

UNSAFE INJECTIONS OR SEXUAL TRANSMISSION?

Is HIV in sub-Saharan Africa predominantly a sexually transmitted infection? Or is the culprit the practice of re-using needles designed for single use? David Gisselquist, John Potterat and Stuart Brody would have us think the latter. This group have recently published extensively, putting forward their theory that the HIV pandemic in sub-Saharan Africa was not as a result of sexual transmission, but as a result of unsafe injection practices. Their ideas have not been popular, and there have been several papers published which attack the rationale behind their allegations. The most recent, in the *Lancet*, is probably the most compelling.

Transmission of HIV-1 infection in sub-Saharan Africa and effect of elimination of unsafe injections

George Schmid, of the World Health Organisation (WHO) in Geneva, and several colleagues, have examined Gisselquist *et al.*'s methodology in some detail. They have reviewed the arguments used to question the epidemiological interpretations on the lead role of unsafe sex in HIV-1 transmission and found no 'compelling evidence' that unsafe injections are the main mode of transmission of HIV-1 in the region. In fact, they conclude that the epidemiological evidence shows that sexual transmission continues to be, '....by far the major mode of spread of HIV-1'.

Recently, Gisselquist and colleagues refuted recent estimates which suggest that only 2.5% of HIV transmission is through unsafe injections, and instead suggest between 20% and 40%. This questions the orthodox epidemiological interpretations of the lead role of unsafe sex in transmission. The danger of this approach is that it could possibly lead to a reduction in efforts to prevent unsafe sex in sub-Saharan Africa. Indeed the US Senate Committee on Health, Education, Labor and Pensions has already started looking at whether funds should be devoted to programmes that target unsafe injections.

In summing up the arguments for the lead role of unsafe injections in transmission of HIV, Schmid and colleagues say:

- Unsafe injections are not common enough to play a significant role in HIV-1 transmission in Africa.

- Transmission efficiency of HIV-1 by injections in the region is overestimated and does not nearly reach the 2.3% proposed by Gisselquist.
- Reverse causality and confounding are not sufficiently accounted for when assessing the association between a history of injections and HIV-1 infection.
- HIV-1 infection in children is rare outside the setting of mother-to-child transmission and the age and sex distribution of HIV-1 is similar to that of other sexually transmitted infections.
- Gisselquist's analyses of sexual behaviour and HIV-1 infection in adults in sub-Saharan Africa are oversimplified and do not take into account measurement of exposure.
- Prevalence of HSV-2 is high, the disease is also sexually transmitted and is demographically similar to HIV-1.
- The South African epidemic has developed in the absence of unsafe injections and with data indicating sexual transmission as the cause.

Frequency of unsafe injections

In sub-Saharan Africa there are an estimated 2.1 injections given per person per year in low-income areas. Of these, about 18% are given with reused equipment — far less than the 50% cited by Gisselquist and colleagues. Furthermore, most injections are intramuscular, with infrequent blood contamination. A threshold of 0.0015 microlitre is thought by some to be the minimum amount needed to transmit HIV-1. Studies in the USA suggest that contamination of needles with sufficient HIV-1 to transmit infection is very uncommon. According to Schmid *et al.*, this means that a careful distinction should be made between injections with needles and syringes that might not be sterile, and those that are capable of actually transmitting HIV-1. In addition to this, washing, soaking or rinsing syringes before reusing will reduce the likelihood of contamination even further. There are several studies that show that reused equipment is often sterilised or boiled, which would destroy HIV-1 in seconds. In Ethiopia, HIV-1 RNA was not detected in 212 reused needles that had been sterilised, boiled or heated with burning alcohol.

Transmission efficiency via unsafe injections

Studies of health care cited by the authors show that the best data on transmission efficiency via injections indicate an estimated risk of 0.3% of HIV-1 infection after direct percutaneous exposure. The figure of 2.3% arrived at by Gisselquist *et al.* came from arguing that the transmission risk associated with unsafe injections in African health care settings is the same as that for deep needle-stick injury, with visible blood on the needle, venous or arterial blood as a source, and high viral loads in the source patient. Schmid *et al.* point out that these factors are unlikely to be present in an African health care setting, where most injections are intramuscular, using cleaned equipment and where patients are unlikely to be terminally ill with high viral loads.

Gisselquist *et al.* also used nosocomial outbreaks of HIV in Russia, Romania and Libya in their arguments. Schmid *et al.* argue that unusual outbreaks are likely to have higher than normal transmission efficiency. The Russian outbreak was probably the result of a combination of intramuscular and intravenous (and possibly transfusion) exposures; the Romanian outbreak involved the sequential immediate use of large-bore needles in children; and there are few epidemiological data from the Libyan outbreak. Generalisation from these situations to Africa is, according to Schmid, erroneous.

Population attributable fractions (PAFs)

Gisselquist and colleagues calculated the PAFs (causal fractions) associated with injections and concluded that 20 - 40% of HIV infections in Africa were associated with injections. They go on to say that these PAFs from general population studies through 1988 suggest that medical exposures were responsible for more HIV infection than sexual exposure.

Schmid and colleagues point out that the association between unsafe injections with prevalent HIV-1 infection has been examined in at least 19 cross-sectional studies. Potential reverse causality and residual confounding factors 'hamper the interpretation of these results on PAF'. To elaborate — people infected with HIV-1 are more likely to be sick than well people, so injections may have been given for primary HIV-1 illness or complications, as was seen in a study in Mwanza, Tanzania. Also, injections may have been given to treat STIs, which are a marker of unprotected sex and so an important co-factor for HIV-1 infection. This leaves STIs as an important confounding factor that distorts the association between injections and HIV-1 infection.

PAF is calculated from the prevalence of the risk factor in the population and the relative risk associated with that risk factor. So if measurement of risk or relative risk is inaccurate, PAF will also be inaccurate. In addition, sexual exposure is notoriously difficult to assess and often

underestimated, which will lead to an underestimation of the relative risk of the association between risky sexual behaviour and HIV-1 infection, and so the corresponding PAF, according to Schmid *et al.* As the authors say, the data on injection exposure should be more accurate because injections are not affected by behavioural considerations. They also go on to say that PAFs should be used with great care for epidemic infections.

Age and sex patterns of infection

The age and sex distribution of HIV-1 in sub-Saharan Africa is extremely consistent. The authors identified 6 population-based studies of the prevalence of HIV-1 infection in sub-Saharan Africa that included children. These showed that there was a much lower HIV-1 prevalence in children aged 5 - 14, than in adolescents and adults aged 15 years or older. They argue that if injections were the main mode of transmission, then a much smaller discrepancy would be expected between HIV-1 prevalence in children and adults, as there is nothing that suggests that children have substantially fewer injections than adolescents and adults. Studies have consistently shown that HIV-1-infected children have infected mothers, or are infected through blood transfusion. There are few which suggest unsafe injection, although this was a recorded possibility for 2 children in one study from Masaka, Uganda. Furthermore, results of longitudinal studies show that seroconversion in uninfected children is rare. A Ugandan study in which 5 451 HIV-1-negative infants and children (0 - 12 years) were followed up for 8 596 person-years, showed only one seroconversion. In Cote d'Ivoire, none of the children born to 266 persistently HIV-1-negative mothers seroconverted over a period of 48 months.

The consistent age and sex distribution of HIV-1 in adolescents and adults also goes against transmission by injection, unless major differences in injection rates between these groups are assumed. The distinct patterns of injection by age and sex differ from the patterns of HIV-1 infection.

Sex as primary mode of HIV-1 transmission

Looking at other STIs, the authors suggest that the fact that sub-Saharan Africa has both the highest rate of infection by the sexually transmitted herpes simplex virus type 2 (HSV-2), and the highest burden of STIs in the world, makes sexual transmission of HIV-1 highly plausible. These two facts also suggest that risky sexual behaviour is common in sub-Saharan Africa.

Rates of infection among couples also suggest that HIV-1 is effectively transmitted by sex. The authors point out that if injections were a frequent mode of transmission, infections clustered exclusively among adults in a household would be unexpected. However, in a study of 228 families, each with one adult infected by HIV-1, Hira *et al.* showed the following: of 150 men, 92 had infected wives; of 78

infected women, 57 had infected husbands; of 144 children aged less than 5 years, 36 were infected and all had infected mothers; and of 120 children between 5 and 10 years, 3 were infected. It would require huge disparities in injection practice between adults and children to explain this pattern of seroprevalence.

Another factor that strongly suggests predominantly sexual transmission is the effect of male circumcision that has been shown by 21 out of 27 studies to have a consistent and protective effect against HIV-1 acquisition. In addition, rates of HIV-1 in Africa are inversely correlated with circumcision status.

South Africa

Finally, the authors take South Africa as an example of a country for which the hypothesis that unsafe injections are the primary mode of HIV-1 transmission does not stand. The argument is that health care practices, including transfusion, are largely safe in South Africa, borne out by personal communication with 10 health care authorities in March 2003. However, the 2002 Household Survey by the South African Human Sciences Research Council showed an unexpectedly high prevalence (5.6%) of HIV-1 infection among 2 - 14-year-olds. This was taken by Brody *et al.* to be evidence of iatrogenic transmission to hundreds and thousands of children. However, as discussed by the survey's authors, but ignored by Brody, there were questions about the exact validity of the survey findings. For example, there was no increase in prevalence with age among children, which might have been expected if the main mode of transmission was injection. The non-response rate in households was high, as 25% of listed visiting points did not participate, nor did 37% of eligible respondents in

the remaining households. Also, prevalence among children by race is the opposite of what other surveillance and death registration data show, and the pattern of HIV-1 by provinces was also inconsistent with previous research. In addition, data from Statistics South Africa do not suggest that AIDS is an important cause of mortality among children and teenagers.

However, according to Schmid *et al.* there is plenty to suggest that unsafe sex is the cause of the epidemic in South Africa. The 1998 survey in Carltonville (a mining community with high quality medical care and good research), showed that the HIV-1 prevalence among women was 57%. Yet, of 118 children aged 13 and 14 years, none were HIV-1-positive. The age of sexual debut among women was 16.3 years and for men, 15.9 years. The acquisition of HIV-1 in men and women began at the age of 15 and escalated sharply, men following women. This curve has also been seen in Zimbabwe.

The authors conclude that re-interpretation of the studies published by Gisselquist and others does not show that unsafe injections are the main mode of transmission of HIV-1 in sub-Saharan Africa, although they do agree that unsafe injection practices should be discontinued. They finally conclude that epidemiological evidence indicates that unsafe sex continues to be the main mode of transmission of HIV-1 in Africa.

Gisselquist DP, *et al.* *Int J STD AIDS* 2003; **14**: 148-161.

Gisselquist DP, *et al.* *Int J STD AIDS* 2002; **13**: 657-666.

Schmid GP, *et al.* *Lancet* 2004; **363**: 482-488.

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SINGLE SUTURE

ROADS KILL

As a cyclist I am increasingly aware of the toll of death and injury among my fellow cyclists around the country during the summer. But cyclists are not the only casualties on the roads. The ninth leading cause of death in the world is road-traffic accidents, and it is predicted that by 2020 this will become the third leading cause of death and disability. As with so many things, the poor come off worst — 90% of deaths related to road-traffic injury occur in middle- and low-income countries. The highest absolute numbers are in Asia and the highest death rates in Africa. Rapid urbanisation and motorisation in low-income countries, such as India, contribute to this. The WHO have declared a World Health Day on road safety in 2004, calling for global action to prevent the annual toll of one million deaths from road-traffic injuries.

Hyder AA, *et al.* *Lancet* 2003; **362**: 2034-2035.