THE ASCHER COMMENTARY

On 11 March 1993, the journal Nature published a commentary by Michael Ascher et al entitled “Does drug use cause AIDS?” Coverage of the commentary in the mainstream press (The New York Times, San Francisco Chronicle, etc.) coincided with the publication of the commentary itself. Richard Strohman writes an unpublished letter to the editor of the San Francisco Chronicle, claiming their coverage of the commentary is a “masterpiece of scientific ignorance.” Strohman further claims in an open letter to the Daily Californian that the “scientific community has shut out dissenting AIDS theories.” Duesberg and Bryan Ellison submit a response to Nature the following January, which is rejected. Neville Hodgkinson picks up on the story in May, claiming that “censorship is blocking the debate vital to discovering the truth about AIDS.”

DCB
To the Council
National Academy of Sciences
2101 Constitution Ave
Washington Dc 20418

Re: Science by press releases

To an extent which undermines classical standards of science, the scientific establishment has handled purported scientific results concerning AIDS by press releases rather than by scientific exchanges, thereby manipulating the media and people at large. I shall give two examples.

(a) Gallo-HHS press conference. Gallo's purported "discovery" of "the AIDS virus" was announced at a press conference by him and HHS Secretary Margaret Heckler on 23 April 1984. Details of the circumstances of this press conference can be found in Crewdson's original Chicago Tribune article of 19 November 1989, section 4. This press conference was a major factor in making people accept that AIDS is caused by a virus and that this virus is HIV. I regard this conclusion as a mere hypothesis, which has been challenged by some scientists.

(b) A press release on a "Commentary" in Nature. A piece "Does drug use cause AIDS?" by M. S. Ascher, H. W. Sheppard, W. Winkelstein Jr. and E. Vittinghoff, was published in the Nature issue of 11 March 1993.1 This piece was not a regular scientific article, but fell under the category "Commentary". About a week before publication, Nature issued a press release headlined without qualification: "DRUG USE DOES NOT CAUSE AIDS." The press release announced the publication of that piece, and concluded: "These findings seriously undermine the argument [sic] put forward by Dr Peter Duesberg, of the University of California at Berkeley, that drug consumption causes AIDS, and instead provides strong support for the hypothesis that HIV causes the disease." Numerous members of the press started calling Duesberg to get his comments on the forthcoming article in Nature, but the article had not been made available to Duesberg. Despite the fact that the press release is marked "Embargoed for release: 6:00 pm EST, Wednesday, March 10, 1993", Duesberg told me that on 4 March he got several calls from journalists, including one from the New Scientist in Washington. These journalists asked for his comments on the forthcoming Nature "Commentary"). Duesberg told these journalists that he could not comment on a piece he had not seen. The New Scientist then faxed him a copy on 4 March. He received a copy from Nature only on 9 March. Thus does Nature and the authors of the article use the media to manipulate public opinion before their article has been submitted to the scientific scrutiny of other scientists, especially Duesberg who is principally concerned.

A misrepresentation in Nature's press release. Among other things, Nature's press release misrepresents how the sample of 1,034 men for the purported study was determined. The press release states: "These were selected by random sampling of San Francisco households regardless of sexual preference, lifestyle, HIV status or drug use." But a qualification from the "Commentary" itself was left out in the press release. Indeed the "Commentary" actually refers to a "random sampling from

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1 Nature identifies the authors as follows: Michael S. Ascher and Haynes W. Sheppard are in the Viral and Rickettsial Disease Laboratory, California Department of Health Services, 2151 Berkeley Way, Berkeley, CA 94704. Warren Winkelstein Jr. and Eric Vittinghoff are in the Department of Biomedical and Environmental Health Sciences, School of Public Health, University of California, Berkeley, CA 94720.
neighborhoods of San Francisco where the AIDS epidemic had been most intense before 1984". Thus the press release suppresses the additional information that the sampling came from a definite segment of San Francisco households rather than random San Francisco households.

Limitation on the length of Duesberg's reply. Incidentally, when Duesberg submitted a reply to the Ascher et al. "Commentary", he was at first told by Nature to limit his reply to at most 500 words. This is less than one-fourth the space (two full pages) allotted to Ascher et al. I hope nevertheless that Duesberg will make available a longer critical analysis, but it may take both more time and more space for him to produce a more extensively documented critique of the "Commentary". In addition, Duesberg has received an answer from CDC to the letter he wrote them on 11 February, and he is also occupied in documenting his criticisms of that answer.

I take no position here on the relative merits of the AIDS virus hypothesis or the AIDS drug hypothesis (in whatever form it may be formulated). I do take a position against the manner Nature handled the "Commentary" by Ascher et al. before Duesberg and other scientists had a chance to evaluate the scientific merits of such "Commentary" and the data on which the "Commentary" was purportedly based.

Objections in letters from Richard Strohman. Some other scientists reacted as negatively as I did to Nature's publication. Among them is Richard Strohman (Professor Emeritus, Molecular and Cell Biology, UC Berkeley), who wrote some of his objections in a letter to the editors of the San Francisco Chronicle which had rushed into print about the "Commentary". I enclose a copy.

The authors of the "Commentary" in Nature ended their piece as follows:

The energies of Duesberg and his followers could better be applied to unraveling the enigmatic mechanism of the HIV pathogenesis of AIDS. To this end, we have proposed an alternative model\textsuperscript{14,15} based on HIV signalling at CD4 cells. This model and others are now being evaluated, and we cordially invite Duesberg to participate in this endeavour. [I omit footnotes 14 and 15.]

I find it presumptuous and objectionable for scientists to tell others where their energies "could better be applied". Especially in connection with this last paragraph, Strohman also wrote an open letter to one of the authors, Warren Winkelstein, a colleague at UC Berkeley. Strohman submitted this letter on 12 March 1993 to the student publication The Daily Californian. I enclose a copy.

Scientific standards as I have known them since I was a freshman at Caltech require that some energies be applied to scrutinize data on which experiments are based, to determine the accuracy of the data, its significance, its completeness, and to determine whether conclusions allegedly based on these data are legitimate or not.

I wish to warn you here against Maddox's unscientific, irresponsible, and manipulative journalism.

Serge Lang

Enclosures: The press release from Nature concerning the Ascher et al. "Commentary" and the "Commentary" itself; Strohman's letters; article from SF Chronicle

c: Duesberg, Maddox, Strohman
PRESS DIGEST OF NATURE ISSUE DATED MARCH 11, 1993

Embargoed for release: 6:00 pm EST, Wednesday, March 10, 1993
For further information please FAX the Request Form on page 5 or call 202/737-2355
Please mention Nature as the source of these items

Please note that Scientific Correspondence, Commentary and News & Views pieces may not be available until the Monday morning prior to embargo.

AIDS: DRUG USE DOES NOT CAUSE AIDS

The first rigorously controlled epidemiological test of the proposed link between drug use and acquired immune deficiency syndrome (AIDS) shows that "there is no evidence of a drug effect," according to Dr Michael S. Ascher at the California Department of Health and Human Services in Berkeley, California, and his colleagues, in this week's Commentary (p103). These findings undermine the premise for the so-called 'Duesberg Hypothesis' which suggests that drugs, and not the human immunodeficiency virus, HIV, causes AIDS.

The study was based on a unique population-based cohort of 1,034 single men aged between 25 and 54 years of age at the time of recruitment in 1984, the San Francisco Men's Health Study (SFMHS). These were selected by random sampling of San Francisco households regardless of sexual preference, lifestyle, HIV status or drug use. The participants were questioned about drug use for the 24-month period before recruitment, and during a 96-month follow-up period, with the outcome that of 812 homosexual/bisexual cohort members, 215 developed AIDS, while none of 215 heterosexual men developed the disease, despite roughly equivalent proportions of drug use in each group.

With regard to HIV status, 45 out of the 812 homosexual/bisexual men seroconverted from HIV-negative to HIV-positive status during the course of the study, 11 of which (24 percent) were reported to have developed AIDS, and 5 (11%) have died; of 400 men in the same group who were seropositive at the start, 204 (51%) have developed AIDS and 169 (42%) have died. In contrast, all of the 215 heterosexual men were HIV-negative at the beginning of the study, with only one seroconverting to become HIV-positive during the 96-month follow-up period; no cases of AIDS and one death (0.5%) was recorded in this group.

These findings seriously undermine the argument put forward by Dr Peter Duesberg of the University of California at Berkeley, that drug consumption causes AIDS, and instead provide strong support for the hypothesis that HIV causes the disease.

CONTACT: Dr Michael S. Ascher 510-540-2573
Does drug use cause AIDS?

M. S. Ascher, H. W. Sheppard, W. Winkelstein Jr & E. Vittinghoff

A hypothesis identifying substance abuse as a main cause of AIDS has naturally excited much publicity. But such claims have no basis in fact.

Since 1987, Peter H. Duesberg, a professor of molecular biology at the University of California, Berkeley, has maintained that the human immunodeficiency virus (HIV) is not the infectious aetiological agent for AIDS (acquired immune deficiency syndrome). Responses to Duesberg have presented a strong case that HIV has a central role in AIDS pathogenesis. Duesberg did not at first present a clear alternative hypothesis, but recently, based on an ecological analysis of drug use in the United States, he has proposed that "either drug consumption (particularly associated with malnutrition) by recently established behavioral groups or conventional clinical deficiencies and their treatments are necessary and sufficient to cause indicator diseases of AIDS." Because of the wide publicity attracted by this assertion, we decided to assess this hypothesis.

In the first case reports of AIDS in the United States, recreational drug use was considered as an aetiological factor. Subsequently, an association between drug use, acquisition of HIV and development of AIDS has been extensively documented among those sharing needles for injecting drugs. But the first major case-control study of AIDS in homosexual men showed no association between drug use and the development of AIDS. Later, Kaslow and colleagues analysed data from more than 4,500 homosexual/bisexual men in the multicenter AIDS Cohort Study (MACS) and found no association between the use of alcohol or other psychoactive drugs and HIV seroconversion or progression of HIV infection to AIDS. Because amyl nitrite inhalants were thought to be aetologically related to Kaposi's sarcoma, Lifson and colleagues compared the use of 10 psychoactive drugs in 72 incident cases of Kaposi's sarcoma with 109 incident AIDS cases without Kaposi's sarcoma from the well-characterized San Francisco City Clinic Cohort, and found no differences. The most commonly used drugs were marijuana, nitrite inhalants, cocaine and amphetamines.

Direct test

To test Duesberg's drug-use hypothesis directly, we analysed data from a unique population-based cohort study, the San Francisco Men's Health Study (SFMSH). This study is based on a cohort of 1,034 single men 25-54 years of age at the time of recruitment (June-December 1984), selected by stratified, random, household sampling from neighbourhoods of San Francisco where the AIDS epidemic had been most intense before 1984. Participants were recruited without regard to sexual preference, lifestyle or HIV serostatus (not known at the time), and thus constitute a representative cross-section of men in this community. We believe that the sampling method is critical in the assessment of drug-use data, which can be strongly affected by recruitment bias.

Duesberg has stated that there are no controlled studies of drug use and AIDS, and that previous studies "failed to match the HIV-free control group with the HIV positives for the extent and duration of drug consumption". We performed our study in part to respond to this criticism. We examined the cohort at 6-monthly intervals for 96 months, and obtained drug-use data and determined HIV serostatus at each examination. Data for the variables we considered were available from 1,027 study subjects.

We compared heavy drug use (weekly or more frequent use of the four recreational drugs mentioned above) for the 24-month period before entry into the study among 215 heterosexual and 812 homosexual/bisexual cohort members. Except for amyl nitrite, with 18% heavy use in homosexsuals versus no heavy use among heterosexuals, the percentage of subjects reporting heavy use of each drug was similar in both sexual preference groups: 36 versus 39% for marijuana; 7 versus 4% for cocaine; and 1 versus 5% for amphetamines, respectively. During 96 months of follow-up, 215 cases of AIDS occurred among the homosexual/bisexual men (cumulative incidence, 26%) compared with none among the heterosexuals. If heavy use of marijuana, cocaine or amphetamines is casually associated with AIDS, a cumulative incidence of 56 (0.26×215) cases among the heterosexual subjects would be expected.

Survey results

Table 1 summarizes the cumulative incidence of AIDS and total mortality according to sexual preference and HIV serostatus on entry into the SFMSH. Of the 215 heterosexual men, none was HIV seropositive on entry and one seroconverted during the follow-up period. Among these men, no cases of AIDS and one death (0.5%) were recorded. Among the 812 homosexual/bisexual study subjects, 367 were HIV seronegative on entry and have remained so for 96 months. No cases of AIDS and seven deaths (2%) have been recorded among these men. Forty-five men seroconverted during the 96-month follow-up period. Among the seroconverters, eleven cases of AIDS (24%) and five deaths (11%) have been recorded. Among the 406 study subjects who were HIV seropositive on entry and throughout the follow-up period, 204 (51%) have developed AIDS and 169 (42%) have died.

Because Duesberg has specifically implicated amyl nitrite in the aetiology of Kaposi's sarcoma, we performed additional analyses to assess this relationship. As can be seen in Table 2, among the 144 homosexual/bisexual men who reported heavy use of amyl nitrite inhalants during the 24 months before study entry, 54 developed AIDS during the ensuing 96 months (cumulative incidence, 37.5%). Among the 668 homosexual/bisexual men reporting none or less than weekly use of amyl nitrite inhalants during the same time period, 161 developed AIDS in 96 months (cumulative incidence, 24%) for a relative risk of 1.56. This crude association is apparently the basis for Duesberg's hypothesis. Further analysis of the data reveals a similar association between...
drug use and HIV positivity, and when controlled for HIV serostatus, there is no overall effect of drug use on AIDS.

A similar effect, a marginal association that drops after controlling for HIV serostatus, is seen in cases which end in Kaposi’s sarcoma. Thus, when proper methods are used to assess the role of confounding variables, there is no evidence of a drug effect. In addition, we have performed a logistic analysis of the longitudinal drug-use data which shows no positive association between long-term or continued drug use and the development of AIDS.

AIDS definition

The clinical case definition for AIDS has been criticized as having subjective features and low specificity. We have attempted to circumvent this problem by assessing the effects of drug use on a more objective and, indeed, the primary pathogonomic feature of AIDS, CD4+ T-lymphocyte depletion. The relationship between HIV serostatus, drug use during the 24 months before entry into the study, and CD4 cell levels is shown in the figure. A consistent loss of CD4+ T-lymphocytes is limited to HIV-seropositive subjects, among whom there is no discernible difference between the counts according to composite drug-use scores. The apparent flattening of the trajectories over time is due to the death of rapidly progressing HIV-seropositive subjects. Among HIV seronegatives, the CD4+ T-lymphocyte count trajectories are essentially flat with slight but consistent differences between the drug-use groups. By contrast with Duesberg’s hypothesis, moderate or heavy drug users have consistently higher counts than non-users, for unknown reasons. Taken together, these data do not support Duesberg’s hypothesis that drug use causes AIDS.

Duesberg has argued repeatedly that studies of the associations of HIV infection, drug use and AIDS have been “uncontrolled”. However, the population-based SFMHS provides a rigorously controlled epidemiological model for the evaluation of aetiological hypotheses. Duesberg has also argued that the case definition of AIDS is “circular” and that HIV-seronegative AIDS cases are excluded by definition. In the

SFMHS, AIDS cases were diagnosed by the clinical criteria defined by the Centers for Disease Control (CDC), which are irrespective of HIV infection status. Incidentally, the CDC’s criteria for defining AIDS do not require HIV positivity, provided that the CD4 count is less than 400 and the clinically defining conditions are not explainable by established aetiologies. Furthermore, in the data presented here, mortality as well as AIDS incidence support the HIV aetiological hypothesis.

Conclusions

The main purpose of the cohort studies conducted in San Francisco and elsewhere has been to look for associations of environmental or behavioural factors with the development of AIDS. Had any factor other than HIV infection been found, it would have been reported immediately. The fact that not every failure to find such associations has been reported does not undermine the well-established causal relationship between HIV and AIDS, particularly as it relates to prevention strategies. The energies of Duesberg and his followers could better be applied to unravelling the enigmatic mechanism of the HIV pathogenesis of AIDS. To this end, we have proposed an alternative model based on HIV signalling at CD4 cells. This model and others are now being evaluated, and we cordially invite Duesberg to participate in this endeavour.

Michael S. Ascher* and Haynes W. Sheppard are in the Viral and Rickettsial Disease Laboratory, California Department of Health Services, 2151 Berkeley Way, Berkeley, California 94704, USA. Warren Winkelstein Jr and Eric Vittinghoff are in the Department of Biomedical and Environmental Health Sciences, School of Public Health, University of California, Berkeley, California 94720, USA.

*Author for correspondence.

Debunking Doubts That H.I.V. Causes AIDS

By GINA KOLATA

Researchers have found evidence that contradicts what has become a tenet of a persistent but widely disparaged theory of the cause of AIDS: that recreational drug use and not the human immunodeficiency virus causes the deadly collapse of the immune system in people with AIDS.

In a commentary published today in Nature, the British science journal, researchers reported data showing that there is no relationship between recreational drug use, excluding intravenous drugs, and the development of AIDS.

The researchers said they had taken a new look at data collected in an eightyear study that began in 1984 in order to demolish the hypothesis that H.I.V. does not cause AIDS. The research team was led by Dr. Michael S. Ascher, an immunologist at the California Department of Health Services in Berkeley, and Dr. Warren Winkelstein Jr., an epidemiologist at the University of California at Berkeley.

Challenge Issued

Dr. Ascher and his colleagues wrote their paper in response to a challenge by Tom Bethell, a media fellow at the Hoover Institution at Stanford University, to compare people who took drugs with those who did not and see whether those who took drugs had a higher incidence of AIDS.

"This study has never been done," Mr. Bethell wrote in an article in the San Francisco Chronicle on Oct. 3. "Why not? Billions of dollars have been spent on AIDS research and little headway has been made. Perhaps, then, the wrong theory has been pursued."

Mr. Bethell discussed the theory proposed six years ago by Dr. Peter H. Duesberg, a molecular biologist at the University of California at Berkeley. Dr. Duesberg holds that AIDS is caused by something other than H.I.V. and that H.I.V. is instead an innocent bystander. He contends that AIDS is not an infectious disease and that the AIDS drug AZT hastens, rather than slows, the immune system's demise.

But, Dr. Ascher replied, such studies have been done by scientists in California and elsewhere who were suspicious of recreational drugs from the very beginning of the AIDS epidemic.

Already Considered

"I felt a little embarrassed" to be going back to such familiar material, Dr. Ascher said. "This was one of the first things the scientific community looked at."

But, Dr. Ascher added, "Tom Bethell threw down the gauntlet," and he and his colleagues accepted the challenge and wrote their commentary.

Dr. Jerome Groopman, an AIDS researcher at New England Deaconess Hospital, said Dr. Ascher and his colleagues should be commended for their article. "Science keeps an open mind at all times, but there comes a time when you have to declare that the earth is not flat," he said. "It is incumbent on those who rejected H.I.V. to come to terms with this."

Dr. Duesberg, who refined his argument in January in an article in the Journal Pharmacology and Therapeutics, said that the new data did not sway him in the least and that he had written a refutation of the Nature paper.

Dr. Duesberg conceded in a telephone interview yesterday that most academic scientists reject his hypothesis, but he said he nevertheless remains convinced that the most likely cause of AIDS is recreational drugs: "Galileo was alone when he started," he said. "So was Max Planck."

Group Questions Standard

He also noted that 150 scientists in the United States and Europe had joined a group, headed by Dr. Charles Thomas, a retired molecular biologist from Harvard Medical School, that questions the standard view that H.I.V. alone causes AIDS.

In their paper, Dr. Ascher and his colleagues described a direct test of the hypothesis that arose from their analysis of the San Francisco Men's Study, a group of 1034 randomly selected single men who lived in San Francisco and were 25 to 54 years old in 1984, when the study began. Every six months for eight years, the researchers examined the men, testing to determine whether they were infected with H.I.V. or had developed AIDS.

Note how Gina Kolata in the New York Times follows the Nature press release in reporting incorrectly "a group of 1034 randomly selected single men who lived in San Francisco and were 25 to 54 years old in 1984, when the study began."
The target of the attackers is Dr. Peter Duesberg, a virus researcher and molecular biologist at the University of California at Berkeley, who for years has waged a lonely and often bitter battle challenging the established doctrine that HIV is the culprit in the epidemic.

Disputing Duesberg's newest claims about drug use, the researchers have analyzed the health records and drug habits of more than 1,000 men and are publishing their findings today in the British scientific journal Nature.

Publication of their article, labeled a "commentary" by Nature's editors, marks a fresh round in a

The scientist's unpopular belief is that illicit drug use causes AIDS

5-year-old controversy pitting Duesberg and his few scientific supporters against the overwhelming majority of AIDS researchers and physicians who monitor progress in the hunt for anti-viral drugs and vaccines.

Duesberg's most recent version of his theory contends that illicit drugs like cocaine, amphetamines and the nitrite inhalants known as "poppers" are the "necessary and sufficient" cause of AIDS in the United States and Europe.

Even powerful drugs like AZT, ddI and ddC, which are widely used to treat AIDS or to delay disease symptoms in HIV-infected patients, can damage immune systems so badly that AIDS is inevitable, Duesberg maintains.
African Version

In Africa, where AIDS ravages entire countries, the sole causes of the epidemic are protein malnutrition, poor sanitation and parasite infections — any of which can ultimately destroy the immune systems of their victims, he says.

Duesberg has argued in several recently published scientific journals that the epidemics in Africa and the industrialized nations are entirely different. But nowhere in the world, he insists, does HIV play any role at all in causing AIDS. In his view, the virus is merely an accidental invader, taking advantage of people whose immune systems are already severely damaged.

The new blast at Duesberg comes from AIDS researchers in the virus laboratory of the State Department of Health Services in Berkeley and the University of California School of Public Health.

Headed by Dr. Michael Ascher and Dr. Haynes Sheppard of the state’s viral disease laboratory, the researchers report that their study of 1,027 gay men in San Francisco establishes that drug use alone cannot trigger the onset of AIDS. Only the men in their study who were infected by HIV — whether they used drugs or not — were killed by the disease.

In 1984, Ascher and his colleagues say, they obtained reliable histories of previous drug use from 812 San Francisco men who were either homosexual or bisexual and from 215 heterosexual men. All had volunteered to join a long-range health study of men randomly selected from the city’s neighborhoods where AIDS was already striking most heavily.

Ascher’s team has now followed the men for up to eight years, questioning them every six months about their patterns of drug use, and determining the state of their health and their immune systems.

The men were divided into three groups according to their use of “recreational” drugs: nonusers, infrequent users and heavy users. The most commonly used drugs were marijuana, nitrite inhalants, cocaine and amphetamines.

HIV’s Role

A total of 215 cases of AIDS have struck the 445 homosexual and bisexual men who were infected with HIV, and 181 of them have died. None of the gay or bisexual men who remained uninfected with HIV has developed AIDS, but even the HIV-infected men who said they used no drugs at all have developed the disease. The drug-use patterns of the gay and heterosexual men were virtually the same, the researchers said.

To Ascher and his colleagues, the development of AIDS and the damaged immune systems among the HIV-infected men — regardless of whether they used drugs — offers striking confirmation that HIV must indeed be the virus that causes AIDS and that drugs alone cannot be responsible for the disease.

In their Nature article, for example, Ascher and his colleagues dismiss Duesberg’s theory as disproved by their data. While they concede that even today scientists cannot explain just how HIV causes AIDS, they throw a challenge to the small circle of anti-HIV theorists:

“The energies of Duesberg and his followers could better be applied to unraveling the enigmatic mechanism” of how HIV operates, they say. And they “cordially invite” Duesberg to join them in unraveling that mystery.

But in an interview yesterday, Duesberg responded by accusing Ascher and his team of sloppy and deliberately misleading use of statistics to back up their claims.

Their data contain no “scientific verification” that the long-term drug-use patterns claimed by the men they studied were valid, he insisted. And the report’s conclusions that drug use does not cause AIDS “are worthless for a scientific appraisal” of Duesberg’s contrary theory, he insisted.

Besides Ascher and Sheppard, the team that wrote the study for Nature included Dr. Warren Winkelstein, the UC professor of epidemiology who launched the pathfinding San Francisco Men’s Health Study, and Eric Vittinghoff, a graduate research statistician for the project.
San Francisco Chronicle  
Letters to the Editor  
San Francisco, CA  
Fax: 415/ 512-8196  

March 11, 1993

Dear Editor:

I am dismayed by your treatment of the AIDS-drug hypothesis (4/11/93). As a piece of reporting it is a masterpiece of scientific ignorance. First, in the article in question all conclusions, dutifully reported by Mr. Perlman, were drawn from hearsay. It is hearsay because the article was not a scientific paper that survived any rigorous review process; it was instead part of what is called "scientific correspondence" that gets by with often cursory review by journal editors. Second, as a result of lack of thorough review there is no detail given on methods used to collect data. Third, without details on methods we can not evaluate the data itself, never mind conclusions drawn from that data. Thus, all standards of real science are violated. What remains is only "scientific correspondence", at best a mechanism for developing opinion or debate. In the mainstream of science or in a court of law it would be thrown out as hearsay evidence. Instead of asking why the authors of this very "important" study did not take the trouble to submit their work through normal channels, but instead chose the less rigorous process, the Chronicle choose to treat the work as valid, proven, information. The Chronicle owes all its readers, and especially all HIV+ people a profound apology.

Sincerely yours,

Richard C. Strohman  
Professor Emeritus  
(510) 642-4941
An open letter on the HIV-AIDS hypothesis

Scientific community has shut out dissenting AIDS theories

Dear Professor Warren Winkelstein:

The HIV-AIDS hypothesis is a crucial problem that must be either discarded or proven. We all agree to that. As stated in your recent Nature magazine article (Mar. 11), scientists still do not know how HIV works, and until that time we must all strive to do what we can to find a solution.

Your own work has striven to develop a strong correlation between HIV and AIDS, but you agree that correlation does not establish cause. More than 90% of a multibillion-dollar budget is dedicated to finding a molecular link between the virus and immunosuppression, with still no definite proof after more than 10 years. Meanwhile, there are some scientists, myself included, calling for approaches to AIDS other than the near-monolithic HIV theory. Perhaps other factors are involved; goodness knows, there certainly is convincing evidence for co-factors, and for Peter Duesberg’s theory that AIDS is caused by drugs alone. The drugs he mentions most often are recreational drugs taken by some, but not all, gay men, and intravenous drug addicts. In addition, AZT, which is prescribed to deal with bacterial and viral infections, is known to be cytotoxic to human cells, and in itself could be the culprit.

My question, really for all of us, is the following. Why is it necessary to insistently call on dissenters from the mainstream theory to abandon their dissent, and to join ranks with those who believe that HIV, and only HIV, causes AIDS? You yourself issue such a call in your recent Nature article (as quoted now in newspapers all over the country, ex-SF Chronicle of Mar. 11). This is not how science is supposed to operate. It is supposed to be pluralistic; it is historically best when dissent is open and wide; results come more quickly when support is given not only to those who follow the major paradigm, but also to those who have reasoned but unpopular approaches.

Our science is already terribly afflicted with a molecular tunnel vision that obscures the whole organism. Do we not need our Peter Duesbergs who, major scientists in their own right, serve us all by their steadfast pursuit of truth, albeit along unfamiliar or controversial paths? Should we not join with him, and others like him, in diversifying our scientific portfolio, in seeking new approaches? Does not his thesis also have scientific merit? Your Nature article, for example, does not address AZT. Also, unfortunately, since your article was published as a “Commentary” rather than as a full report it does not contain sufficient information on methods for us other scientists to clearly understand the correctness of your conclusions.

Warren, while AIDS remains the devastating mystery that it is, can we not all join forces, not for a cooperative single approach, but for a cooperative pluralistic approach, especially when those approaches are made by intelligent scientists, with or without excellent track records and when such approaches meet sound scientific criteria? Can we have a meeting in which we discuss how best to approach funding agencies so that a healthy, robust attack on AIDS is mounted, one which includes your approach, the HIV mechanism, the co-factor hypothesis, and the hypothesis that HIV itself may be only a marker rather than a cause?

Sincerely yours,

Richard C. Strohman
Professor Emeritus,
Distinguished Wellness Lecturer
for 1992 at UC Berkeley

DAILY CALIFORNIAN 1 April 1993

Note: In his open letter, Strohman included his address: Dept of Molecular & Cell Biology U of C, Berkeley Calif 94720; 510-642-4941
Dissenting scientists: earth is not flat

Dear Professor Richard Strohm-

I hasten to respond to your letter on the April 1 opinion page ("Scientific community has shut out dissenting AIDS theories"), regarding the commentary article in Nature authored by my colleagues and me. You accuse us of calling on, in your words, "...dissenters from the mainstream theory to abandon their dissent and to join ranks with those who believe that HIV, and only HIV, causes AIDS. . . ." You cite Peter Duesberg's theory, "that AIDS is caused by drugs alone" as an example of such dissent. You point out correctly, in my view, that when understanding is incomplete, a "pluralistic" approach is most likely to yield answers to nature's secrets. However, advocating a pluralistic approach does not automatically validate every alternative theory. That can only be accomplished by rigorous research.

Our commentary (Nature, Mar.11) reviewed studies published by others which did not support Duesberg's hypothesis and added data from our own nine-year follow-up of a cohort of homosexual men from San Francisco. Our data showed that among 367 men who remained uninfected by HIV for nine years, none developed AIDS while among 400 men already infected on entering the study in 1984, 204 developed AIDS of whom 169 died. After controlling for HIV serostatus, we found no difference in the occurrence of AIDS between heavy users of recreational drugs, light users and non-users. Thus, we were not able to support Duesberg's hypothesis.

Your assertions regarding alternative approaches and dissenting opinions is best answered by quoting what we actually wrote in the Nature commentary: "The main purpose of the cohort studies conducted in San Francisco and elsewhere has been to look for associations of environmental or behavioral factors with the development of AIDS. Had any factor other than HIV infections been found, it would have been reported immediately.... The energies of Duesberg and his followers could better be applied to unravelling the enigmatic mechanism of the HIV pathogenesis of AIDS. To this end, we have proposed an alternative model based on HIV signalling at CD4 cells. This model and others are now being evaluated, and we cordially invite Duesberg to participate in this endeavor."

In a New York Times article reporting the content of our Nature commentary, Dr. Jerome Groopman, a distinguished medical scientist, is quoted as follows: "Science keeps an open mind at all times, but there comes a time when you have to declare that the earth is not flat. It is incumbent on those who rejected HIV to come to terms with this."

Sincerely yours,
Warren Winkelstein, Jr.
Professor of epidemiology (Emeritus)
John Maddox, Editor  
*Nature*  
4 Little Essex Street  
London WC2R 3LF, UK

Dear Dr. Maddox:

We submit the enclosed paper, entitled "HIV as a surrogate marker for drug use: A re-analysis of the San Francisco Men's Health Study," for publication in *Nature*. One original and four copies are enclosed.

This paper has been prepared in response to the Commentary by Ascher et al., published last March in *Nature* ("Does drug use cause AIDS?", 362:103-104), which purported to prove an epidemiological association between HIV infection and AIDS, versus no association between long-term drug use and AIDS. We have examined the database of the San Francisco Men's Health Study (SFMHS) for ourselves and, using a more accurate analysis, have invalidated the conclusions reached by Ascher et al.

In order for us to do a proper analysis of the SFMHS, it was necessary for us to write a paper that is longer than the original Ascher et al. Commentary, and which includes more tables and figures. But the importance of the issues involved is such that we decided to make a full and clear presentation of the facts.

Among the most egregious distortions of the Ascher et al. paper, we have uncovered the following:

1) Ascher et al. reported no AIDS cases among the HIV-seronegative men in the cohort. We have found 45 HIV-free AIDS cases, and have circumstantial evidence indicating many more.

2) Ascher et al. drew a curve of T cell loss over time representing a group of seropositive men who used no drugs. We found that 17 of these 20 men did, in fact, use recreational drugs, or AZT, or both.

3) Ascher et al. presented a figure with six remarkably straight curves representing average T cell counts over time. None of these curves were given error bars, and even their paper acknowledged that the data had been altered with some undescribed "adjustment." We present some of the original data, without alteration or distortion, showing T cell curves fluctuating over time, and with extreme variability between individuals. Had the unadulterated data been presented by Ascher et al., no reasonable statistician would have drawn any serious conclusions from the figure.
4) Ascher et al. claimed that no significant difference in drug use existed between homosexual and heterosexual men in the cohort. We, on the other hand, have found a tremendous and statistically significant difference in drug use.

Warren Winkelstein examined the paper for over a week, and was unable to contradict any of our conclusions. Indeed, he further confirmed our finding of HIV-free AIDS cases with a previously published paper of his (now included in our paper).

We believe that, despite the gross inaccuracies and misrepresentations of the Ascher et al. Commentary, a retraction of their paper should not be necessary if this new data is published.

We are submitting this paper to take you up on your offer made last May that "When he [Duesberg] offers a text for publication that can be authenticated, it will if possible be published" ("Has Duesberg a right of reply?", Nature 363:109). Naturally, we presume this offer, made no doubt in the spirit of scientific inquiry, still holds.

Thank you for your attention to this matter. We look forward to hearing from you shortly.

Sincerely,

Bryan J. Ellison

Note by Serge Lang: The paper was turned down by Nature. It appeared in Genetica, Volume 95 no. 1-3 (1995) and was reprinted in a collection published by Kluwer, 1996, in the form that follows. S.L. March 1996
HIV as a surrogate marker for drug use: a re-analysis of the San Francisco Men's Health Study

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Abstract

Our analysis of drug use and morbidity data from a cohort of 1034 men yields the following results: 1) HIV infection is a strong indicator of drug use – HIV-positive respondents reported an average lifetime dose of recrecational drugs (excluding marijuana) 2.3 times higher than HIV-negative respondents. 2) Homosexuality is a strong indicator of drug use – homosexual respondents reported an average lifetime dose 2.0 times higher than heterosexual respondents. 3) The incidence of AIDS-defining diseases was not limited to respondents infected with HIV, but was almost completely limited (98%) to respondents who reported using drugs. We also address a previous report (Ascher et al., 1993) that was based on the same database and purported to show that HIV alone correlates with the development of AIDS. Specifically, we show that the relationship between HIV infection and CD4+ T Cell loss is weaker than reported by Ascher et al., and provides little evidence for a causative relationship. These results support the hypothesis that long-term, habitual drug use can cause the conditions known as AIDS (independent of the presence of HIV), and refute the hypothesis that HIV alone causes these conditions independent of drug use.

Introduction

A Nature Commentary by Ascher et al. purported to show that infection by the human immunodeficiency virus (HIV) alone correlates with the development of the acquired immune deficiency syndrome (AIDS) (Ascher et al., 1993). According to their analysis of the San Francisco Men’s Health Study (SFMHS), drug use had no effect on T cell loss over time, while all cases of AIDS and all T cell depletion occurred among HIV-positive men. Ascher et al. interpret this apparent correlation between HIV and AIDS as support for ‘the well-established causal relationship between HIV and AIDS’ (Ascher et al., 1993).

The power of the statistical tests Ascher et al. use is often insufficient to justify the conclusions they draw. This paper will discuss the deficiency of these tests. In some cases, however, the absence of a detailed description of the methods they used made it impossible for us to verify their results.

Ascher et al. also selectively cited existing literature on the debate over AIDS etiology, ignoring a wealth of evidence arguing against the HIV-AIDS hypothesis and for a drug-AIDS hypothesis. The molecular and epidemiological inconsistencies of the HIV hypothesis include the inability of the virus to induce AIDS in chimpanzees and the existence of HIV-free AIDS cases (Duesberg, 1992; Duesberg, 1993a). There is ample evidence that alkyl nitrates, recreational drugs primarily used by male homosexuals at risk for AIDS, and related compounds produce irreversible immune suppression and pneumonia in mice after long-term exposure, and that the nitrates follow a dose-dependent relationship with the incidence of AIDS in humans (Holt et al., 1979; Haverkos, 1988; Newell, Spitz & Wilson, 1988; Ortiz & Rivera, 1988). Cocaine and heroin, moreover, have long been associated with severe immune deficiencies in humans, independently of HIV infection (Duesberg, 1992).

In addition to reviewing the data cited by Ascher et al., we were also able to perform our own analysis of the primary data. This paper presents some of our findings. Despite the extremely sparse reporting of AIDS indicator diseases in the database, we found 45 cases of these diseases among HIV negative respondents. Also, we quantified a higher level of drug use among HIV
positive men than among their HIV negative counterparts. These results suggest a direct link between drug use and AIDS independent of HIV infection.

The SFMH Study

The SFMHS is a population-based longitudinal survey of 1034 men, recruited in 1984 from the San Francisco precincts most heavily populated with homosexual men. (For reasons unknown to us, Ascher et al. used only 1027 of these men in their analysis). Of these subjects, 816 identified themselves as homosexual or bisexual and 215 as heterosexual. At the end of the study’s seventh year, 578 men remained HIV negative, 46 had seroconverted, 400 had entered the study already seropositive, and 10 remained undetermined; 215 men had been officially recorded with diagnoses of AIDS. Data are collected by semi-annual interviews, which tabulate such self-reported data as medical conditions, use of pharmaceutical or recreational drugs, and a number of other responses that are difficult to verify.

The SFMH Study, however, was not designed to test for the cause of AIDS. HIV was presumed from the beginning to be the etiological agent, so that no attempt was made to account for the inherent problems of self-reported answers, nor for the preceding years of unrecorded drug use (especially among HIV-positives). Inadequate records were also kept of specific AIDS diseases and of drug use patterns occurring during the course of the study.

We shall document these and other defects of the SFMHS study as well as of the Commentary by Ascher et al. based on that study. Our analysis will show that Ascher et al.‘s claim that ‘the population-based SFMHS provides a rigorously controlled epidemiological model for the evaluation of aetiological hypotheses’ is unjustified (Ascher et al., 1993).

The Ascher et al. Commentary

The Commentary reported a perfect association between HIV and AIDS, as well as between HIV and a progressive decline in CD4+ T cells. It also found no relationship between drug use and T cell loss. But the analysis suffers from several logical flaws:

1) The HIV-based clinical definition of AIDS is circular, because it fails to report AIDS-defining conditions in the absence of HIV infection. Conventional diseases such as pneumonia or tuberculosis are only reclassified as AIDS in the presence of antibodies against HIV, or on the presumption of infection (Institute of Medicine and National Academy of Sciences, 1986; Centers for Disease Control, 1987; Centers for Disease Control and Prevention, 1992). Ascher et al. imply they have taken all such diseases into account. The Commentary notes ‘Duesberg has also argued that the case definition of AIDS is ‘circular’ and that HIV-seronegative AIDS cases are excluded by definition. In the SFMHS, AIDS cases were diagnosed by the clinical criteria defined by the Centers for Disease Control (CDC), which are irrespective of HIV infection status.’ (Ascher et al., 1993). However, our review of the SFMHS database indicates that for the first five years of the study, respondents were only asked whether they had been diagnosed with AIDS or Kaposi’s Sarcoma, not whether they had been diagnosed with any of the AIDS indicator diseases. In the latter part of the study, the surveys included questions about some AIDS indicator diseases, but in total more than two-thirds of the data about these diseases is missing.

2) HIV infection and drug use have been shown to correlate with one another. Risk behaviors for virus transmission, including extreme sexual activity and sharing of injection equipment, generally involve use of such recreational drugs as heroin, cocaine, alkyl nitrites, and others (Jaffe et al., 1983; Newell, Spitz & Wilson, 1988; Schechter et al., 1993). For this reason any epidemiological study of HIV infection must carefully control for drug use. The authors compare drug use among the homosexual or bisexual respondents and the heterosexual respondents, using sexual preference

<table>
<thead>
<tr>
<th>AIDS diagnostic disease</th>
<th>Number (%)</th>
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<tr>
<td>Salmonella</td>
<td>18 (40)</td>
</tr>
<tr>
<td>Non-pulmonary tuberculosis</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Thrush/oral candidiasis</td>
<td>6 (13)</td>
</tr>
<tr>
<td>Immune thrombocytopenic purpura (ITP)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>9 (20)</td>
</tr>
<tr>
<td>&lt;200 CD4+ T cells</td>
<td>14 (31)</td>
</tr>
<tr>
<td>total</td>
<td>45 (100)</td>
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<tr>
<td>Single condition</td>
<td>40 (89)</td>
</tr>
<tr>
<td>Double condition</td>
<td>5 (11)</td>
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</tbody>
</table>
as a proxy for serostatus. They thereby imply that there is no difference in drug use between HIV positive and HIV negative respondents. According to Ascher et al., 'Except for amyl nitrite . . . the percentage of subjects reporting heavy use of each drug was similar in both sexual preference groups.' (Ascher et al., 1993). While heterosexuality is an effective proxy for HIV-negative serostatus (all but one of the heterosexual respondents was HIV-negative), homosexuality is not a reasonable proxy for HIV-positive serostatus (almost half of the 816 homosexual respondents were HIV-negative). Our analysis (below) shows that there is a significant correlation between drug use and serostatus.

3) The hypothesis of drug use as the cause of AIDS is analogous to the cigarette-smoking hypothesis of lung cancer and the alcohol hypothesis of liver cirrhosis (Lauritsen & Wilson, 1986; Duesberg, 1992). That is, disease symptoms depend primarily on the lifetime dose of the relevant drug, a function of both quantity and number of years of consumption. Thus a proper longitudinal study would quantify each respondent’s total lifetime drug use. Ascher et al. imply that they have done this: ‘We examined the cohort at 6-monthly [sic] intervals for 96 months, and obtained drug-use data and determined HIV serostatus at each examination’ (Ascher et al., 1993). But in the Commentary, all study subjects were stratified according to a single drug use report, taken during the first wave of the study. Furthermore, although the respondents were asked about use of nine to ten different psychoactive drugs (see below), only four of those drugs were incorporated into the paper’s analysis. Moreover, no mention was made of AZT, the toxic and immune-suppressive DNA nucleoside analogue prescribed as AIDS therapy.

Our analysis of the data and our results

Statistical tests are based on Cochran and Cox t-tests (with unequal variances), or on univariate linear regression.

AIDS without HIV

Clinically, AIDS is defined entirely in terms of about 30 conventional diseases presumed to have been comparatively rare in 20- to 55-year-old men before 1980. If a patient with one or more of these indicator diseases tests positive for HIV antibodies, he is usually diagnosed with AIDS. The AIDS case definition has been expanded several times by the CDC, each time adding new diseases to the diagnostic list. The 1987 CDC definition incorporated some two dozen diseases, and was the universal standard for diagnosis until January 1, 1993, when five new conditions were added (Centers for Disease Control, 1987; Centers for Disease Control and Prevention, 1992). As of 1992, 39% of the AIDS-defining conditions reported in the United States were not diseases of immunodeficiency, including Kaposi’s sarcoma, several lymphomas, dementia, and wasting disease (Centers for Disease Control, 1993).

Despite the absence of most of the relevant disease data, we found 45 HIV-negative men with AIDS-defining conditions (according to the CDC), as listed in Table 1. Of those, 34 qualified under the older (1987) definition; 11 qualified only under the 1993 definition, having either <200 CD4+ T cells or thrombocytopenia. Fifteen of the 45 were reported in the first round of interviews in 1984. Many HIV-negative men were followed up only inconsistently thereafter or were lost altogether, and were therefore inadequately monitored for AIDS diseases. Given the missing data on many of the study subjects and on other potential AIDS-defining conditions, this must be taken as a minimum estimate.

At least eight of these cases were published a few years earlier by Winkelstein and other researchers with the SFMHS (Lang et al., 1987). The earlier study also included as many as 133 other cases of AIDS- or early-AIDS-related symptoms, such as lymphadenopathies, persistent rashes, wasting conditions, or histories of worsening herpes infections. This earlier paper, and our finding of HIV-free AIDS indicator diseases, undermine the claim of Ascher et al. that ‘No cases of AIDS . . . have been recorded among these [seronegative] men’ (Ascher et al., 1993).

The relatively high incidence of opportunistic diseases listed in Table 1, found in men recruited between the ages of 25 and 54, is particularly revealing, for such conditions would normally not be expected to occur among the healthiest age group in the population. The presence of these diseases indicates some non-HIV factor at work. It is important to emphasize that had any of these 45 men been positive for antibodies against HIV, they would likely have been recorded as AIDS cases.

An analysis of the ‘no drug use’ subgroup

A second question arose over the figure displayed in the Commentary. One of the six longitudinal T cell
curves purported to describe HIV-positive men reporting ‘no drug use’. The authors’ criteria for this classification were based on self-reported use of four drugs—marijuana, cocaine, nitrites, and amphetamines—during the two years prior to the beginning of the study. We examined the database to find the subjects who met these criteria, and inspected these men’s recorded answers to check whether they remained a truly drug-free control group, looking at all other drugs and at AZT.

That ‘no drug use’ curve was apparently based on twenty seropositive men in the database who reported no use of the four drugs upon entry. Of these men, one reported using a different drug (downers) immediately prior to entry, five others admitted using various drugs (marijuana, nitrites, cocaine, and hallucinogens) at later times during the study; thirteen reported taking AZT. After accounting for overlaps, this left only three of the original twenty who claimed to be completely drug-free, at least during the study. One of these men showed a sharp decline in CD4+ T cell counts during the first two years of the study, was diagnosed with AIDS, developed a Pneumocystis carinii pneumonia, and died months later. The remaining two individuals appear not to have declining T cell counts, and neither was diagnosed with AIDS or died.

Even if the ‘no drug use’ group were well-defined, it would still be inappropriate to present a simple average of T-cell counts, especially, as in the Commentary, without providing error bars to indicate the variation within the group. First, an individual’s T-cell count varies widely over time, making time-series data of this kind dubious. Secondly, not all subjects participated in all waves; thus the ‘group’ represented at each wave is made up of different respondents. Finally, the use of unnormalized T-cell counts weights individuals with naturally high T-cell count more than individuals with naturally lower counts. The unreliability of T-cell counts as a measure of the health of the immune system is well-known; averaging this data over ill-defined and varying groups does not help—it only obscures whatever conclusions might be drawn from individual trends. Figure 1 shows the T-cell counts for each of the 20 ‘drug-free’ subjects over time. Any decline in the average T-cell count in this group is primarily due to a single individual with an unusually high and sharply-declining T-cell count. Generalizations about the health of the members of this group on the basis of this chart would be entirely unjustified.

**Drug use as a correlate of HIV infection and AIDS**

The SFMHS database suffers several shortcomings that limit its ability to test the drug- and HIV-hypotheses of AIDS. Because many of the drug-use questions were not answered by many of the subjects at various times throughout the study and all drug data were self-reported and unverified, it was difficult to construct a reliable measure of lifetime drug use. Nevertheless, we were able to convert data about frequency of drug use into an estimate of total doses, and to integrate this data over time into an estimate of total lifetime dose. For example, if an individual reporting annual use of a drug was assigned one dose unit, another individual reporting weekly use would be assigned 52 dose units.

Data were available from fourteen semi-annual surveys; we added a fifteenth data point representing the eighteen months preceding the beginning of the study. Drug use was condensed into two indices for each individual—the total combined drug use reported over the 8.5 years (marijuana, nitrites, cocaine, ‘crack’ cocaine, amphetamines, hallucinogens, uppers, downers, ethyl chloride, heroin, and ‘other’), and a similar index without marijuana. The category ‘crack cocaine’ was added in wave 10, at which point the category ‘other’ was no
among homosexual and heterosexual respondents. It confirms the role of HIV as a surrogate marker for drug use. HIV-positive men on average used 128% more drugs (ignoring marijuana) than did the HIV-negative subjects (the difference is statistically significant). Moreover, the drug use data from later in the study contradict the claim of Ascher et al., based on data from the first survey, that drug use is similar among homosexuals and heterosexuals. Table 3 shows that homosexuals used twice as many drugs as the heterosexuals (again ignoring marijuana), a statistically significant difference. Use of nitrite inhalants was particularly heavy among homosexuals, and AZT (naturally) was used almost exclusively by HIV positives respondents (Ascher et al., 1993).

Among HIV-positive subjects, we looked for a difference in total lifetime drug use between respondents who had been diagnosed with AIDS and those who had not. Contrary to our expectations, we did not find a statistically significant difference. The statistical power of the test was limited by some of the problems we have mentioned above, as well as the following:

a) Associations between drug use and AIDS are obscured by the likelihood that by the time an individual develops serious illness, he will begin to reduce his drug use. In order to demonstrate this effect, we compared the level of drug use reported by respondents who used AZT before and after they began AZT treatment. Average drug use before AZT treatment is 169% higher than after (26.4 ± 1.3 before versus 9.84 ± 1.3 after, p = 0.0001), suggesting that recreational drug use declines when patients become ill.

b) If the drug hypothesis is correct, respondents who developed AIDS during the course of the study, especially during the first few years, must have used drugs prior to the beginning of the study. Table 2 shows that men reporting AIDS or AIDS diseases were significantly older than other HIV-positive respondents. This discrepancy indicates that our estimates of lifetime drug dose are less accurate for the respondents who developed AIDS, because more of their lifetimes fall outside of the study.

c) Much of the drug use data is missing from the study altogether. Only 17% of the respondents answered all drug use questions during the first seven years; 22% of the respondents answered half or fewer of the questions. Furthermore, there is a strong negative correlation between reported level of drug use and number of responses to drug use questions (slope = −1.76 ± 0.32, p < 0.0001), meaning.

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![Graphs showing individual CD4+ cell counts and average adjusted CD4 counts over time.](image-url)
Table 3. Average doses of drugs (other than marijuana) per year, HIV+ vs. HIV- and homosexuals vs. heterosexuals.

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Mean ± SE</th>
<th></th>
<th>Number</th>
<th>Mean ± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+</td>
<td>400</td>
<td>29.7 ± 2.8</td>
<td>Homosexual</td>
<td>816</td>
<td>22.8 ± 1.5</td>
</tr>
<tr>
<td>HIV-</td>
<td>578</td>
<td>13.0 ± 1.2</td>
<td>Heterosexual</td>
<td>215</td>
<td>11.7 ± 2.6</td>
</tr>
<tr>
<td>Ratio</td>
<td>2.28</td>
<td></td>
<td></td>
<td>1.94</td>
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<tr>
<td>t-test</td>
<td>p = 0.0001</td>
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<td>p = 0.0002</td>
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that those subjects who responded the fewest times claimed the highest average drug use. This result indicates that men using the most drugs were least reliable in their responses.

Conclusions

The Ascher et al. Commentary was a faulty analysis of the SFMHS database:

a) Because of the authors’ dependence on the circular CDC definition of AIDS, they ignored the incidence of AIDS indicator diseases among the HIV-negative respondents. One consequence of their artificially perfect association between HIV and AIDS is that all other correlations between risk factors and AIDS are obscured.

b) By failing to quantify the enormous difference in drug use between HIV-positives and -negatives, they overlooked this potential explanation of the greater decline in CD4+ counts among HIV antibody-positive men.

c) By stratifying subjects according to a single drug use report, they included users of recreational drugs and AZT in their ‘no drug use’ group, and were able to ignore the problem of missing data later in study.

d) By failing to analyze the data with and without marijuana they allowed some drug associations to be obscured or minimized. Study subjects reported large amounts of marijuana use, which numerically tended to drown out reported use of more powerful drugs. The general willingness to admit marijuana use may reflect the lesser degree of social stigma attached to this particular drug. In any case, marijuana is less cytotoxic than other drugs examined in the study (such as nitrates [Haverkos & Dougherty 1988]), and is likely to be insignificant in the etiology of AIDS.

e) T cell counts provide a questionable marker of AIDS progression, especially in the SFMHSstudy. For one thing, several important AIDS-defining diseases do not result from immunodeficiency; Kaposi’s sarcoma, for example, has been described in homosexual men without measurable immune deficiencies (Murray et al., 1988; Spornraff et al., 1988; Friedman-Kien et al., 1990). Furthermore, the individual T cell counts recorded in the database often fluctuated greatly with time, and the average T cell curves (not reproduced here) showed major irregularities that Ascher et al. smoothed out with some undescribed adjustment (Fig. 1). Finally, many CD4+ counts were missing throughout the study, apparently for individuals who could not be contacted at various waves. The average T cell curves therefore reflect a constantly changing subset of men over time.

Furthermore, the SFMHS database may be inadequate to test drugs, HIV, or any other agent as a proposed cause of AIDS:

a) Of the 446 men who were seropositive after seven years, only 46 had seroconverted at known times during the study; the other 400 had been infected at unknown times preceding the study.

b) AIDS-defining diseases were poorly monitored. The SFMHSstudied relied at times on self-reported answers rather than medical records and only inquired about a changing and severely incomplete list of those diseases. Many of the men were followed up inconsistently after the first six months, which may explain the observation that 15 of the 45 cases of AIDS indicator diseases among HIV-negative respondents were recorded during the first wave.

c) No data about drug use exist for most of the years preceding the study, so that it is impossible to quantify lifetime drug consumption. Without more reliable data on lifetime drug use, no controlled anal-
ysis of drug-AIDS associations is possible in this cohort.

Nevertheless, some conclusions can be drawn from the SFMHS study. Perhaps most significant of these is our finding of 45 HIV-free cases of CDC-defined AIDS diseases. These can be added to the list of nearly 5000 cases of HIV-free AIDS-defining diseases and immunodeficiencies already uncovered in at least 75 references in the existing literature (compiled in a review paper) (Duesberg, 1993a). The seronegative AIDS conditions have been found primarily in the same risk groups as seropositive AIDS, including central Africans, male homosexuals, intravenous drug users, and hemophiliacs.

The association between drugs and AIDS-defining diseases in this database appears to be greater than the association between HIV and AIDS. AIDS conditions were reported among 260 men, 215 of whom were infected with HIV—a total of 82%. Of the same group, 93% admit using drugs other than marijuana, a total of 96% including marijuana, and a total of 98% including both marijuana and AZT.

The most compelling argument against the drug hypothesis of AIDS would be the existence of a group of drug-free, HIV-positive AIDS cases, but such could not be found in the SFMHS. On the other hand, the strongest argument against the virus-AIDS hypothesis would be a group of drug-using, HIV-negative AIDS cases, which may indeed exist in the SFMHS cohort (see above).

Further results might possibly still be extracted from the SFMHS database, including an analysis of the effects of AZT; of the 400 seropositive men in the study, 215 (54%) reported use of this DNA chain-terminating chemotherapy. But an epidemiological study of the causality of AIDS, controlling for both HIV and lifetime drug exposure, will require some other more adequate cohort. From the standpoint of biological plausibility, the toxicity of long-term drug use makes much more sense as a damaging agent to the immune system than do the 'enigmatic mechanisms' of the conventional retrovirus HIV (Ascher et al., 1993).

References


Acknowledgements

We are indebted to Warren Winkelstein, Jr., for providing access to the data from the SFMHS study, and to Eric Vittinghoff for technical assistance. We also thank Phillip Johnson, Richard Strohman, Malcolm Zaretsky, John Lauritsen, Charles A. Thomas, Steve Smale, and Harvey Bialy for critical reviews. Supported in part by the Council for Tobacco Research, USA, and private donations from Glenn Braswell (Los Angeles, Calif., USA), Dr. Richard Fischer (Annapolis, Va., USA), Dr. Fabio Franchi (Trieste, Italy) and Dr. Friedrich Luft (Berlin, Germany).


Poppers and propaganda

Censorship is blocking the debate vital to discovering the truth about Aids, argues Neville Hodgkinson

If Hansard, the official record of proceedings in Parliament, is anything to go by, homosexual men who use the inhalant drug amyl nitrite to boost their sex lives do not face any increased risks of developing Aids, apart from being more exposed to HIV through having more partners.

This reassurance has been offered in both Houses by health ministers, after The Sunday Times reported new evidence three weeks ago supporting long-standing claims that the drug, marketed as "poppers" and sold widely in gay clubs, discos, shops and through gay newspapers, is an important cause of Aids.

The ministers cited two statistical analyses, published in March last year in Nature and The Lancet, which purported to give poppers the all-clear. In the light of this evidence, they said, no further research was planned.

What they did not say was that both analyses were specifically aimed at silencing Professor Peter Duesberg, a distinguished American molecular biologist and virus expert who has enlivened the scientific establishment by arguing that HIV is harmless and that long-term drug abuse, especially of amyl nitrites, is a main cause of the catastrophic collapse of the immune system seen in Aids.

Nor did they mention — indeed, they could not have known — that in the case of Nature, repeated efforts by Duesberg and others to reply to the attacks on him have been frustrated by John Maddox, the journal's editor. Their latest effort, re-analysing data from an eight-year study of homosexual men in San Francisco, was rejected two weeks ago. It reaches conclusions that directly contradict those in the original article. Almost 100% of the men who died had used poppers, and there was a much higher level of general drug use (including heroin and cocaine) among HIV-positive men than their HIV-negative counterparts.

The Lancet study quoted by health ministers to justify their inaction on poppers was published as a "short report". It too dismissed Duesberg's claims, which it described as "a hindrance to public health initiatives".

But as Duesberg pointed out in a letter in The Lancet, 88% of the HIV-positive men in this survey among homosexual men in Vancouver had used nitrites, and up to 100% had used drugs of some sort.

Drug use was also widespread in men who did not get Aids, but that may simply mean other factors, such as genetic susceptibility, are involved, as with smoking and cancer.

Poppers are volatile, mutagenic, carcinogenic chemicals, scientifically established as potent inhibitors of the human immune system, and causally linked by several studies to Kaposi's sarcoma (KS) — a form of cancer characteristic of Aids. They came into widespread use in the gay community a few years before Aids appeared.

In a sane world, faced with the tragic and continuing reality of the Aids epidemic in the gay and drug-abusing communities — and the failure of predictions that the syndrome would soon spread to the sexually active population at large — health authorities would be doing everything possible to alert potential poppers users to the dangers, and funding intensive research efforts to try to establish how much of a contribution these and other drugs may be making to Aids. Instead, they are turning a blind eye to the unlicensed, uncontrolled manufacture and sale of these powerful chemicals.

A kind of collective insanity over HIV and Aids has gripped leaders of the scientific and medical professions. They have stopped behaving as scientists, and instead are working as propagandists, trying desperately to keep alive a failed theory.

A press release issued by Nature on the original "commentary" — it was not even presented as a scientific paper — was baldly headlined "Drug use does not cause Aids" and declared that the findings "seriously undermine" Duesberg's arguments. To refuse Duesberg and colleagues any right of reply is an act of censorship on one of the most important scientific debates of our time.

Another example of this "science by press release" came last week. The Lancet, attacking what it called "a few maverick researchers and journalists", said a study it had published about Aids in Africa "squelches the mischievous claim of some that HIV on that continent and the Aids that results from it are unimportant".

The study — whose key results were first announced last June, and discussed in this newspaper last October — found far higher death rates among HIV-positive villagers in rural Uganda than in those who tested HIV-negative. But it failed to address scientific concerns that the HIV test has never been validated as specifying the presence of a virus. It simply detects the presence of certain proteins, and there is much evidence that these may enter the bloodstream as a result of the immune system becoming stressed by a wide variety of insults apart from HIV, including drugs, malnutrition, repeated blood transfusions and chronic infections of the kind common in Africa.

In fact, the study strengthens these concerns, for during the entire two-year period that it lasted only five Aids cases were diagnosed. On that basis, a whole continent is said to be doomed. When will this madness end?