relationships could be considered a form of group monogamy) or in a series of monogamous relationships, with occasional external sexual partners. How then can an epidemic of the magnitude we are experiencing occur? What are the key differences in sexual behaviour in Africa which could account for the rapid growth of the epidemic among heterosexuals on this continent?

It is unlikely that the average rate of partner change in the population could, by itself, account for the size of the African epidemic. Although marginal differences in the basic reproductive rate (the average number of new infections produced by an infected individual) of HIV-1 can lead to huge differences in the course of the epidemic#, to account for the magnitude of the epidemic in Africa, average rates of partner change in African populations would need to be as great as 10 to 1000 fold higher than in western populations. This seems improbable if not impossible. However, it is not only the average rate of partner change in the population which determines the spread of HIV-1, but also the heterogeneity of the rate of partner change and the way in which population subgroups mix sexually5 ie., who is having sex with whom.

Certain subgroups of men and women in the population have very rapid changes in sexual partners and very large numbers of sexual partners. Through their sexual activity, they are frequently exposed to and acquire sexually transmitted infections. Once infected, again because of their high level of sexual activity, they are efficient transmitters of sexually transmitted infections to others with similar behaviour and, at a lower (but very important!) rate, to individuals who do are less sexually active. Yorke, Hethcote and Nold have termed such population sub groups of men and women, "high frequency transmitter core groups"3.

A core group was originally defined as a subpopulation of individuals who each transmit an STD to more than one susceptible person3. However, this definition does not convey the essential idea that in order to spread the epidemic beyond the core group<sup>1</sup> to the general population, core groups must mix sexually with otherwise low risk individuals. New infections are produced both among other members of the core group and among individuals outside the core group such as monogamous wives, girlfriends, husbands and boyfriends. If core group members only had sex with

1'

I

each other, no STD transmission to the general population would occur. Another definition, which we offer here, is that a core group for a given STD is the smallest subpopulation which is necessary to sustain transmission of an infection transmitted by sex. Thus, the core group for an STD is the smallest possible subpopulation such that removal of its members from the population would bring the basic reproductive rate of the STD below one. The core group for each STD is not necessarily the same, although there is certainly considerable overlap<sup>6</sup>.

Infection specific factors such as the duration of the infectious period, the effect of immunity and the transmissibility of the agent determines the size and to some extent the composition of the core group, for each sexually transmitted infection<sup>6</sup>.

Considering the specific case of HIV-1, one can begin to understand how the average number of infections produced by an infected person could exceed one through the operation of the core group principle. An illustrative example is the HIV-1 epidemic among core group prostitute women in Nairobi and their clients<sup>78</sup>. In Pumwani, a low income area of Nairobi, women working as prostitutes report they have three to four sex partners per day. Thus, each woman has approximately 1000 to 1200 sex partners per year. With this level of exposure, it is easy to see how these women would eventually become infected, even with a low prevalence among their clients and low transmission rates at the beginning of the epidemic. Since these women often are infected with other STD, their susceptibility to HIV-1 is increased<sup>9</sup>. Once infected with HIV-1, they are efficient transmitters of HIV-1 infection both because of their large number of sex partners and the increased infectivity caused by concurrent STD<sup>10</sup>. In a year, one HIV-1 infected woman could infect several men with HIV-1, even with low rates of transmission per sexual encounter.

Yet, these women do not necessarily constitute a core group. They are only one component of the HIV-1 core group. If their sexual contacts were limited to a small group of men who had sex exclusively with prostitutes, they would have no important role in the overall dynamics of the HIV-1 epidemic. The fact that the group of clients is not confined, but comprises a sizable proportion of the (male) population at large, who sexually mix with the female population at large, makes these prostitutes an important core group for HIV-1 and other STD. Most newly infected clients have additional sex partners - wives, girlfriends and other prostitutes - to whom they may transmit the virus, making them another component of the core group for HIV-1 and STD.

Prostitutes and their clients are not the only type of core group for HIV-1, but it should be apparent how important they may be in continued transmission of the virus. The usual compositions of core groups in Africa seems to be a few women and

a large number of men. This sexual behavioural pattern or social dynamic is very efficient in transmitting STD, more so than the dynamic where everybody is having sex with everybody. This is principally because the women involved have very large number of sexual contacts and a consequent high probability of being infected with any particular STD, relative to the general population. Thus, men who have sex with prostitutes will have much greater frequencies of STD, including HIV-1, than men who have the same number of female sexual partners who are not prostitutes. This is simply because the probability of contact with an infected woman is so much greater among men who have sex with prostitutes. The opposite situation, a large number of women having sex with a small number of men, would probably be similarly efficient, but it does not seem to be a feature of sexual behaviour in modern societies. One known situation of a "male" core group is that of long distance truck drivers<sup>n3</sup>. They constitute an essential part of the HIV-1 core group in East Africa, which is separate from the more familiar one of prostitute-clients. It is probable that other male core groups exist, but our knowledge of them is rudimentary.

The core groups for any specific STD should not be conceptualized as an immutable group of individuals within the population, but as a very dynamic one. Individuals move in and out of the core group sexual behavioural pattern, possibly very rapidly. The absolute number of HIV-1 core group members is probably continually expanding and contracting with changes in disease prevalence, as new individuals enter the behavioural pattern and as others become ill, die or alter their behaviour. The effect of a prostitute-client core group on a hypothetical HIV-1 epidemic is illustrated by the simulations shown in figures 1 and 2. The details of the model are given in Appendix 1. Figure 1 shows the percentage of men and women, in the general population, infected with HIV-1 while prostitute client interactions continue uninterrupted. Figure 2 presents the same situation, but transmission from prostitutes to clients is interrupted (e.g., through condoms) at seven years. In this simulation, parameters were chosen in a way that interruption of core group transmission sufficed to interrupt the epidemic. This model, should not be taken literally, but it serves to illustrate how significant the contribution of a core group can be to the dynamics of an HIV-1 epidemic in the whole population.

Social and economic forces creating core groups in Africa High frequency transmitter core groups are an important theoretical concept, but who are they in the population? Women who sell sex and men who buy it are obvious examples of core groups; long distance truck distance drivers are becoming another familiar one. What other subsets of the population are possible or likely core group members and why has this social situation

I

I

developed to such an extent in African societies?

Economic forces, rapid modernization and urbanization and changes in people's aspirations in African countries results in selective male migration to major cities in search of work.

These men are single or have left their spouses in the rural areas. At the same time, the limited economic opportunities for women in both rural and urban Africa have created a large underclass of women willing to sell sex for survival and/or advancement. These unattached men frequently seek comfort and sexual gratification from women whose only economic recourse is the exchange of sexual favors for money - prostitution. As noted above, this type of sexual mixing (a large number of men having sex with a small number of women) is very efficient for the transmission of STD, including HIV-1.

Outside the cities a similar social dynamic is created by mobile male populations (eg., miners, soldiers and truck drivers) and the disruption of rural agrarian life resulting from famine, poverty, war and selective migration of men to the cities. In this setting, unattached mobile men encounter rural women who are willing to sell sex.

The men and women who are involved in this social dynamic are both the major victims and the major transmitters of STD and HIV-1. The social and economic forces that result in migration of labour to cities or to mines and which deny women sufficient means to participate in the economy should be recognized as co-factors in the HIV-1 epidemic.

The interaction of STD and HIV-1 in core groups

A discussion of the importance of core groups would be incomplete without consideration of how HIV-1 and other STD interact to amplify transmission. The effect of core groups on the epidemic of HIV-1 is magnified, perhaps many times, by the interactions between sexually transmitted infections.

A number of epidemiologic studies have implicated other STD in facilitating the transmission of HIV-1. There appear to be several effects. Ulcerative STD and perhaps non-ulcerative STD result in increased susceptibility of women to HIV-1A0Hi.

Ulcerative STD increase the infectivity of women for male sex partners by increasing the shedding of virus in the genital tract". There are possible roles for STD in increasing the infectivity and susceptibility of men as well, but these have not been studied to any great extent. Increasing evidence indicates that HIV-1 infection alters susceptibility to STD as well, completing a loop of mutual facilitation. The loop is further amplified by the higher frequency of both HIV-1 and STD in core groups.

.  
hx

The loop of amplification is currently understood as follows. Genital ulcers, and probably other STD, increase the susceptibility of core group women to HIV-1 and they become infected rapidly. Genital ulcers increase the infectivity of HIV-1 infected women by increasing genital tract viral shedding, resulting in relatively frequent transmission of the infection to core group men. As more core group men become infected the risk to core group women increases. There is gradual spillover to the non-core group female and male population. Finally, HIV-1 induced immune deficiency results in an increased prevalence of genital ulcers among the core group, facilitating transmission in both directions.

The effect of STD on HIV-1 disease progression in core groups may accelerate the HIV-1 epidemic

Recent evidence that a more rapid rate of progression from initial HIV-1 infection to disease may be occurring in prostitutes has potentially important implications for the epidemiology of HIV-1.

It appears probable that HIV-1 infectivity is not continuous throughout the period an individual is infected. Infectivity probably parallels viremia, which occurs initially, soon after infection and for a longer period later, as immune deficiency develops. Peak infectivity and presumably peak transmission occurs during these two periods, with the latter being relatively more important because of its longer duration. Factors which affect the rate of development of immune deficiency would thus have an effect on the spread of HIV-1 in the population. Evidence from our work in Kenya, suggests that progression to disease is more rapid in women working as prostitutes than in other populations. The mean time to development of symptomatic disease among one group of women working as prostitutes was estimated at 27.8 months by Markov modelling. It appears that this more rapid progression may be related to the frequency of STD, in that women with more frequent episodes of gonococcal infection progress to symptomatic disease more quickly and that women who use condoms more frequently progress at a slower rate.

If these data are confirmed, then STD and HIV-1 would have an important interaction, which once again is mutually facilitating. Frequent STD would increase the rate of development of immune deficiency resulting in earlier development of peak infectivity. This could have an important effect on accelerating the epidemic and would result in further amplification of the interactions of HIV-1 and STD noted above. The period of increased viremia related to immune deficiency would coincide with a period of increased susceptibility to the STD which increases viral shedding in the genital tract, maximizing infectivity.

,

The overall effect of an accelerated disease progression would probably be to increase the initial rate of growth of the epidemic, as newly infected individuals would enter the peak period of infectivity earlier. The effect on HIV-1 prevalence at equilibrium might be less important, if the duration of the infectious period were unaffected or shortened.

The role of core group interventions in control programs The major emphasis of AIDS control programs thus far, has been to provide information to the general public. While this is important for creating awareness, so that a public discussion can begin and that people don't die of ignorance, it probably does little to effect real behavioral change. In a study of sexual risk taking behavior among truck drivers, Bwayo et al<sup>13</sup> found very high levels of high risk sexual contact and infrequent condom use, despite a high level of awareness of AIDS and STD and an accurate knowledge of preventive methods. A potentially more effective approach to HIV-1 control would be to incorporate into current efforts, intensive information, education and behavioural programs (including condom promotion) targeting high frequency transmitter core groups. One model of such a comprehensive program consists of a four tiered approach:

- 1) information and education for the general population,
- 2) intensive information and education programs for core groups, -
- 3) programs for the promotion of condom use core group members who do not limit their sexual risk,
- 4) reducing the likelihood of transmission by reducing the prevalence of factors such as sexually transmitted diseases which promote transmission of HIV-1.

The educational and behavioural components should have the effect of reducing the size of core group populations and reducing contact between core groups and the population at large. There are several aspects of this intervention model which exploit the mutually facilitating relationship between STD and HIV-1. First, women and men in core group populations would be protected from HIV-1 and STD through the barrier effect of condoms. There would be an increased effect on prevention of HIV-1. Because STD are also prevented women, at least, would be less susceptible to HIV-1 infection when condoms are not used, or when they fail.

Provision of services for earlier STD detection and treatment among core groups would also have the effect of decreasing susceptibility to HIV-1 when condoms are not used.

Among core group members, the ultimate effect of such programs is however to delay HIV-1 infection rather than prevent

(  
I

it absolutely. Even with very high levels of condom use, many core group members would probably eventually become infected. However, infection may be delayed sufficiently that the individuals remove themselves from the core group prior to becoming infected. The most important, effect (in terms of the overall HIV-1 epidemic) of programs targeted to core groups would be to reduce transmission of HIV-1 to the sexual contacts of core group members. This effect is achieved not only through the barrier effect of condom use, but also by the reduction in infectivity resulting from a lower STD prevalence and incidence within core group members (both through condom use and STD treatment).

The effect of these programs is not limited to the core groups, but by reducing the incidence and prevalence of STD in the general population the infectivity and susceptibility for HIV-1 outside core groups is decreased.

The constraints of condom promotion programs aimed at the general population, illustrate another benefit of targeted programs. The cost of purchasing and the logistics of distributing condoms to the entire sexually active population of a country are immense. It may prove simpler, less expensive, more sustainable and just as effective to provide condoms to population subsets at highest risk, the core groups.

one of the longest running core group interventions in Africa is the program among the women of Pumwani. We began this program in 1985 to investigate the epidemiology of STD. When HIV-1 infection was recognized as a severe problem, it became the main focus of the program. Although general STD education was an element of the program from the outset, these efforts were intensified and a condom distribution program was initiated when the problem of HIV-1 infection was recognized. The program was successful in persuading the women to have their clients use condoms, resulting in fewer cases of gonococcal infection and genital ulcer disease and Preventing or at least delaying HIV-1 infection among the women. While these effects are important, the most important effect in terms of the overall HIV-1 epidemic, is the efficiency of this program in preventing transmission of HIV-1. At the current level of self-reported condom use, transmission of HIV-1 is more than halvedn. An equally important effect is that men who are prevented from becoming infected through the use of a condom cannot transmit the .. W infection to other sexual partners. In a recent study of the effectiveness and cost of the intervention program, we estimated that between 6000 and 10,000 primary and secondary cases of HIV-1 infection are prevented per yearn. The cost per case prevented is approximately \$8-12 US. This compares well with other public health interventions and is much less expensive than screening blood, per case of HIV-1 prevented.

I

z

If one accepts the fundamental epidemiologic principle that high frequency transmitter core groups play a major role in sustaining the HIV-1 epidemic, the conclusion that they are a key target in programs for control of sexual transmission of HIV-1 is inescapable.

It is often stated that core groups are only important for HIV-1 transmission early in an epidemic, when the prevalence of HIV-1 is relatively low and that when the prevalence is high, targeting core groups is no longer effective. The reasoning being, because the number of infected individuals with low rates of sex partner change is greater, many more individuals have the potential to transmit HIV-1. This logic is incorrect. High prevalence does not change the basic epidemiologic principle that the core group accounts for a disproportionate amount of HIV-1 transmission.

In an epidemic in equilibrium, new infections are always occurring. In fact, in a high prevalence equilibrium new infections must occur at an extremely high rate to replace the large number of individuals dying of AIDS. Even if the difference in HIV-1 prevalence between core group and non-core group population subsets is narrower, later in the epidemic, core groups still account for a disproportionate number of new infections. The number of new infections resulting from the sexual activity of any one core group member will be several orders of magnitude greater than that of a non core group member, because of the great difference in the rate of-partner change. This point is illustrated by the simulations in our model. In the intervention simulation, the prevalence had reached a very high level, yet the core group intervention had a dramatic effect on the epidemic. Given the presence of an epidemic and the fact that some people live monogamously or without a sex partner, a core group always exists. In effect, in these very high prevalence situations, the core group has expanded in size. It is not that the core group is unimportant, but rather that the identification of the core group for targeting is more difficult.

However, within the expanded core group population some individuals will be more effective transmitters of HIV-1 than others. If these individuals can be identified for targeted interventions, at least some level of control can be achieved. Balancing disease control with the potential for victimization While it is important to understand the role played by core groups in sustaining transmission of HIV-1 and other STD; the purpose of understanding is not to affix blame on these subsets of the population. Indeed the understanding is superficial and callous without acknowledging that these men and women are already victims of the societal inequities which result in their circumstance. Added to this is the additional burden of ill health, suffering and premature death from HIV-1 andSTD.

Further victimization by punitive interventions is misguided and ineffective. Passing laws or rounding up core group members (usually women) will not control the spread of HIV-1.

If interventions programs targeting core groups are to succeed, they must be undertaken in full partnership with the targeted population. For partnership to develop common interests and goals must be identified and trust must be nurtured. These populations are often already alienated and marginalized, with a strong distrust of officialdom and authority. Achieving a partnership can require great effort and time but is essential. It certainly cannot be achieved under the threat of punishment or proscription.

#### Research needs

While programs for core groups must be incorporated into HIV-1 and STD control programs now, our understanding of the issues involved is still superficial. We do not understand the psychologic and sociologic motivations for core group behaviour beyond the obvious - economic necessity, libido and loneliness. We do not understand the dynamics of this behavioural pattern. Is it a transient behavioural pattern? If so, what are the determinants of entry and exit? How do peer groups influence these behaviours and how can they be manipulated in control programs? How common is this behavioural pattern in societies? How much STD and HIV-1 are attributable solely to the core group behavioural pattern? How long is the chain of transmission from core groups to non core group? What are the contributions of the behavioural and the biological factors to the HIV-1 epidemic? How can we identify core group members for targeting of interventions? What is the fraction of HIV-1 infection in the population which is attributable to the interaction of STD and HIV-1 in core groups? Which of the STD associated with HIV-1 transmission are most important in core groups and which at the level of the entire population? Clearly, optimal program implementation requires additional knowledge.

#### Conclusion

High frequency transmitter core groups are key to the epidemiology of HIV-1 and STD. The rapid growth of the HIV-1 epidemic in Africa appears to have resulted, in part, from the social and economic factors which result in frequent participation in the core group pattern of sexual behaviour. An understanding of the importance of core groups in HIV-1 transmission is key to developing more effective programs for the control of HIV-1.

iV'L

## Simulation mode;

To explore the effect of prostitute-client core group on the course of the HIV-1 epidemic we considered a population of an equal number of men and women (for simulation purposes taken to be 2000) plus a number (the actual number is unimportant) of prostitutes who are already infected with HIV-1 time zero. The model assumes that 30% of men and 30 % of women are in stable relationships and do not participate in the epidemic at all.

Forty percent of both men and women change partners at a rate of every 2 years and 30 % of both men and women do so once a year. However, in addition to these "normal" contacts, men have contacts with HIV-1 infected prostitutes. Those in stable relationships are modelled not to have any such contacts. Those who change partners every two years are modelled to visit a prostitute between .1 and 4 times a year and those changing partner every year to visit a prostitute between 4 and 7 times a year. The probability of acquiring HIV-1 during a single contact with a prostitute is assumed to be 1%, while the male to female and female to male infection rates per new partner assumed to be 0.25 and 0.2 respectively. Infected individuals die. --v exponentially at a rate of 20% per year and are automatically replaced by uninfected individuals (so we have left population growth out of the model). In Figure 1 we have plotted the results of one simulation run with the above parameters, while in figure 2 we set the transmission rate from prostitutes to clients equal to zero after 7 years.

IV'L

Table 1. Serial HIV-1 Prevalence in pregnant women in Nairobi,  
1986-1990

Year No. Screened Per cent Prevalence

1986 1 2256 2.6

1987 2070 3.2

1988 1623 4.1

1989 1446 4.8

1990<sup>t</sup> 1091 5.5

t

1990 data are through October 1990.

"x

15

2 Figure 1. Simulation of an HIV-1 epidemic in a constant  
3 population of 1000 men and 1000 women with prostitute  
client sexual contact uninterrupted.

Per Cent HIV Prevalence

30 40 50

. Year

4- Males 96 -9- Females 9%

K'x

Figure 2. Simulation of an HIV-1 epidemic in a constant population of 1000 men and 1000 women, where prostitute client sexual contact is interrupted at seven years by a successful (100%) condom promotion program.

Per Cent Prevalence HIV

H" - Males 'k 4- Females 96

mX

## References

1. Piot P, Plummer FA, Mhalu FS et al. AIDS: An international perspective. *Science* 1988;239:573-9.
2. Chin J, Mann J. Global surveillance and forecasting of AIDS. *Bull World Health Organ* 1989, 67: 1-7.
3. Yorke JA, Hethcote HW, Nold A. Dynamics and control of transmission of gonorrhoea. *Sex Transm Dis* 1978, 5:31v6.
4. Anderson RM, May RM. Epidemiologic parameters of HIV transmission. *Nature* 1988, 333:514-9.
5. Anderson RM. Mathematical and statistical studies of the epidemiology of HIV. *AIDS* 1989, 6:333-46.
6. Brunham RB, Plummer PA. A general model of sexually transmitted disease epidemiology and its implications for control. *Med Clin N Amer* 1990; 74: 1339- -52.
7. Piot P, Plummer FA, Rey M-A et al. Retrospective epidemiology of AIDS virus infection in Nairobi populations. *J Infect Dis* 1987, 155: 1108- 12.
8. Kreiss JK, Koech D, Plummer FA et al. AIDS virus infection in Nairobi prostitutes: extension of the epidemic to East Africa. *N Engl J Med* 1986, 314:414-8.
9. Plummer FA, Simonsen JN, Cameron DW et al. Co-factors in male to female transmission of HIV-1. *J Infect Dis* (in press).
10. Cameron DW, Simonsen JN, D'Costa LJ et al. Female to male transmission of HIV-1: risk factors for seroconversion in men. *Lancet* 1989, ii:403-8.
11. Kreiss JK, Coombs R, Plummer FA et al. Isolation of HIV-1 from, genital ulcers in prostitutes. *J Infect Dis* 1989, 160:380-4. -'
12. Carswell JW. IV infection in healthy persons in Uganda. *AIDS* 1987, 1:223-7.
13. Bwayo JJ, Omare M, Mutere A et al. HIV- 1 infection in long distance truck. *East Afr Med J* (submitted). ;  
I

14. Laga M, Nzila N et al. Non ulcerative STD and risk of HIV-1 seroconversion. VI International Conference on AIDS, San Francisco, June 1990.
15. Cameron DW, Plummer FA et al. Genital ulcers and HIV-1. Sex Transm Dis. (in press).
16. Plummer FA, Simonsen JN, Chubb H et al. Epidemiologic evidence for serovar specific immunity after gonococcal infection. J Clin Invest 1989, 83:1472-6.
17. Goedart JJ, Eyster ME, Biggar RJ. Heterosexual transmission of human deficiency virus infection: association with severe depletion of T-helper cells in men with hemophilia. AIDS Res Hum Retroviruses 1987, 4:335-61.
18. Medley GF, Anderson RM, Cox DR, Billard IL. Incubation period of AIDS in patients infected via blood transfusion. Nature 1987, 328:719-21.
19. Nagelkerke NJD, Plummer FA, Holton D et al. Transition dynamics of HIV disease in a cohort of African prostitutes. AIDS 1990, 8:743-8.
20. Bolton D, Plummer FA, Odour D et al. Condom use reduces the risk of HIV-1 disease progression in women working as prostitutes in Nairobi. Lancet (submitted).
21. Ngugi EN, Plummer FA, Simonsen JN et al. Prevention of IV transmission in Africa: the effectiveness of condom promotion and health education among high risk prostitutes. Lancet 1988, 11:887-90.
22. Moses S, Plummer FA et al. Controlling HIV in Africa: cost and effectiveness of a program among high frequency STD transmitters. AIDS (in press).