

EDITORIAL REVIEW

# HIV infections in sub-Saharan Africa not explained by sexual or vertical transmission

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**Summary:** An expanding body of evidence challenges the conventional hypothesis that sexual transmission is responsible for more than 90% of adult HIV infections in Africa. Differences in epidemic trajectories across Africa do not correspond to differences in sexual behaviour. Studies among African couples find low rates of heterosexual transmission, as in developed countries. Many studies report HIV infections in African adults with no sexual exposure to HIV and in children with HIV-negative mothers. Unexplained high rates of HIV incidence have been observed in African women during antenatal and postpartum periods. Many studies show 20%–40% of HIV infections in African adults associated with injections (though direction of causation is unknown). These and other findings that challenge the conventional hypothesis point to the possibility that HIV transmission through unsafe medical care may be an important factor in Africa's HIV epidemic. More research is warranted to clarify risks for HIV transmission through health care.

**Keywords:** iatrogenic, nosocomial, HIV, AIDS, sub-Saharan Africa

## INTRODUCTION

Within two years after the first AIDS cases were described in homosexual men in Los Angeles in 1981, AIDS was diagnosed in Haitians<sup>1</sup> and among Africans in Europe<sup>2</sup>, Zaire<sup>3</sup> (now Democratic Republic of Congo [DRC]), Rwanda<sup>4</sup>, and Zambia<sup>5</sup>. Unlike AIDS in the US and Europe, which seemed concentrated among injection drug users (IDUs), men-who-have-sex-with-men (MSM), and haemophiliacs, AIDS in Haitians and Africans occurred about equally in women and men, and was found among the well-to-do, including those who could afford to go to Europe for medical care.

Experts at a World Health Organization (WHO) meeting on AIDS in November 1983 puzzled over possible channels for HIV transmission among Africans and Haitians<sup>6</sup>. While noting that spouses of AIDS patients were at risk, experts were undecided about heterosexual promiscuity, concluding that 'whether persons with multiple heterosexual sex partners are at greater risk of acquiring AIDS is unknown...'. Meeting participants considered that 'injections with unsterile needles and syringes may play a role...'. WHO's

1983 recommendations focused on sterilization of medical equipment, blood safety, and MSMs.

During 1983–88, researchers in Africa found high rates of HIV prevalence among female commercial sex workers (CSWs) and patients at sexually transmitted disease (STD) clinics<sup>7–9</sup>. By the end of the 1980s, a consensus emerged among AIDS experts dealing with Africa that over 90% of adult HIV infections in sub-Saharan Africa were acquired through heterosexual contact and less than 2% through unsafe injections<sup>10–13</sup>. Unfortunately, this consensus was achieved without research to address confound between sexual and medical exposures. As Packard, Epstein, Minkin, and others have noted, CSWs and STD patients have relatively high levels of medical exposures that may be channels for transmission of blood borne pathogens<sup>14,15</sup>. Further, the consensus ignored evidence from 1980s research suggesting non-trivial levels of HIV transmission to African children and adults through unsafe injections and other medical care<sup>16–19</sup>.

## OBSERVATIONS ON HETEROSEXUAL TRANSMISSION

During the past decade, researchers have struggled to fit emerging facts about Africa's evolving HIV epidemic into the consensus view that heterosexual transmission accounts for nearly all adult infections

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and that iatrogenic transmission is minimal. Many facts do not fit well.

### Divergent epidemic trajectories

Differences in sexual behaviour across countries do not explain differences in epidemic trajectories. In some countries and regions with high HIV prevalence during the second half of the 1980s, such as DRC, Uganda, and Kagera in Tanzania, the epidemic has been stable or declining during the 1990s. In others, such as South Africa and Botswana, the epidemic reportedly doubled in less than two years among the low risk population (*viz.*, antenatal women) during the early 1990s. A series of sexual behaviour surveys in 12 African countries during 1989–93 shows no apparent correlation between the per cent of adults in a country reporting non-regular sexual partners in the last year and HIV prevalence<sup>20</sup>. A more recent study of sexual behaviour and HIV prevalence in four African cities reports that partner change, contacts with sex workers, and concurrent partnerships were no more common in the two high prevalence cities studied than in the two low prevalence cities<sup>21,22</sup>.

### Unexplained high implicit rates of heterosexual transmission in Africa

The assumption that historic and continuing high rates of epidemic increases among African adults are almost exclusively due to sexual transmission requires much higher rates of heterosexual transmission in Africa than in the developed world. However, a recent study of HIV incidence in serodiscordant couples in Africa (only 1.2% reported consistent condom use) estimated a rate of transmission per coital act of only 0.0011<sup>23</sup>, comparable to rates of 0.0003–0.0015 from similar studies in the US and Europe<sup>24–26</sup>. In four other studies of HIV transmission in serodiscordant African couples (with most individuals not aware of their HIV status and/or with continuing unprotected sex), the unweighted average HIV-incidence for men (women) was 7.6 (10.0) per 100 person years (PYs)<sup>27–30</sup>, comparable to an incidence of 4.8–7.2 per 100 PYs in European men and/or women with HIV-positive partners who continued unprotected sex<sup>25,31,32</sup>. Moreover, these data may overstate heterosexual transmission in African couples; a Zambian study that sequenced viruses to determine epidemiological linkage reported at least 13% of sequences in newly infected persons were not related to their partner's HIV<sup>33</sup>.

In the US, recent estimates of average lifetime heterosexual transmission (from a survey of sexual behaviour and research-based estimates of per coital act transmission) from infected heterosexual and bisexual males to females range from 0.19–0.40 with various assumptions and from infected females to males range from 0.09–0.18<sup>34</sup>. With these

estimates, the HIV epidemic in the US does not reproduce—much less expand—through heterosexual transmission alone. In contrast, Anderson *et al.* estimated average unconstrained (assuming all partners are susceptible) lifetime heterosexual transmission of 4.7 new infections per infected person to explain observed epidemic growth in Africa<sup>35</sup>.

Epidemiologists who design computer models to support heterosexual transmission's role in fuelling Africa's HIV epidemic characteristically choose and/or adjust assumptions about sexual behaviour, rates of heterosexual transmission, and/or other parameters to allow the model to reproduce observed prevalence<sup>35–38</sup>. These assumptions are often distant from empiric observations from African studies. While such models show that it is possible to imagine patterns of heterosexual transmission that can 'explain' the epidemic, they do not show that imagined patterns are realistic.

In one model, for example, Anderson and colleagues assumed a mean rate of annual partner change of 3.4<sup>35</sup>. In contrast, surveys in 12 African countries show unweighted averages of 74% of men and 91% of women aged 15–49 years with no non-regular sex partners in the past year, and only 3.7% of men and 0.7% of women with more than four non-regular partners<sup>20</sup>. At about the same time, a survey in Denmark found that 19% of adults aged 18–59 years reported more than one sex partner in the past year<sup>39</sup>; a survey in France found that 17% of men and 7.9% of women aged 18–44 years reported more than one sex partner in the past year<sup>40</sup>; and a survey in the UK found that 17% of men and 8.4% of women aged 16–44 years reported more than one sex partner in the past year<sup>41</sup>. Studies of sexual behaviour do not show as much partner change in Africa as modellers have assumed, nor do they show differences in heterosexual behaviour between Africa and Europe that could explain major differences in epidemic growth.

Model-builders often use the transmission co-factor effect imputed to STDs to generate desired rates of heterosexual propagation. For example, Korenromp and colleagues<sup>37</sup> assumed that genital ulcers from syphilis or chancroid in either partner enhance HIV transmission by a factor of 100, implying an HIV transmission risk from a single coital act of 30% from men to women and 8% from women to men. These rates are at odds with most empiric studies. Assumed high co-factor effects for STDs are based on findings from two prospective studies in Kenya that enrolled cohorts of CSWs and male clients visiting STD clinics<sup>42</sup>. In such studies, the cohort are not representative, and STD treatments—through injections—may be a source of risk.

Although information about the structure of sexual networks in Africa is sparse, many studies of incidence show over two-thirds of HIV occurring in African adults reporting only one

sexual partner in the reporting period<sup>27,43–45</sup>. The network geometry of such a pattern would be predominantly dendritic, with open ends formed by infected spouses with no outside partners. Rapid STD/HIV transmission has been associated with cyclic (with closed loops providing network cohesion) rather than dendritic networks<sup>46,47</sup>.

### Adult HIV without sexual exposure to HIV

During the last 14 years, a number of studies have reported adults contracting HIV without sexual exposures to HIV. A study in Zimbabwe in the 1990s found 2.1% HIV prevalence among 933 women with no sexual experience<sup>48</sup>. In a 1988 study of discordant couples in Rwanda, 15 of 25 HIV-positive women with HIV-negative partners reported only one lifetime sex partner<sup>49</sup>. In a 1990 study of teenagers in Uganda, 6.9% of women with no sex partners in the last five years were HIV-positive *vs* 23% for those with one or more partners; for men, 1% with no partners in the last five years were HIV-positive *vs* 2.5% of those reporting partners<sup>50</sup>. Among young adults 15–24 years old in Tanzania, a 1995 study found HIV prevalence of 5.6% among men and 3.6% among women who did not report any lifetime sexual activity *vs* 4.8% and 12% for men and women reporting one or more sexual partners<sup>51</sup>. In a 1999 study in South Africa, 6.8% of women and 1.2% of men 14–24 years old who reported never having sex were HIV positive; however, a validation study found some under-reporting of sexual activity<sup>52</sup>. In a case-control study in Uganda, in two of seven cases with only one lifetime sexual partner, the partner was HIV-negative, three were HIV-positive, and two others not tested<sup>53</sup>.

When HIV prevalence or incidence is found in adults and adolescents with no reported sexual exposures to HIV, it may be assumed that a proportion of the HIV in those who are sexually exposed comes from non-sexual transmission as well. Moreover, that proportion may be larger than observed HIV prevalence or incidence in those who are not sexually exposed, since whatever exposures are responsible for non-sexual transmission—injections or vaginal examinations, for example—may well increase with age and sexual activity.

## OBSERVATIONS SUGGESTING MEDICAL TRANSMISSION

### HIV-positive children with HIV-negative mothers

A study in Kinshasha in 1985 found 39% (16 of 44) of HIV-positive inpatient and outpatient children 1–24 months old to have HIV-negative mothers; only five of 16 had been transfused<sup>17</sup>. A study in Rwanda in 1984–86 found that 20% (15 of 76) of children 1–48 months old with AIDS or AIDS related complex had HIV-negative mothers

(initially 18 mothers were HIV-negative, but three were positive on a later test); only six of the 15 children had been transfused<sup>18</sup>. In a later report from Rwanda, 7.3% (54 of 704) of mothers of children with AIDS were HIV-negative; transfusions were identified as the risk factor for 22 of the 54 children<sup>54</sup>. Of 26 children less than 15 years old admitted to the Uganda Cancer Institute with Kaposi's sarcoma during 1989–94 for which the mother was tested for HIV, 19% (five of 26) had HIV-negative mothers<sup>55</sup>. A study in Burkina Faso in 1989–90 found 23% (11 of 48) of HIV-positive children to have HIV-negative mothers; six of 11 had been transfused, and the others reported multiple injections<sup>56</sup>. In a 1994 report from Côte d'Ivoire, De Cock and colleagues report that 21% (three of 14) of children with HIV-1 had mothers without HIV-1, and one of two with HIV-2 had a mother without HIV-2<sup>57</sup>. Tests of stored sera from 1994 in Ethiopia found three HIV-positive children less than five years old, of which one had an HIV-negative mother; HIV status for the other mothers was not known<sup>58</sup>. Two of 654 children tested in Guinea Bissau in 1989 were HIV-positive; the mother of one was HIV-negative, while the other mother was not tested<sup>59</sup>. These and other findings suggest that a significant proportion of paediatric HIV in Africa—as much as a fifth or more in many studies—has been acquired through health care rather than through vertical transmission from mothers.

### Shortfalls in accounting for incidence during antenatal and postpartum periods

Studies from seven African countries over the last 15 years show rates of HIV incidence during antenatal and/or post-partum periods exceeding what could be expected solely from sexual transmission (Table 1)<sup>43,45,60–68</sup>. The risk of infection from sexual transmission for women in these studies can be estimated as  $I_{WD} \times D$ , where  $I_{WD}$  is incidence for women in serodiscordant couples and  $D$  is the per cent of women in the studies who are in serodiscordant couples. We can estimate  $I_{WD}$  at 10 per 100 PYs from studies of serodiscordant African couples with continuing unprotected sex<sup>27–30</sup>. In one of the seven studies of antenatal and post-partum women<sup>68</sup>, 30 of 634 women had HIV positive partners; three of these 30 women seroconverted in a year. Unfortunately, the study did not say how many other husbands were negative or were tested, and none of the other studies report husbands' HIV status. Nevertheless, an upper bound estimate for  $D$  can be set at  $P_W$ , HIV prevalence among women in the population from which the study cohort is drawn. HIV prevalence in African men is generally lower than in women, and many infected men are partnered with infected women. In eight studies of African couples with HIV in one or both partners<sup>27–29,49,69–72</sup>, the average per cent of women

Table 1. HIV incidence in antenatal and post-partum periods vs expected incidence from heterosexual transmission

Location and years of study	Number of HIV-negative women	Incidence observed during ANC and PP (per 100 PYs)	Maximum expected incidence from sexual transmission* (per 100 PYs)	Incidence not explained by sexual transmission (per 100 PYs)
Blantyre, Malawi, 1990–95 (43, 60)	>1,000	21 during ANC and PP in 1990 12 during ANC and PP in 1991 8.0 during ANC 1990–93	2.2–3.3	19 during ANC and PP in 1990 10 during ANC and PP in 1991 5 during ANC 1990–93
Harare, Zimbabwe, 1990–94 (61, 62)	372	17 during ANC <sup>†</sup> ≥13 during 0–6 months PP	2.4–3.0	14 during ANC ≥10 during 0–6 months PP
Durban, South Africa, 1993 (63)	178	9.0 during ANC <sup>†</sup>	0.7	8 during ANC
Nairobi, Kenya, 1986–91 (64, 65)	353	6.2 during 0–6 months PP	0.27–1.6	5 during 0–6 months PP
Kigali, Rwanda, 1988–90 (66, 67)	216	7.2 during 0–6 months PP 4.2 during 7–18 months PP	3.0–3.2	4 during 0–6 months PP 1 during 7–18 months PP
Rakai, Uganda, 1994–96 (45)	1,305	3.2 during pregnancy	1.4 <sup>‡</sup>	1.8 during pregnancy
Lusaka, Zambia, 1987–88 (68)	634	3.0 during first year PP	1.2	1.8 during first year PP

\*See text

<sup>†</sup>Estimated from reported seroconversions from first antenatal visit to delivery, assuming three months in antenatal care<sup>‡</sup>Observed incidence in women during all other intervals

ANC = Antenatal care; PP = post-partum period; PYs = person years

with HIV was more than double the per cent without HIV who had HIV-positive partners. Hence,  $D < P_w$ , and expected HIV incidence from sexual transmission for antenatal and postpartum women—when one does not know the HIV status of their partners—is less than 10 per 100 PYs times  $P_w$ , or 10% of HIV prevalence among women from which the cohort of HIV-negative women is selected.

A study in Malawi reported incidence of 8.0 per 100 PYs for more than 1000 HIV-negative women from first antenatal visit in 1990 or 1993 to delivery, with an odds ratio of 1.4 for spending more than the median 3.4 months in antenatal care<sup>43</sup>. Combined antenatal and postpartum incidence in 1990, 1991, 1992, 1993, and 1994–95 was 21.3, 12.8, 8.2, 3.3, and 1.1 per 100 PYs<sup>60</sup>. HIV prevalence in antenatal women rose from 22% in 1990 to 26% in 1991 and 33% in 1996<sup>60</sup>, so that maximum expected annual incidence from sexual transmission rose during the period from 2.2% to 3.3% (i.e. from 2.2 to 3.3 per 100 PYs) only. The study shows average unexplained incidence during antenatal care of about five (8.0 minus 3) per 100 PYs, with unexplained or excess incidence of 19 (21.3 minus 2.2) and 10 (12.8 minus 2.6) per 100 PYs in 1990 and 1991, respectively, for antenatal and postpartum periods combined. The study also shows a large fall in antenatal and post-partum incidence during 1990–95 despite increasing HIV prevalence in the community—and presumably rising heterosexual transmission. No mention is made of the introduction of a remarkably effective intervention, but such a trend raises the possibility, at least, of a change in medical practice.

In a 1990–94 study in Harare, Zimbabwe, 18% (66 of 372) of women seronegative at first antenatal visit seroconverted within two years post-partum (many were lost to follow-up, so that average follow-up was much less, but no details are available)<sup>61</sup>. Sixteen women seroconverted by delivery; the report does not state the period; if average time from enrolment to delivery was three months, incidence during antenatal care was 17 per 100 PYs ( $[12 \times 16/3]/372$ ). Another 23 seroconverted in the first six months post-partum; if all women HIV-negative at birth were followed to six months post-partum, incidence during this period would be 13 per 100 PYs ( $[2 \times 23]/[372 - 16]$ ). During 1990–94, the maximum reported HIV prevalence in Harare antenatal clinics rose from 24% to 30%<sup>62</sup>, so that maximum expected incidence from heterosexual transmission was 2.4–3.0 per 100 PYs. The study suggests unexplained or excess incidence in antenatal and post-partum women, respectively, of at least 14 (17 minus 3) and 10 (13 minus 3) per 100 PYs.

Overall, four studies—in Malawi, Zimbabwe, South Africa, and Kenya—show unexplained HIV-incidence ranging from 5–19 per 100 PYs during antenatal and post-partum periods (see Table 1). These rates of unexplained incidence among African women are comparable to rates of maternal mortality from puerperal fever of 6% to 16% observed by Semmelweis during 1841–46 in the First Clinic at the University of Vienna's obstetric department<sup>73</sup>. For three other studies—in Uganda, Rwanda, and Zambia—unexplained incidence during antenatal and post-partum

periods ranged from 1.8–4 per 100 PYs, lower but still worrisome (see Table 1).

Variation of unexplained incidence from country-to-country and over time—most notably within the Malawi study—suggests that something more than simply heterosexual transmission is involved. Excess HIV incidence associated with pregnancy—whatever its cause—helps to explain the spread of HIV among low-risk populations in many African countries. In Malawi, for example, antenatal and post-partum women seroconverted at the rate of 21.3 and 12.8 per 100 PYs in 1990 and 1991, so that within one year, prevalence among women who were HIV-negative at first antenatal visit was well over half of observed prevalence from sentinel surveys of 22% and 26% in 1990 and 1991<sup>60</sup>. In Zimbabwe during 1990–94, HIV prevalence among women who were HIV-negative at first antenatal visit reached 18% within two years postpartum, which is more than half of observed prevalence of 30% in antenatal clinics in 1994<sup>61,62</sup>. In other words, whatever happens during one or two pregnancies and post-partum periods—whether iatrogenic or sexual or something else—may largely account for observed high levels of HIV among low risk women in at least some African communities.

#### HIV infections associated with induced abortions and assisted delivery

In addition to these prospective studies of pregnant and postpartum women, some other studies also suggest that health care for pregnant women may be a risk factor for HIV. In Congo, among 1770 women at an antenatal clinic in 1987–88, 17 of 282 with a history of induced abortions were HIV-positive *vs* 54 of 1488 without for a crude population attributable fraction (PAF) of HIV associated with induced abortions of 5%; complications from abortions were a common cause of hospitalization, which was also associated with HIV infection<sup>74</sup>. Among 4548 wives of workers in Kinshasha in 1987–88, 9.2% of 175 HIV-positive women *vs* 3.9% of 4373 HIV-negative women reported induced abortions for a crude PAF of 10%<sup>69</sup>. In a study among pregnant women in Ethiopia in 1993–95, 28 of 92 HIV-positive cases and 14 of 173 controls reported induced abortions for a crude PAF of 24% (calculated from the odds ratio and per cent of controls with induced abortions)<sup>75</sup>.

Finally, a study of 5690 pregnant women in Rwanda in 1989–91 reports an odds ratio of 2.7 (95% confidence interval 1.9–3.6) for last delivery with assistance by medical personnel *vs* unassisted delivery<sup>76</sup>. From reported data (221 HIV-positive out of 1872 with last delivery assisted by medical personnel *vs* 130 HIV positive out of 2422 with assistance by traditional birth assistant or no one), the crude PAF for last delivery assisted by medical personnel can be calculated as being 34%.

#### Studies associating African HIV infections with injections

At least 15 large studies (with more than 500 subjects or 50 cases in a case-control study) of risk factors for HIV prevalence or incidence in a general population sample (i.e. not CSWs or patients seeking treatment for an STD or other illness) in Africa have reported sufficient data to calculate crude PAFs associated with one or more *vs* no injections over some period ranging from 4 months to lifetime (see Table 2)<sup>16,19,77–89</sup>. Of the 20 PAFs calculated from these 15 studies (with PAFs for two samples in five studies), only four are below 22%, and the unweighted average is 29%. In the four studies of HIV incidence, the unweighted average of five PAFs is 28%<sup>19,80,86,87</sup>. Six of the studies report a positive (but not always significant) dose-response for seropositivity associated with injection frequency<sup>16,77,83–85,87</sup>. High PAFs are in most cases due to high exposures with relatively modest risk ratios. Although the crude PAFs in Table 1 ignore the associated influence of other potential risks, they provide first estimates for comparison with other studies and risks.

Several investigators<sup>19,85,90</sup> noted that some of the association may be due to people seeking treatment for HIV/AIDS symptoms or STDs, but the assertion is not adequately supported by research. A study that provides sufficient information to separate risk due to heterosexual transmission while infected with an STD from risk due to injections for STD indicates a much greater risk associated with injections (although the data have arguably been misinterpreted to support the opposite conclusion): among 302 factory workers in Rwanda in 1985, HIV prevalence for those with STDs in the last two years but without injections for STDs in that period (9.7%) was lower than for those without STDs (11%), while those with injections for STDs had much higher prevalence (27%). In a parallel survey among 150 health workers, prevalence for those with STDs and injections for STDs (47%) was almost double prevalence for those with STDs only (24%)<sup>90</sup>.

#### DISCUSSION

The recognition that significant proportions of HIV in African adults and children cannot be explained on the basis of current knowledge about sexual and vertical transmission leaves open several transmission hypotheses. There may, for example, be co-factors for sexual transmission not yet identified that are particularly influential during pregnancy or for young women. However, an accumulating body of evidence from Africa and other countries suggests that iatrogenic transmission may explain many if not most of the observations previously held to be anomalous and detailed in this review.

Table 2. Crude population attributable fractions (PAFs) associated with medical injections in studies of HIV prevalence and incidence in Africa

Location, year of study	Type of data	Type of cohort	RR for >0 vs 0 injections	$\rho$ with >0 injections* (%)	PAF
DRC, 1984 (16)	P	Adults	1.82	81	40
DRC, 1984–86 (19)	I	Adults	1.54 <sup>†</sup>	73 <sup>†</sup>	28 <sup>†</sup>
Uganda, 1987 (77)	P	Adults	1.68	66.0	31
Zimbabwe, 1987 <sup>†</sup> (78)	P	Men	3.61 <sup>†</sup>	95.0 <sup>†</sup>	71 <sup>†</sup>
Tanzania, 1987 (81)	P	Rural adults	2.6	79.2	56
		Urban adults	3.0	89.7	64
Uganda, 1989 (79)	P	Men	1.67	41.8	22
		Women	1.75	57.2	30
Uganda, 1989–90 (80)	I	Adults	1.12	75.7	8
Malawi, 1989–90 (88)	P	Women	0.91	64	–6
Kenya, 1989–90 (89)	P	Women	0.73	96.6	–3
					5
Tanzania, 1990–91 (82)	P	Men	1.98	42.9	30
		Women	1.66	58.2	28
Tanzania, 1991–92 (83)	P	Women	1.38	98.9	27
Tanzania, 1991–92 (84)	P	Men	2.19	36.8	30
Tanzania, 1991–92 (84)	P	Men	2.24	32.7	29
		Women	1.59	46.9	22
Rwanda, 1989–93 (86)	I	Women	2.42 <sup>†</sup>	58.6 <sup>†</sup>	45 <sup>†</sup>
Uganda, 1990–97 <sup>†</sup> (87)	I	Men	5.21 <sup>†</sup>	16.9 <sup>†</sup>	41 <sup>†</sup>
		Women	1.60 <sup>†</sup>	32.2 <sup>†</sup>	16 <sup>†</sup>

\*During an interval which varies from four months to lifetime

<sup>†</sup>Case-control studies, for which the table shows the odds ratio instead of the rate ratio and  $\rho$  is per cent exposed to injections among controls only. The PAF is approximated from the standard formula:  $(\rho[OR-1])/(1+\rho[OR-1])$

<sup>‡</sup>In calculating RR,  $\rho$ , and PAF, seroconversion is assumed to have occurred at the mid-point of the observation interval

DRC=Democratic Republic of Congo; P=prevalence; I=incidence; RR=rate ratio;  $\rho$ =per cent of study cohort

### HIV survival and transmission through medical instruments

HIV can survive in syringes at room temperature for more than four weeks<sup>91</sup>. One study found HIV-RNA in three of 80 syringes after subcutaneous or intramuscular injections of infected patients; since the volume of blood in the syringes was too low to explain the observed HIV-RNA, the study team hypothesized that the RNA had been released by follicular dendritic cells into interstitial fluid<sup>92</sup>.

An early prospective study among health care workers estimated the probability of seroconversion after work-related percutaneous exposure to HIV of approximately 0.3%<sup>93</sup>. However, a case-control study of percutaneous exposures by the Centers for Disease Control (CDC) and health authorities in the United Kingdom and France assessed risks for deep injuries (6.8% of controls vs 52% of cases) to be 15 times greater than for other percutaneous exposures<sup>94,95</sup>. Furthermore, many health care workers were treated with zidovudine for post-exposure prophylaxis, which reportedly reduced seroconversion rates by over 80%<sup>95</sup>. Because medical injections occasion a deep injury and are not countered by antivirals, HIV transmission during unsafe injections may well be an order of magnitude greater than 0.3%<sup>96</sup>.

### Epidemic of unsafe injections in much of Africa and South Asia

In a recent review, Simonsen *et al.*<sup>97</sup> concluded that the average person in the developing world received 1.5 injections per year (range 0.9 to 8.5). In the majority of studies reviewed, the proportion of injections that were unsafe was greater than 50%. Despite the lack of systematic data collection noted by the authors, these findings were consistent over a range of developing world settings. In a companion piece, Kane *et al.*<sup>98</sup> estimated that 80 000 to 160 000 HIV infections occur worldwide each year (two-thirds of these in Africa) from unsafe injections. These model-based estimates assume a transmission efficiency of 0.5% through unsafe injections, which as noted above, may be an order of magnitude too low. Further, these estimates do not consider the concentration of medical injections in certain groups (e.g., CSWs, STD patients, pregnant women) and settings with high HIV prevalence.

Starting in the 1950s Africans experienced a massive increase in medical injections associated with mass injection campaigns targeted at yaws, with introduction and spread of parenteral therapies to treat other diseases, and with plummeting prices for antibodies and injection equipment<sup>99</sup>. For example, UNICEF administered 12 million injections

for yaws in Central Africa alone during 1952–57<sup>99</sup>. From the 1950s into the 1980s, unsafe injections may have contributed to the silent spread of HIV in Africa in much the same way that unsafe injections for schistosomiasis and other treatments in Egypt established hepatitis C as a major blood-borne pathogen, infecting about 15% to 20% of the general population at the end of the 1990s<sup>100</sup>.

### Documented iatrogenic outbreaks

The unexpected discovery of HIV in a 12-year-old Romanian girl in a Bucharest hospital in June 1989 led to extensive testing to uncover the extent and channels for iatrogenic transmission<sup>101</sup>. Tests during 1989–90 found 1086 HIV-positive Romanian children less than four years old. Medical injections were the only apparent risk factor for more than half of these children; fewer than 40% had been transfused with untested blood (even so, in 1990 only 0.0006% of Romanian blood donors were HIV-positive), and fewer than 8% of tested mothers were infected<sup>101,102</sup>.

In the former Soviet Union, about 250 children reportedly acquired HIV from hospital exposures in 1988–89<sup>103</sup>. More recently, nearly 400 children attending a single hospital in Libya apparently contracted HIV<sup>104,105</sup> and thousands of paid plasma donors in China may have been iatrogenically infected<sup>106</sup>. Smaller iatrogenic outbreaks have been reported among patients and plasma donors in other countries.

### CONCLUSION

Taken together, our observations raise the serious possibility that an important portion of HIV transmission in Africa may occur through unsafe injections and other unsterile medical procedures. After some early interest and research on iatrogenic transmission in Africa, most notably in Kinshasha during the 1980s, the topic all but vanished from the research agenda. Considering the aggressive reactions to evidence of iatrogenic HIV infections in Russia, Romania, Libya, and China, and considering as well international attention to the transmission of Ebola virus through health care practice, the absence of thorough investigation into documented incidents of multiple HIV infections suspected from health care in Africa (e.g. HIV-positive children with HIV-negative mothers cited above) is noteworthy. Fortunately, there are recent indications, at WHO<sup>97,98</sup> and elsewhere, of increasing attention to iatrogenic risks of blood-borne microbes. To the extent that unsterile procedures in routine medical care represent a possibly major route of HIV transmission in countries with high HIV prevalence, the current tenets on which HIV prevention programmes in Africa are based need reassessment. Though promotion of safe sexual practices remains a priority, new interventions may be required to minimize risk from iatrogenic transmission.

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