Letters to the Editor

High rates of HIV seropositivity in Africa — alternative explanation

Sir: It is gratifying that Gissselquist *et al*.[1], albeit from a different perspective, conclude as we have that heterosexual and mother to child transmission cannot account for the high rates of HIV seropositivity in sub-Saharan Africa[2–4]. Gisselquist and his colleagues' argument, that African statistics are explicable in terms of an iatrogenic mechanism involving unsterile injections, presents at least two difficulties. First, given that many infectious agents existed in Africans prior to the AIDS era and undisputedly survive in needles and syringes longer than HIV, and are more readily transmitted[5], such agents should be more prevalent than HIV. Second, their belief that HIV can survive for more than four weeks' is not shared by other HIV experts including the Center for Disease Control and Prevention: '. . . drying of HIV-infected human blood or other body fluids reduces the theoretical risk of environmental transmission to that which has been observed — essentially zero'[6].

An alternative, and in our view more plausible, explanation may be found in an examination of the specificity of the antibody tests[2]. The only way to determine their specificity is to use HIV isolation as a gold standard. However, at present some of the best known HIV/AIDS experts agree there is no such gold standard. 'One difficulty in assaying the specificity and sensitivity of human retroviruses [including HIV] is the absence of a final ''gold standard'' '[7,8]. According to one antibody test manufacturer 'At present there is no recognized standard for establishing the presence or absence of HIV-1 antibody in human blood'[9].

Given also that (a) antibodies directed against the infectious agents which cause the fungal and mycobacterial diseases highly prevalent in Africa cross-react with the HIV antigens[10–13], (b) 60% of infants born to HIV positive mothers serorevert after maternal antibodies have disappeared from the infant circulation[3,14,15]; the only explanations being either children cure themselves of HIV or the tests are non-specific[3]; (c) the criteria which define a positive Western blood vary widely between institutions and laboratories and are least stringent in Africa[16] (see Appendix); it is credible that the disparate number of positive antibody tests in sub-Saharan Africa are due to cross-reacting antibodies.

Although to some it may seem 'curious indeed'[17], a non-retroviral explanation for the correlation between 'seropositivity' and morbidity, mortality and AIDS in Africa[18] is eminently possible. Clinical practitioners are no strangers to tests of significant utility and predictive ability which are nonetheless devoid of specificity. Arguably the test which provides the best example is the erythrocyte sedimentation rate (ESR) because it, like the HIV antibody tests, is associated with elevations of antibodies and acute phase reactant proteins. Indeed, there is evidence that an elevated ESR is a superior predictive marker for the development of clinical AIDS than is a decrease in the CD4 cell count[19], although the latter is said to be the cause of the syndrome. A positive antibody test, like the ESR, may indicate a propensity to the development of particular diseases without necessarily being linked to HIV infection.

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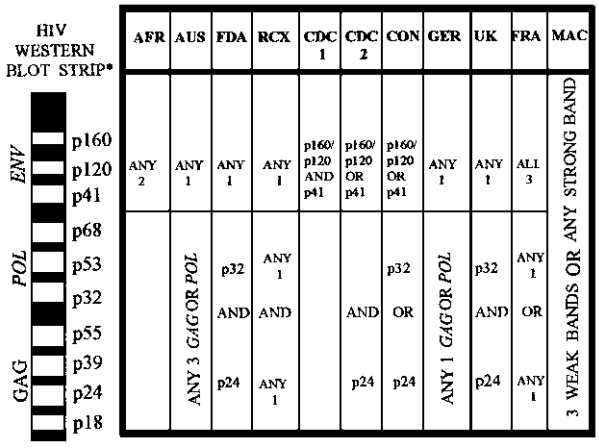
Appendix

Criteria defining a positive HIV Western blot



	AFR	AUS	FDA	RCX	CDC 1	CDC 2	CON	GER	UK	FRA	MAC
	ANY 2	ANY 1	ANY 1	ANY 1	p160/ p120 AND p41	p160/ p120 OR p41	p160/ p120 OR p41	ANY 1	ANY 1	ALL 3	3 WEAK BANDS OR ANY STRONG BAND
		ANY 3 *GAG* OR *POL*	p32 AND p24	ANY 1 AND ANY 1		AND p24	p32 OR p24	ANY 1 *GAG* OR *POL*	p32 AND p24	ANY 1 OR ANY 1	

AFR=Africa[1]; AUS=Australia[2]; FDA=US Food and Drug Administration[3]; RCX=US Red Cross[3]; CDC=US Center for Disease Control[3]; CON=US Consortium for Retrovirus Serology Standardization[3]; GER=Germany; UK=United Kingdom; FRA= France; MACS=US Multicenter AIDS Cohort Study 1983–1992. *Bands not in electrophoretic order

Notes

I 'The Association of Public Health Laboratories now recommends that patients who have minimal positive results on the Western blot, eg p24 and gp160 only, or gp41 and gp160 only, be told that these patterns have been seen in persons who are not infected with HIV and that follow-up testing is required to determine actual infective status'[4].

II In February 1993 the US Food and Drug Administration relaxed their criteria in order to 'reduce the number of HIV-1 seroindeterminate Western blot interpretations', that is, to increase the number of HIV positive individuals[5].

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Heterosexual HIV transmission in Africa: recent findings and future directions

Sir: Contrary to several reports that the HIV epidemic in sub-Saharan Africa has been largely driven by heterosexual transmission, Gisselquist and colleagues[1–3] have argued, based on extensive literature review and statistical analyses, that there is no documented evidence to justify previous reports. The findings of Gisselquist and colleagues have significant implications for HIV/AIDS research, public health policy and scientific publication criteria; yet, is the scientific community prepared for such a dramatic paradigm shift?

While Gisselquist and colleagues must be commended for planning and implementing such an innovative study, as well as extensively documenting their findings, at stake is the re-evaluation of the predominant heterosexual hypothesis, as well as other potential modes implicated in HIV transmission within the context of sub-Saharan Africa, and not merely the medical model as they had hypothesized as the missing variable for HIV transmission in sub-Saharan Africa. Yes, there will be enormous social and financial commitments but such concerns do not outweigh the benefit and growth of science, the global impact of the HIV/AIDS epidemic and the advances in HIV/AIDS research attributed to the global public health initiatives. Therefore, this deeply embedded heterosexual hypothesis must be re-evaluated since the findings may have profound public health implications for HIV/AIDS prevention, treatment, support and care, especially in the context of sub-Saharan Africa. In addition, current efforts initiated by the Joint United Nations Programme on HIV/AIDS (UNAIDS), the United States Agency for International Development (USAID) and other scientific organizations directed at reassessing the findings of Gisselquist and colleagues are encouraging and must be strongly applauded. Such directions, policy statements and perspectives by international organizations could immensely contribute to and subsequently benefit health policy, young and emerging scientists, and at-risk populations.

Finally, HIV/AIDS research is replete with controversy. We have been plagued with issues, for example, concerning the origin of HIV, the discovery of HIV, and whether HIV causes AIDS. Arguments and counter-arguments abound; yet, those debates have germinated alternative hypotheses and paradigm shifts, and some of the findings have had both practical and policy implications. Accordingly, the findings by Gisselquist and colleagues, if viewed and reassessed from such scientific prism, may have potential relevance for HIV/AIDS treatment, support and care, especially for sub-Saharan Africa and the global fight against HIV/AIDS.

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HIV infections in sub-Saharan Africa

Sir: The study by Gisselquist *et al*.[1] is of the utmost importance, as it helps health professionals and policy makers to face the bitter reality of a broken health system. In my opinion as a medical graduate with experience in practice in Cameroon, Central Africa in both rural and urban areas, it seems extremely unlikely that sexual behaviour or vertical transmission could explain the large number of new cases diagnosed daily. I do not, however, agree with the authors' analysis of other possible causes; I believe that too much importance is placed on unsafe injections by health professionals. Injections are not an isolated medical procedure but an integrated component of care delivery. Rather than doing a critical analysis of the health system, Gisselquist *et al*. use injections as a scapegoat and the complexity of health care delivery in Africa is totally ignored. Indeed, from my daily experience, injections administered in hospitals are safe, and there is no multiple use of needles. Nurses performing injections take appropriate care; for example, as we showed, 80% of nurses take the precaution of recapping the syringe[2].

I believe that the whole public health and medical care system is to blame for much of the high level of HIV transmission in some African countries. Salaries of health professionals are low and irregular and motivation is low as well. Budgets in hospitals are extremely low. There is no health insurance scheme and medical care is acquired through various means other than conventional hospitals, even in the biggest cities.

Inadequate funding leads to questionable cleaning and sterilization procedures in hospitals. Sterilization of instruments by flaming or simply cleaning in a solution of povidone–iodine between two surgical procedures are still common. The result is that simply cleaning a wound is likely to be at least as dangerous as a sexual act. Most

medical procedures are still performed by unqualified medical personnel because of the shortage or lack of motivation of doctors with limited knowledge of nosocomial transmissions of HIV. Disturbingly, even when the knowledge is available, it is not always translated into practice[2].

In Africa, either because of financial reasons or cultural beliefs, a substantial proportion of medical procedures are not performed in a recognized health care structure. Most patients and people requiring health monitoring (e.g., pregnant women) seek parallel and sometimes exclusive health care outside the hospital setting, in either an illegal health care structure or among traditional doctors where they face a high risk of HIV.

In most African countries, abortion is illegal but common, with an estimate of 4.2 million per year[3]. Most of them are performed clandestinely in poor conditions by untrained personnel with the same non-sterilized instruments for many cases. Practices like clitoral excision are still common and, like abortions, coincide with the period of high sexual activity and constitute confounding factors. Decision to keep a pregnancy may follow a missed abortion attempt with the serological window ending during the ante-natal care.

Activities involving contact with blood are not subject to public health controls. A good example is hair-cutting which is performed by untrained personnel in the absence of any regulation using a single sharp razor which can be used for up to 10 people per day with absolutely no sterilization between customers. This affects mainly young men, but also young women of an age at which sexual activity his high.

Finally, the monitoring and control of blood products are poor. It seems likely that the HIV/AIDS epidemic is just another manifestation of the inefficiency of health care systems in sub-Saharan Africa. This is already seen in the persistence at high prevalence of other infectious diseases such as malaria and tuberculosis. Can a system that is unable to contain these preventable and treatable diseases be expected to control HIV/AIDS?

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Is offering same day HIV testing appropriate?

Sir: Same day HIV testing (SDT) has been available in Edinburgh since 1995 on the assumption that anxious patients would appreciate this service[1] and uptake would be high. Same day testing is routinely offered in antenatal settings[2] in some centres.

The records of all genitourinary medicine clinic patients at the Royal Infirmary of Edinburgh who had blood taken for SDT in February 2001 were reviewed.

Seventy-four patients were tested and told the result would be available the same day. Nineteen (25%) patients had prearranged an appointment specifically for SDT. Fifty-five (75%) patients had testing offered as sexually transmitted diseases screening.

Sixty-six (89%) patients were of low risk category and eight (11%) were medium or high risk category with sexual contact in Africa or Far East, multiple heterosexual partners, homosexual anal intercourse with HIV positive partners. Forty-four (60%) returned for the result on the same day, 19 (25%) on another day and 11 (15%) never attended to receive their results.

Only 11 (57%) of the 19 who had specifically asked for SDT returned on the same day for their results. Of 66 patients in the low risk category, 40 (66%) returned the same day for their results and of the eight in the medium or high risk category only four (50%) returned for their results on the same day. The cost of each test was £32 (staffing and clinic costs were not included in this amount).

Anxiety levels so low such that 40% of patients are not interested in their SDT results coupled with a low HIV positivity rate suggests that SDT should not be offered routinely. However, it should be available for those who request it.

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Antibiotic treatment of PID

Sir: Peter Watson makes a number of interesting points in his recent letter about the antibiotic treatment of pelvic inflammatory disease (PID)[1],

but I fear there remains some confusion and misunderstanding.

Firstly the use of evidence-based guidelines. Few would disagree that where clinical trial evidence is available for a particular treatment, then that treatment should be used in preference to one for which there is no evidence. The commonest antibiotic regimen used in the UK prior to and immediately after the publication of the national PID guideline was some variation of doxycycline and metronidazole. Historical precedent in the UK supported their use, doxycycline covers *Chlamydia trachomatis* and metronidazole should kill the anaerobes. Were there no alternative therapies then doxycycline and metronidazole would probably be the recommended treatment based on 'expert opinion' (level IV evidence). But of course there are other treatments. Treatments which, unlike doxycycline and metronidazole, have been subjected to randomized controlled trials and found to be effective. Treatments which cover *Neisseria gonorrhoeae* effectively (unlike doxycycline)[2] and are effective against the myriad of other bacteria isolated in women with PID (also unlike doxycycline where 85% of isolates are resistant)[3]. All the currently recommended regimens in the national PID guidelines have at least one randomized controlled trial (and often many) to support their use, and have *in vitro* sensitivity patterns which cover the relevant organisms. I would welcome the chance to debate against anyone who wishes to defend the use of doxycycline and metronidazole to treat PID based on current evidence.

Next, the difficulty in making an accurate diagnosis of PID. Certainly the sensitivity of a clinical diagnosis is little better than 50–60%, but every day in our clinics we are faced by women who may have PID and in whom a delay in diagnosis increases the risk of subsequent ectopic pregnancy and infertility. Because of this we accept that a low threshold for diagnosis is appropriate and that significant over treatment therefore occurs. This is acceptable because the potential harm to the patient of receiving unnecessary antibiotics is low, while the potential benefits are great. Such an approach does not excuse the use of less effective therapy however.

Finally, the question of consensus. The UK PID Guidelines, in common with all the UK STD Guidelines were reviewed by the Medical Society for the Study of Venereal Disease (MSSVD), Association for Genitourinary Medicine (AGUM) and all the UK regional audit chairmen. A variety of changes were made in response to the comments received and the guidelines were posted on the internet for comment prior to publication. The final guideline was then accepted by the Clinical Effectiveness Group on behalf of MSSVD and AGUM.

The production of a guideline will not change clinical practice overnight, but I believe the current UK guideline on PID is both evidence based and has been subjected to a rigorous peer review prior to acceptance by the professional bodies representing GU Medicine in the UK.

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Antibiotic treatment of PID — Reply from Peter Watson

Sir: I welcome Jonathan Ross's reply to my letter, which was not an argument that we require a new national guideline on the management of pelvic infection. I observed that the data from Kuchimanchi's and McClean's audit[1] indicated that the guideline was not being followed in Yorkshire, I suggested that this might be due to a lack of consensus and I tried to discuss reasons why there might not be a consensus. The statement by Walker and colleagues[2] that the development of treatment guidelines requires consensus-building is their opinion. Perhaps they are wrong but it is an opinion which I share. If national guidelines are to be a valuable tool, it is reasonable to monitor their use and to explain why they are not used.

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