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BACK

The Perth Group

AIDS – SEXUALLY TRANSMITTED OR SEXUALLY ACQUIRED?

NOTE

This manuscript was submitted to four scientific journals beginning in 2010 but rejected by all.

The first submission – “AIDS - SEXUALLY TRANSMITTED OR SEXUALLY ACQUIRED?” (YMEHY-D-10-00541) was to *Medical Hypotheses* accompanied by a second manuscript – "WOULD MONTAGNIER PLEASE CLARIFY WHAT METHOD HE USED TO PROVE THE EXISTENCE OF HIV?" (YMEHY-D-10-00397)

Both were accepted for publication by the editor Professor Bruce Charlton who upon our later enquiry emailed: “Unfortunately, I have already been deprived of editorial control of Medical Hypotheses. After I accepted your submitted paper for publication, and without my knowledge, it was 'intercepted by the Elsevier management who are apparently holding it for some kind of evaluation. Presumably you have not had an acknowledgement of the paper so far? This is why. However, since I as editor accepted the paper for publication, and there is no process in the journal's official organization which allows for managers to counter this decision - your paper counts as 'in press'”.

After Charlton was dismissed and his decision revoked, *Elsevier* appointed Dr. M. Manku new editor-in-chief. In August 2010 Dr. Manku rejected both submissions informing us, “your manuscript was one that I felt I had to send out for review. Unfortunately I have not had any luck from 3 reviewers who declined to review. I have also looked at your paper carefully and reached conclusion that it should be published in an AIDS specialist journal where it will get right readership and also go through a formal review process”.

In regard to the second manuscript Dr. Manku wrote, “I also formally reject your YMEHY-D-10-00397 - entitled "WOULD MONTAGNIER PLEASE CLARIFY WHAT METHOD HE USED TO PROVE THE EXISTENCE OF HIV”….I would not like to publish such commentary in Medical Hypotheses I would rather you take your question up directly with Professor Luc Montagnier, a noble (*sic*) laureate, to ‘clarify inconsistencies’. I will not use Medical Hypotheses as platform for such discussion, I would rather you submit your commentary to more suitable journal which will have attention from HIV/AIDS specialists ”.

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ABSTRACT

It is claimed that tens of millions of people have acquired AIDS as a result of sexual transmission of HIV. Sexually transmitted diseases or infections are invariably spread from active to passive partners and *vice versa*. We have critically analysed the published data on AIDS acquisition. These data indicate that AIDS is certainly sexually acquired but not sexually transmitted. Conceptually the difference is subtle indeed but nonetheless pivotal in the understanding of AIDS pathogenesis.

In his Nobel lecture published in V*irology* this year [1] Montagnier stated “changes in sexual behaviours” and “immune depression caused by malnutrition, drug abuse and increased co-infections, are probably the causes of emergence of AIDS as a global epidemic, affecting most if not all continents including recently Polynesia islands”. Elsewhere [2] we have published evidence on the relationship between drug abuse, malnutrition, co-infections and AIDS. We have also put forward a mechanism by which the risk factors cause their effects, a mechanism which Montagnier has embraced [3 ,4]. In this paper we critically analyse the relationship between sexual activity and AIDS.

In 1981 an uncommon malignancy, Kaposi's sarcoma and a few infrequent opportunistic infections, principally *Pneumocystis carinii* pneumonia, were diagnosed with high frequency in young, gay men. This precipitated a concerted effort to find the cause(s) and, since the afflicted individuals were extremely promiscuous, a cause related to sexual intercourse was justifiably high on the list of priorities.

The first study to define the relationship between sexual activity and AIDS in gay men was published pre-HIV in *Lancet* in 1982 by Michael Marmor, Alvin Friedman-Kien and their colleagues. They compared various characteristics of 20 men with biopsy-proven Kaposi’s sarcoma with 40 controls. "The distributions of the number of different sex partners per month in different time periods before disease showed that patients were more promiscuous than controls. 50% of patients reported having sex with 10 or more different partners during an average month in the year before onset of disease, compared with 17% of controls. Some reported extreme levels of sexual activity: the most promiscuous patient estimated that he had had sexual intercourse with an average of 90 different partners per month in the year preceding disease…The initial models, constructed to test our primary hypotheses of (1) infection through sexual activity and (2) a carcinogenic effect of amyl nitrite exposure, indicated statistically significant effects of each of these variables after adjustment for the effects of the other."

In their updated paper published in 1984 they concluded, "Many sexual behaviours listed as risk factors in Table 4 were highly correlated with one another, with nitrite use or with cytomegalovirus antibody titers. Therefore, multiple logistic regression analysis of this data set, including sexual activities, nitrite use, cytomegalovirus antibody titers, and additional variables describing lifetime incidence of amebiasis, giardiasis, gonorrohea, and syphilis, were done to determine which variables were statistically independent in their associations with disease. Stepwise logistic regression analysis indicated that the number of partners per month in receptive anal-genital intercourse with ejaculation, the number of occasions of "fisting", and cytomegalovirus antibody titers were the only independent and statistically significant variables for discriminating patients from controls". Given the nature of sexually transmitted diseases (agents) it is enigmatic that “receptive anal-genital” but not insertive anal intercourse was documented as a risk factor.

The *sine qua non* of sexually transmitted diseases is their bidirectional transmission. For example, both males and females are at risk of acquiring infection with *N. gonorrohea* and *T. pallidum* as a result of sexual intercourse with an infected partner. A disease acquired by a female as a result of sex with a male but not *vice versa* could not be classified as sexually transmitted. The best illustration of this is pregnancy – a condition that is sexually acquired but not sexually transmitted. Because the sexual roles of gay men cannot be assigned by gender, epidemiologists characterise sexual partners as either active (insertive) or passive (receptive). The active partner is the penis inserting, semen donating gay or heterosexual male. The passive partner is the penis accepting, semen accepting gay male or female. Proof a disease is sexually transmitted requires demonstration of a chain of transmission and acquisition from active partner 1 → passive partner 1 → active partner 2 and so on.

Because gay men commonly practise both active and passive sex, documenting the chain of transmission requires data on exclusively active partners. If this fact is ignored it is impossible to prove bidirectional spread amongst gay men.

Following the discovery of HIV and general acceptance of its role in AIDS, studies of the relationship between sexual activity and AIDS were replaced by studies of sexual activity and HIV infection (a positive antibody test). However, unlike for example, *N. gonorrohea* and *T. pallidum*, at no stage was (or has) proof of bidirectional sexual transmission been sought microbiologically. That is, by isolating HIV from the genital (penile, vaginal, rectal) secretions of a series of index cases whose transmission is then proven to uninfected sexual partners by means of contact tracing. In fact, according to Harry Haverkos, at the time when investigations into sexual activity and HIV were initiated, "Sexual contact tracing, the standard practice in public health to combat such sexually transmitted diseases as gonorrhea and syphilis, has been avoided for tracing of HIV infected persons. Health department personnel are concerned about possible discrimination associated with AIDS, plus the fact that there is no cure for the disease" [5]. Rather, to investigate sexual transmission between both gay and heterosexuals, HIV experts have resorted to epidemiological studies. However, epidemiological studies are less precise and are associated with a number of significant caveats:

1. “Evidence from a randomised trial carries the greatest weight, compared to other types of epidemiological study, because they are most likely to be free of a range of biases and other errors that can arise in non-randomised studies”. In regard to sexual transmission and HIV such studies are impossible to perform because this would “involve recruiting a group of people and randomly assigning half to become the sexual partners of people with HIV infection, and then comparing the proportion that developed HIV infection in this group to the corresponding proportion in the group who did not have sexual partners with HIV infection” [6].
2. Sexual behaviours are not observed but self-reported. Yet, as the novelist George Eliot observed in 1866, “Man cannot be defined as an evidence-giving animal; and in the difficulty of getting up evidence on any subject, there is room for much unrecognised action of diligent persons who have the extra stimulus of some private motive” [7]. This view is confirmed by the need many epidemiologists feel to qualify their data. For example:
    a. Over two decades ago Padian and Francis wrote, "Over the years, a constant theme in the AIDS field has emerged from groups working in settings as different as blood bank donor referral and AIDS-case categorisation. Every group has found that extracting sensitive risk-behaviour information is often difficult for even the most experienced interviewer" [8].
    b. “The behavioral reclassification of a relative small number of seroconvertors would have a major impact on our findings” [9]. "[W]e cannot be absolutely certain that we correctly classified this case as female-to-male transmission…Of course, because we are relying on risk histories, the same caveats apply to classification of male-to-female cases of transmission as well" [10].
    c. "[S]tudies may not have been adequately controlled for other confounding non-sexual routes of transmission such as risks associated with intravenous drug use. At first blush, cases that appear attributed to heterosexual transmission may, after in depth interviewing, actually be linked to other sources of risk” [10].
    d. Self-reporting even the act of sexual intercourse is significantly error prone. In 2006 Maria Gallo from the Centers for Disease Control published a study of 332 female sex workers where exposure to semen was assessed using vaginal prostate specific antigen (PSA). “Among women who reported no sex or protected sex only within the past 48 hours, 21% and 39%, respectively, tested positive for PSA. Among those testing positive for PSA, no differences in PSA concentrations were found among those reporting no sex, protected sex only, or at least one unprotected act”. She concluded, “Self-reported data are used for informing policy, research, and funding decisions

regarding STI/HIV and pregnancy prevention efforts. Participants might give inaccurate responses as a result of self-presentation or courtesy bias, imperfect recall, poor question comprehension, limited topical vocabulary, exaggeration resulting from social norms or to comply with study eligibility criteria, personal salience of the sexual event, or emotional responses to sensitive questions. The high level of misreported recent exposure to semen that we demonstrated substantiates that self-reports of unprotected sex cannot be assumed to be valid measures. Future STI/HIV and pregnancy prevention studies should establish the veracity of self-reported measures of sex and condom use or should use end points that do not rely on self-reported data" [11].

e. The interpretation of many epidemiological studies is premised on the veracity of HIV partner status. The latter are obtained from questionnaires filled in by study subjects who rely on self-reporting by their sexual partners. This is a far cry from scientific proof. The unreliability of partner HIV serostatus is frequently invoked to explain anomalous results. For example, gay passive sexual partners found at increased risk of seroconversion from HIV negative partners. Yet outcomes that do accord with transmission of an infectious agent are not similarly qualified [12]. Epidemiologists appear very reluctant to consider what appear to be anomalous results in terms of reliable data, thereby prejudicing opportunities to envisage other hypotheses.

3. Most significantly, the pivotal interpretations of epidemiological data are predicated on findings in a single digit number of individuals. Why should this be so when millions of individuals are said to have acquired HIV following sexual contact?

In the absence of randomised trials epidemiological investigations have to rely on less rigorous methods, either non-randomised and/or observational study designs which, unfortunately, are unable to provide definitive answers. Indeed, the studies on sexual transmission are mostly cross-sectional analyses performed on certain groups of individuals where the investigators document risk factors for the presence of a positive antibody test or AIDS. However, abundant as they are, cross-sectional analyses cannot prove sexual transmission because (a) HIV experts accept there are non-sexual modes of "HIV" transmission; (b) in serologically concordant partners infection of both partners is already present; (c) proof of transmission does not follow merely because there are no other explanations for the data. Hence epidemiologists have resorted to conducting the more difficult, costly and time consuming prospective studies in which the sexual behaviour risk factors related to seroconversion are documented. Such studies invariably include an initial cross-sectional component which is usually published separately before the completed study. Here we examine data from what are accepted to be the most conclusive studies.

GAY MEN

In 1984 Robert Gallo and his associates were among the first to report a cross-sectional study, "…of eight different sex acts, seropositivity correlated only with receptive anal intercourse…and with manual stimulation of the subject's rectum…and was inversely correlated with insertive anal intercourse". Hence Gallo confirmed Marmot's finding but documented a second enigma: An inverse relationship between insertive sex and HIV. This is completely at odds with a sexually transmitted agent. It is no different from asserting the more often a person crosses the road the less likely he is to be struck by a car. In an updated study published in 1986 Gallo wrote: "Data from this and previous studies have shown that receptive rectal intercourse…is an important risk factor for HTLV-III [HIV] infection…We found no evidence that other forms of sexual activity contributed to the risk" [13].

Unquestionably, the largest, longest, best designed and executed study in gay men is the Multicenter AIDS Cohort (MAC) study. Amongst their 900 scientific publications (which include prospective studies) there are many confirmations that "receptive anal intercourse was the **only** sexual practice shown to be independently associated with an increased risk of seroconversion to HIV in this study".

Significantly, in one MAC study publication it was reported: "…greater sexual activity [receptive anal intercourse] following establishment of HIV-1 infection leads to exposure to promoters or co-factors that augment (or **determine**) the rate of progression to AIDS"[14] (emphasis added). This finding presents a third enigma. The generally accepted view for sexually transmitted diseases is that a person needs to be infected only once in order to develop or die from an illness.

By 1994 many epidemiological studies, including prospective studies, had been conducted in gay men. Reviewing more than 20 such studies Caceres and van Griensven concluded, "the cited reports yield convincing evidence that unprotected anogenital receptive intercourse poses the highest risk for the sexual acquisition of HIV-1 infection…there is mounting epidemiological evidence for a small risk attached to orogenital receptive sex, biologic plausibility, credible case reports and some studies show a modest risk, detectable only with powerful designs;…no or no consistent risk of the acquisition of HIV-1 infection has been reported regarding insertive intercourse and oro-anal sex".

There have been some reports which suggest the insertive partner is at increased risk of acquiring HIV. Obviously this is the critical issue but detailed analyses of such reports is unconvincing. For example, in a MAC study reported by Kingsley *et al*,[15] 2507 seronegative gay men were followed for six months. During this time seroconversions occurred in 95 men (3.8%), 9 of whom claimed they did not practise passive anal sex. However, when further questioned, 6 of the 9 men admitted to practising passive anal sex in the months prior to the commencement of the study. Of the 3 remaining men the authors wrote, they "may reflect misclassification of men who actually did participate in receptive anal intercourse". Even if these 3 men did not "reflect misclassification", such small numbers, typical of such claims, lack the power to define an increased or even absolute risk greater than the zero risk observed in the 220 men in this study who did not practise receptive or insertive anal intercourse. The implication of this finding does not appear to have been appreciated.

HETEROSEXUALS

To date there have been only two prospective studies in heterosexuals: those of Isabelle de Vincenzi and her colleagues (the European Study Group) and Nancy Padian and her associates (in the USA). Both sets of studies consist of cross-sectional and prospective components and both report data on male-to-female and female-to-male transmission. As mentioned, studies in heterosexuals are not complicated by the problem of distinguishing between the passive and active partners.

In their cross-sectional studies de Vincenzi reported that sexual practices "other than anal intercourse...were not associated with infection of the [female] partner". In other words, heterosexual women have the same risk factor for a positive antibody test as gay men. In their four year prospective study the European Study Group claimed 4 men and 8 women became infected by having sex with the seropositive partner. This study was criticised by other researchers including Stuart Brody [16] who pointed out, "The problem of subjects' lying (often euphemistically termed "social desirability responding") about engaging in anal intercourse and intravenous drug use plagues most studies of behavioral risk factors for the transmission of HIV, and the study by de Vincenzi and colleagues is no exception. How was the absence of homosexual contact [for the male partners] verified? How was the absence of anal intercourse among the women verified? If only 4 men and 6 women among the 121 couples inconsistently using condoms lied when they denied engaging in anal intercourse (or misreported the facts for other reasons), there would be no cases attributable to vaginal intercourse without a condom. At least this much lying should be expected. Before vaginal and anal intercourse are assigned comparable degrees of risk and condoms given the credit for saving lives, the alternative explanation that the disease is spread almost exclusively by anal and intravenous transmission must be more rigorously examined. Other investigators found that HIV infection in women was related to anal intercourse (especially among partners of bisexual men) and the number of exposures to the index patient, but not to condom use or the total number of sexual partners".

Responding, de Vincenzi wrote, "We agree with Dr Brody that our prospective analysis lacks statistical power to show an increased risk associated with anal intercourse. [That is, de Vincenzi could not exclude the possibility that anal intercourse and not vaginal intercourse was the cause of the positive antibody tests acquired by the 8 women; which means she accepted her study could not prove transmission from vaginal intercourse]. Indeed, we found such an association in the cross-sectional analysis. However, from a public health point of view, no one should state that there is no risk of HIV transmission through vaginal sex, since the vast majority of cases of AIDS throughout the world are acquired in this manner". Since de Vincenzi did not (and could not) claim her evidence proved HIV transmission by penile-vaginal intercourse one can only conclude she was unable to prove sexual transmission of HIV, either male-to-female or female-to-male. Despite this and without citing any other evidence, she claimed, "the vast majority of cases of AIDS throughout the world are acquired" by penile-vaginal transmission [17]. One should note that to enrol the 378 couples in her prospective study de Vincenzi had to recruit from 10 centres in eight European countries. Despite the fact that millions of humans are said to have acquired HIV heterosexually she could document only 4 men and 8 women who developed a positive antibody test. With such small numbers de Vincenzi should justify why her "prospective analysis" has "the statistical power" to prove anything.

Unquestionably Padian's study, which began in 1985, is the longest, largest, best designed and executed study ever conducted in heterosexuals. Padian announced this study at the 1988 Amsterdam, International AIDS Conference: "Objective. **To examine the efficiency of heterosexual transmission of HIV and associated risk factors**. Methods: We enrolled the opposite sex partners of individuals infected with HIV or diagnosed with AIDS or ARC throughout California. Participants were interviewed about their sexual practices and medical history; Laboratory tests for HIV and other co-factors were conducted, as were physical examinations…Results:…in multivariate analysis, only the practice of anal intercourse (p-.003) and non-white race (p-.013) were significantly associated with infection…We have also enrolled male partners of infected women. In spite of reported unprotected sexual intercourse (median number of sexual contacts = 399) **none of the twenty male partners were infected**" [18] (emphasis ours).

Padian *et al's* "Male-to-Female Transmission of Human Immunodeficiency Virus" cross-sectional study was published in 1987 [19]. "Ninety-seven female sexual partners of 93 men infected with human immunodeficiency virus were studied…23% of the women were infected…Anal intercourse significantly discriminated between seronegative and seropositive women…The number of sexual contacts (whether vaginal, anal or oral, was significantly associated with infection…whereas general sexual activity (as measured by number of sexual partners [median 2,5 for seropositive; 4 for seronegative women] and number of sexually transmitted diseases) was not associated with HIV infection". The data on "The number of sexual contacts" *versus* the "general sexual activity" are unexpected findings (see below).

The "Female-to-Male Transmission of Human Immunodeficiency Virus" cross-sectional study was published in 1991 [10]. Here Padian *et al* pointed out, "since 1985, we have been conducting a study of the heterosexual transmission of AIDS", but by 1991 of 72 infected women, only the partner of one of them was found positive. However, for a number of reasons they could not say with certainty that the man was infected by his female partner. "…we cannot be absolutely certain that we correctly classified this case as female-to-male transmission…Of course, because we are relying on risk histories, the same caveats apply to classification of male-to-female cases of transmission as well". By 1997, in the cross-sectional part of the study, Padian and her colleagues described one further case of female-to-male transmission but were also uncertain about this man. Attempting to explain the differences between their findings and those who claimed high rates of female-to-male transmissions, they wrote, "studies may not have been adequately controlled for other confounding non-sexual routes of transmission such as risks associated with intravenous drug use. At first blush,

cases that appear attributed to heterosexual transmission may, after in depth interviewing, actually be linked to other sources of risk".

The results of Padian *et al's* prospective study were published in 1997 in a paper [20] entitled "Heterosexual Transmission of Human Immunodeficiency Virus (HIV) in Northern California: Results from a Ten-year Study". "We followed 175 HIV-discordant couples over time for a total of approximately 282 couple-years of follow-up…The longest duration of follow-up was 12 visits (6 years). Table 3 summarises behaviour change over time, comparing behaviours of the entry visit with those reported at the last follow-up visit".

"TABLE 3. Risk behavior at baseline and most recent (final) follow-up visit among 175 human immunodeficiency virus (HIV)-discordant couples recruited in Northern California from 1985 to 1996 (*n* = 175 couples with a total of 3,384 couple-months of follow-up)

	Baseline Visit (%)	Final follow-up visit (%)
Abstention	0	14.5*
Consistent condom use	32.2	74*
Any anal intercourse	37.9	8.1*

* $p < 0.0005$ (by McNemar's test for matched pairs)."

As can be seen from their Table 3, at the beginning of the study, nearly 70% of participants were not using condoms consistently. And, despite diligent efforts promoting safe sexual practices, Padian and her colleagues were not entirely successful in improving this situation. At the end of the study 25% of participants still did not consistently use condoms. Furthermore, "approximately 97% of behaviour changes was reported between baseline and the first follow-up visit". Yet, they "observed no seroconversion", that is, no person who had a negative test at the beginning of the study developed a positive antibody test over the course of the study. Discussing the lack of sexual transmission Padian and her associates wrote, "Nevertheless, the absence of seroincident infection over the course of the study cannot be entirely attributed to significant behaviour change. No transmission occurred among the 25% of couples who did not use condoms consistently at their last follow-up nor among the 47 couples who intermittently practiced unsafe sex during the entire duration of follow-up" [20].

Several times recently Padian has defended her prospective study against assertions her data prove HIV is not heterosexually transmitted. In a commentary posted at the AIDSTruth website she claimed her study was not designed to prove HIV transmission but to examine the effects of "behavioral interventions" on sexual transmission of HIV. In other words, Padian accepted there is proof HIV is sexually transmitted and "Any attempt to refer to this or other of our publications and studies to bolster the fallacy that HIV is not transmitted heterosexually or homosexually is a gross misrepresentation of the facts and a travesty of the research that I have been involved in for more than a decade". However, as cited above, when Padian first announced her ongoing study at the 1988 Amsterdam International AIDS Conference, she did not describe it in terms of "behavioral interventions" but as "Objective. To examine the efficiency of heterosexual transmission of HIV and associated risk factors". Her 1991 paper began with "**Objective. –** To examine rates of heterosexual transmission of human immunodeficiency virus (HIV) and associated risk factors and to determine the relative efficiency of female-to-male and male-to-female transmission". The abstract of her 1997 paper opens with "To examine rates of and risk factors for heterosexual transmission of human immunodeficiency virus (HIV), the authors conducted a prospective study of infected individuals and their heterosexual partners who have been recruited since 1985". Neither does the title of the 1997 paper reflect a change of focus: "Heterosexual transmission of human immunodeficiency virus (HIV) in

Northern California: results from a ten-year study". And while at AIDSTruth Padian states, "That we witnessed no HIV transmissions after the intervention documents the success of the interventions in preventing the sexual transmission of HIV", in her 1997 paper she wrote, "Nevertheless, the absence of seroincident infection over the course of the study cannot be entirely attributed to significant behavior change. No transmission occurred among the 25 percent of couples who did not use condoms consistently at their last follow-up nor among the 47 couples who intermittently practiced unsafe sex during the entire duration of follow-up".

The fact is that in the Padian study there were many serodiscordant heterosexual couples who continued to practise unsafe sex who, nonetheless, did not seroconvert. The proportion who practised unsafe sex did decrease over time but no scientist can claim the zero transmission rate observed in any couple was due to the success of "behavioral interventions" when, at the beginning of the study, approximately 70% of the couples were not practising safe sex, as were 25% at the completion, despite the many and constant "behavioral interventions". Most significantly, over the 12 years she conducted her study, Padian could document only two men who were HIV positive, both in the cross-sectional component. Not only does this vanishingly small, cross-sectional statistic not prove transmission, Padian herself expressed doubts about the validity of either man (see above). Hence Padian's study did not provide evidence beyond reasonable doubt of female-to-male transmission and, on the basis of this study, the acquisition of a positive antibody test cannot be substantiated as caused by a sexually transmitted agent. It is also significant that in her AIDSTruth commentary Padian does not cite any of her own research as proof of heterosexual transmission. In fact she could not cite her prospective study because there were zero transmissions. Rather Padian, like de Vincenzi, cites "everyone else", while "everyone else" cites de Vincenzi and Padian.

The reliability of the evidence which is said to prove heterosexual (vaginal/penile) transmission has been questioned by other scientists [16 ,21-25]. Our group has repeatedly requested such evidence from leading HIV epidemiologists but, despite assurances, no such evidence has eventuated.

In summary the presently available data show that the epidemiology of a positive antibody test and AIDS is the same as pregnancy. The passive partner may acquire either or both through sexual activity but cannot transmit either to the active partner. In terms of a retroviral infection this can only signify the male partner first acquiring HIV by non-sexual means following which he transmits it to the passive partner. However, unless one accepts that millions of heterosexual males (including Africans) are haemophiliacs, transfusion recipients or drug addicts, this is a highly unlikely explanation. Hence, one is obliged to search for evidence for an alternative interpretation in the passive partners (male and female). That is, factors other than a retroviral infection that can explain acquired immune deficiency (low T4 cell count) and antibody reactions with test kit antigens. There are at least two possibilities, either or both of which may be operative.

Non-HIV causes of a low T4 cell count, AIDS and positive antibody tests

A. Microbial factors

The traditional but problematic [26] view of AIDS pathogenesis is that HIV causes immune deficiency (T4 cell depletion) which directly causes the clinical AID syndrome. Furthermore, the T4 cell depletion is driven by viral expression. If this is the case the plasma HIV RNA ("viral load") must predict the decline in the number of T4 cells. This view, which has been accepted for more than two decades, has been proven wrong. In 2006, Rodriguez and his associates from the Universities of Case Western Reserve, Harvard, Washington and California concluded, "Presenting HIV RNA level predicts the rate of CD4 cell decline only minimally in untreated persons. Other factors, as yet undefined, likely drive CD4 cell losses in HIV infection" [27]. Many HIV experts, including Anthony Fauci, Daniel Douek, David Ho, [28] Keith Henry, Pablo Tebas and Clifford Lane [29] share this view. The latter three authors wrote: "The provocative main finding from their [the Rodriguez] study was that the presenting plasma

HIV RNA load predicted no more than 10% of the observed CD4 cell loss in patients with chronic untreated HIV infection. What factor(s) explain the other 90%? Twenty-five years into the HIV epidemic, a complete understanding of what drives the decay of CD4 cells – the essential event of HIV disease – is still lacking…The findings presented by Rodriguez et al provide support to those who favour **nonvirological mechanisms as the predominant cause of CD4 cell loss**" (emphasis added).

Evidence published in 2007 led to the paradoxical situation where the central role played by "immune deficiency" (low T4 cells) has been replaced by "immune activation". What was for over two decades considered the "hallmark" of AIDS is no longer the central, distinctive attribute of the HIV theory of AIDS. Ivona Pandera and her associates from the Tulane National Primate Centre, Tulane University, the Los Alamos National Laboratory, University of Pennsylvania and National Institute of Allergy and Infectious Diseases, wrote, "Therefore, our data support a revised paradigm wherein severe GALT [gut associated lymphoid tissue] $CD4^+$ T cell depletion during acute pathogenic HIV and SIV infections of humans and Rh [rhesus macaques] is necessary but neither sufficient nor predictive of disease progression, with levels of immune activation, proliferation and apoptosis being key factors involved in determining progression to AIDS" [30]. In the same year and the same journal Jeffrey Milush from the University of Texas and his associates from 8 institutions in the USA, wrote, "The original observation that clinical AIDS was associated with peripheral blood CD4 T cell loss due to the direct and indirect effects of HIV infection led to the paradigm that depletion of peripheral blood $CD4^+$ T cells is the major determinant of immune dysfunction, ultimately resulting in the opportunistic infections and cancers characteristic of AIDS". "Rather, AIDS pathogenesis appears to be the cumulative result of multiple aberrant immunologic parameters that include CD4 T cell depletion, generalized immune activation, and depletion/dysfunction of non-CD4 T cells. Therefore, these data provide a rationale for investigating multifaceted therapeutic strategies to prevent progression to AIDS, even following dramatic CD4 depletion, such that HIV^+ humans can survive normal life spans analogous to what occurs naturally in SIV^+ mangabeys", which remain healthy despite systemic T4 cell loss [31]. The idea that "activation is a fundamental driving force" in AIDS pathogenesis is not new, and at present it seems to be embraced by all AIDS experts. Nonetheless, the mechanism remains obscure [32].

Recently, to account for the immune activation in AIDS patients, researchers from the National Institute of Allergy and Infectious Diseases, National Institute of Health, USA, put forward the following: "We propose the hypothesis that the effects of HIV during the acute phase of infection and the consequent localized immune perturbation ["HIV infection depletes the mucosa of CD4 T cells"] compromise the integrity of the mucosal surfaces, thereby leading to increased translocation of intestinal flora and subsequent systemic immune activation" [33].

In the same year, the above researchers from the National Institute of Allergy and Infectious Diseases, and from several other Institutions from the USA as well as researchers from France and England [34] published a paper entitled "Microbial translocation is a cause of systemic immune activation in chronic HIV infection". Summarising their findings they wrote, "Chronic activation of the immune system is a hallmark of progressive HIV infection and better predicts disease outcome than plasma viral load, yet its aetiology remains obscure. Here we show that circulating microbial products, probably derived from the gastrointestinal tract, are a cause of HIV-related systemic immune activation. Circulating lipopolysaccharide, which we used as an indicator of microbial translocation, was significantly increased in chronically HIV-infected individuals and in simian immunodeficiency virus (SIV)-infected rhesus macaques ($P <= 0.002$). We show that increased lipopolysaccharide is bioactive *in vivo* and correlates with measures of innate and adaptive immune activation". However:

1. While there is evidence that lipopolysaccharides (LPS) cause immune activation [35] there is no evidence that HIV-induced gut T4 depletion is either necessary or sufficient for LPS translocation, or that LPS are necessary for immune activation in AIDS [32,36 ,37].
2. As mentioned, from the very beginning the epidemiological evidence showed that "fisting" and "manual stimulation of the subject's rectum" (physical injuries to the intestinal mucosa and wall) are independent risk factors for AIDS and a positive antibody test. Such injuries represent an open wound bathed in bacterial-laden intestinal fluids – a ready source of microbial (LPS) translocation even in the absence of HIV-induced "compromise [of] the integrity of the mucosal surfaces". It is significant that the bacterium *E. coli* is highly prevalent in the gut and is a source of LPS.
3. Commenting more than 20 years ago on Gallo's experimental findings we wrote [2], "In a paper published this year in which Gallo is a co-author, it is stated, "In the present study T4 cells from normal donors that were infected with HTLV-III [HIV] *in vitro*, after stimulation with PHA followed the same pattern of secretion of IL-2 [interleukin-2] (day 1), production of HTLV-III and cell death", that is the same pattern as PHA-stimulated cells from AIDS donors. Whereas the same infected cells...did not produce IL-2 or express virus without immunological activation" (PHA stimulation). Since this is the case, even assuming that HTLV-III/LAV exists *in vivo* and is transmitted from a sick individual to a normal one, the normal person would never become ill unless he is exposed to high concentrations of mitogenic agents. In other words HTLV-III/LAV by itself cannot produce ill effects while the mitogenic agents would produce the immunological and clinical abnormalities associated with AIDS irrespective of HTLV-III/LAV infection. It is important to note that in the above-mentioned paper evidence is presented that PHA produces immunological abnormalities in normal non-infected cell cultures, including T4 loss...The situation is as follows: There are two agents A (HTLV-III/LAV) and B (sperm, nitrites, opiates, Factor VIII), however only B is pathogenic on its own. Yet A is considered as the primary causative agent".
4. At a National Institute for Drug Abuse meeting held in Washington, May 1994, Gallo said: "Inflammatory cytokines are usually promoted by immune activation, not by immune suppression…In gay men, the inflammatory cytokines are increased *before* HIV infection."[38].
5. Nine years later, in a paper published by researchers from Amsterdam, one reads, "In conclusion, our data show that chronic immune activation and the size of the CD4 T cell pool are critical factors in HIV-1 pathogenesis, even when measured before seroconversion". The finding that "Increased T cell activation has predictive value for HIV-1 disease progression **even before seroconversion**" is as good a proof as one can obtain that HIV is not necessary for the T4 cell decrease and immune activation present in AIDS patients [39] (emphasis added).

There is also ample evidence that microbial products may also cause a positive HIV antibody test.

1. As far back as 1993 Essex and his associates showed that "[L]eprosy patients and their contacts show an unexpectedly high rate of false-positive reactivity of HIV-1 proteins on both WB [76.7%] and ELISA [63.6% -- a lower figure because some negative ELISAs tested positive on the WB]. Our observations of cross-reactivity between LAM [lipoarabinomannan], and to a lesser extent PGL-I [phenolic glycolipid I], with HIV-1 antigens suggest that HIV-1 ELISA and WB results should be interpreted with caution when screening individuals infected with *M. tuberculosis* or other mycobacterial species. ELISA and WB may not be sufficient for HIV diagnosis in AIDS-endemic areas of Central Africa where the prevalence of mycobacterial diseases is quite high" [40].
2. Collizzi and his colleagues from Rome have shown that healthy mice injected LPS develop antibodies to the HIV p120 and p41 proteins [41] (and V. Colizzi *et al.*, personal

communication). Given that 30% of the normal population have an HIV p24 band on the Western blot this may lead to a positive "confirmatory" test under the criteria of most institutions.

B. SEMEN

At the beginning of the AIDS era many scientists considered a role for semen in the genesis of AIDS. However, following the discovery of HIV and its general acceptance as the cause of AIDS, semen was discounted, albeit with two exceptions – our group and Robert Root-Bernstein. We postulated semen plays a principal role in AIDS by causing generalised cellular oxidation [2 ,42]. According to Root-Bernstein, exposure to semen "is theoretically capable of initiating lymphocytotoxic autoimmunity" [43]. The presently available data show that:

(a) AIDS and a positive antibody test are not bidirectionally sexually transmitted;
(b) Trauma to the rectum is a risk factor;
(c) Ejaculation of semen is a risk factor;
(d) Immune activation is an oxidative process; [2 ,42 ,44]
(e) Semen is a potent oxidant. In fact its biological effects depend on this property; [2]
(f) In 1986 Gallo and his colleagues [45] performed experiments which showed that:
HIV + stimulating (activating) agents → decrease in T4 cells
Activating agents by themselves → decrease in T4 cells.
HIV by itself → no evidence reported.
Commenting on these findings they wrote, "The results revealed a cytopathogenic mechanism that may account for T4 cell depletion in AIDS patients and suggest how repeated antigenic stimulation by infectious agents, such as malaria in Africa, or by allogenic blood or **semen**, may be important determinants of the latency period in AIDS" (emphasis ours).

Given the above data one must conclude semen is amply able to produce immune activation. Indeed, semen has been proven to cause immune activation [46]. The question then arises: Can semen cause a positive antibody test in the absence of HIV?

According to some of the pre-eminent experts in HIV antibody testing "The best antigen preparations to detect established HIV infection are viral lysates because these contain native antigens from virtually all structural components of the virus" [47]. The most important antigens in the Western blot test have molecular weights of 24,000 (p24), 32,000 (p32), 41,000 (p41), 121,000 (p120) and 160,000 (p160). p120 and p160 have been shown to be polymers of p41 [48] and, according to the data published by researchers at the US National Cancer Institute,[49] all the proteins with molecular weight higher than 24,000 are cellular proteins.

Luc Montagnier is credited with the discovery of the HIV p24 protein but it appears even this protein is cellular. Montagnier claimed p24 originated from T lymphocyte cell cultures of a patient BRU, which Montagnier ultimately detected in material he referred to as the "purified" virus. However, 14 years after the discovery of the p24 protein, Montagnier admitted that no electron micrographs of the "purified" virus were published because, even after a "Roman effort", they were unable to find particles with "the morphology typical of retroviruses" [50]. This was corroborated by Montagnier's electron microscopist and co-author Charles Dauguet, who said all there was present in the "purified" virus was cellular debris (D. Tahi, personal communication). This is as good evidence as one can get that p24 is a cellular protein.

This means that the main antigens present in the WB kits, at least when they are obtained from viral lysates, are cellular proteins. In this case a positive antibody test in the passive partner may be the result of:

1. the reaction of these cellular antigens with antibodies directed against sperm or lymphocytes present in semen.
2. reactions induced by other antigens in the ejaculate.

Ample evidence exists that:

(a) a large and ever increasing number and variety of autoantibodies is present in AIDS patients; [51]
(b) hypergammaglobulinemia is present in the vast majority of seropositive and AIDS patients; [52]
(c) immunoglobulins present even in normal individuals exhibit auto-antibody binding reactivity. Their appearance and disappearance is redox dependent. This finding has such a profound effect that it constitutes one of the main arguments "...for rethinking much of what we assume to be true in basic immunology, including tolerance"; [53]
(d) semen is a potent oxidising agent; [2]
(e) the tissues of AIDS patients and those at risk are oxidised [54,55]. In other words, semen may transform the immunoglobulins into auto-antibodies which, in turn, will cause a positive HIV antibody test.

It must also be pointed out that physical injury to the gut will not only facilitate translocation of endogenous bacterial products, but also exogenous material including bacteria, foreign proteins and cells, such as lymphocytes and spermatozoa. There is evidence that such exposure induces antibody formation including antibodies that react with HIV antigens, gp120, p24 and gp41 [56,57].

The claim that semen may play a role in the acquisition by the passive partner of AIDS and a positive test can only be proved or disproved by studying a sufficiently large sample of men/women who have no other risk factors for HIV/AIDS but a high frequency of passive anal intercourse with HIV negative men. Unfortunately, because of the substantive bias towards HIV, no such studies have been conducted. However, there is at least some supportive evidence.

If the quantity of semen is the cause of a positive antibody test and AIDS, rather than an infectious agent present in semen, the number of episodes of passive anal sex with ejaculation will prove to be a greater risk than the number of different sexual partners. In case this distinction is not clear consider the following: Assume the average volume of the male ejaculate is 5 ml. In three months, for example, a gay man could have sex with 100 partners, each once, which would expose him to 500 ml of semen. Or he could have 50 partners, four times, which would expose him to 1000 ml of semen. In other words, half as many partners could expose him to twice the dose of semen. If HIV is the only cause of a positive antibody test and thus AIDS, then the 100 partners should pose a far greater risk than the 50 partners. Epidemiologists have had many opportunities to obtain and report these data but we could find only one such study.

"In the year before testing, homosexual men who were seropositive tended to have a greater number of sexual partners ($p = 0.009$), more episodes of receptive anal intercourse ($p < 0.001$), and more frequent active ($p < 0.001$) and receptive ($p = 0.023$) insertion of hands into the rectum…The number of episodes of receptive anal intercourse per year was the variable most highly associated with HTLV-III/LAV [HIV] seropositivity ($F = 27$. $p < 0.001$). After adjustment for this variable, no other variable was statistically significant". In other words, in this study the number of episodes of receptive anal sex had more statistical significance than the number of partners. And in a subgroup of men analysed the quantity of semen was the only significant risk factor [58].

Conclusion

The presently available epidemiological evidence shows that a positive antibody test and AIDS are not sexually transmitted. A positive antibody test and AIDS, like pregnancy, can be only sexually acquired and thus, as with pregnancy, cannot be due to an infectious agent.

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***Conflicts of Interest Statement**

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