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LETTERS

"The Duesberg Phenomenon": Duesberg and Other Voices

In the Special News Report of 9 December (p. 1642) by Jon Cohen, *Science* struggles with what is called "The Duesberg phenomenon"—"a Berkeley virologist and his supporters continue to argue that HIV [human immunodeficiency virus] is not the cause of AIDS [acquired immunodeficiency syndrome]." Cohen tries to explain why "mainstream AIDS researchers" believe that HIV causes AIDS and why "HIV now fulfills the classic postulates . . . by Robert Koch." One week later (16 Dec., p. 1803), Cohen himself appears to become part of the phenomenon, when he writes, "Is a new virus the cause of KS [Kaposi's sarcoma]?" One should realize the heresy of this question. *KS has been and still is the signal disease of the AIDSyndrome.* The Centers for Disease Control includes it in its list of 29 diseases defining AIDS in the presence of HIV (*1*). No other AIDS-defining disease has increased more than KS over its long-established background. It was so rare before AIDS that many doctors told me that they had never seen it before in young men. This is the reason why KS has become a hallmark for AIDS. And now, according to Cohen, "solid headway will have been made . . ." if HIV is found *not* to be the cause of KS.

Since "mainstream AIDS researchers" now consider one non-HIV cause for AIDS, why not consider others? Accordingly, I submit two experimental tests to find such causes.

1) Cohen wonders (16 Dec., p. 1803) about the "mystery" that "KS is almost exclusively confined to male homosexuals," but he reports (9 Dec., p. 1648) that "use of nitrite inhalants known as 'poppers' . . . has been high among some subgroups in the homosexual population" and that "nitrite inhalants [are] popular among gay men" (16 Dec., p. 1803). Cohen also interviewed the authors of a study that had shown in 1993 that every one of 213 homosexual AIDS patients from San Francisco had used poppers in addition to other recreational drugs and AZT (*2*).

Since nitrites are some of the best known mutagens and carcinogens (*3*) and AIDS KS typically occurs on the skin and in the lungs, the primary site of nitrite inhalant exposure, I propose to solve the "mystery": Expose 100 mice, or cats, or monkeys to nitrite inhalants at doses comparable with human recreational use and for time periods approximating the so-called 10-year latent period between infection by HIV to the onset of AIDS—possibly a euphemism for the time of drug use necessary for AIDS to develop. (It takes 10 to 20 years of smoking for emphysema or lung cancer to develop.) I would predict this result: immunodeficiency, pneumonia, and pulmonary KS in animals.

2) According to Cohen, mainstream AIDS researchers argue that it is "impossible" to eliminate confounding factors from HIV in typical AIDS risk groups, as for example in hemophiliacs "because [they] do not keep track of each factor VIII treatment" (9 Dec., p. 1645). Therefore, we are asked to accept confounded epidemiological studies of HIV-positives—who are either male homosexuals using immunotoxic nitrites (*2*), or are intravenous drug users, or are hemophiliacs subject to immunosuppressive transfusions, or are being treated with AZT, or are subject to exotic lifestyles—as evidence that HIV causes AIDS.

In view of this, I propose a very possible epidemiological test of whether HIV or nonHIV factors cause AIDS: Compare the incidence of AIDS-defining diseases in 3650 homo- or heterosexual American men, who are not on transfusions and recreational drugs or AZT, but are HIV-positive, to the incidence in 3650 HIV-negative counterparts. These healthy subjects could be found by the U.S. Army, which tests more than 2.5 million per year, or among those contributing to the blood banks, which test more than 12 million a year. If the 3650-day latent period is correct, every 2 days one of the people that are HIV-positive would develop AIDS. I would predict this result: The percentage incidence in the HIV-positive group will be the same as in the HIV-negative group.

If the mainstream AIDS researchers are not already doing these experiments, I would be delighted to do them provided I can get funded.

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References

1. Centers for Disease Control and Prevention, *Morb. Mort. Weekly Rep.* **41(No. RR17)**, 1 (1992).
2. M. S. Ascher, H. W. Sheppard, W. Winkelstein, E. Vittinghoff, *Nature* **362**, 103 (1993); P. Duesberg, *Lancet* **341**, 1544 (1993); *ibid.*, p. 957; *AIDS-Fors-*

chung **12**, 627 (1993).
3. H. W. Haverkos and J. A. Dougherty, Eds., *Health Hazards of Nitrite Inhalants* (NIDA Research Monograph 83, U.S. Department of Health and Human Services, Washington, DC, 1988).

One point in Cohen's excellent article about the "Duesberg phenomenon" may have left a sour taste in the mouths of many young scientists. The article shows repeated examples of how the professor from Berkeley has built a case on what to some looks like possible misinterpretation, misuse of statistics, and highly selective cherry-picking of the data while contrary evidence is ignored. Yet there is still a surprising sentiment of support expressed by those who disagree with his conclusions but seem to argue that none of this should have any impact on his ability to be funded. We are talking about a scientist who repeatedly and publicly has accused many of those who disagree with him of fraud and "genocide" and who has undermined public health efforts to educate young people about the need for safe sex practices. Were similar behaviors and data management tactics exhibited by any younger or less well-known scientist, especially one swimming against the scientific consensus in a field rife with public health considerations, would this not affect his or her ability to be funded?

Neither government nor private sources owe any scientist one single dollar in funding. Funding is tight, highly competitive, and subject to peer review. Not all ideas or specific proposals are equally worthy of support, and even many sound ideas and well-constructed proposals go unfunded every month. Certainly one factor worth considering in a grant review is how the applicant handles data in drawing conclusions. There is no sound reason for exempting Duesberg from the kind of scrutiny that any other scientist must undergo to receive funding. The fact that his views are unconventional should not qualify for automatic sympathy points. His grant applications should be neither rejected nor favored because of his unconventional views, but he should be held accountable for his public statements as well as what they demonstrate about the ways in which he uses data to reach conclusions. To set any lower standard would be an insult to all of science.

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We, the undersigned gay men, do not accept the reasons for Peter Duesberg's alleged decline in popularity as related by Cohen.

Although there may have been some resistance to accepting responsibility for our own illness, I am sure if we had been presented with the facts only, the gay community would have responded in an appropriate manner. Instead, we were bombarded with a relentless propaganda campaign funded by the drug companies and the government to accept the HIV-AIDS-DEATH paradigm. Then, to the dismay of all of us who understood what was happening, AZT was approved and distributed as the only approved therapy. We believe this has resulted in an untold number of unnecessary deaths and, at this time, we have no idea how many would have actually been stricken with a fatal disease and how many have been poisoned by prescription.

The political reasons that Cohen gives, quoting Steven Epstein, have little to do with the events as they transpired. This is nothing more than a case of obfuscation designed to diffuse the growing discontent with the established paradigm in the gay community. This paradigm (that is, the HIV theory of AIDS) has resulted in billions of dollars in government money being spent on research, with not one life having been saved by this enormous effort.

Since the Concorde trials, there has been a growing disaffection with AZT ther-

apy, and Burroughs Wellcome reports a 20% drop in its sale of this poison. To many of us, this is good news. As more and more victims become aware of the harm that has been done, there are more and more lawsuits being mounted. Perhaps this whole issue will not be settled in a scientific debate, but in the courts.

In the meantime, we as gay men, are working together to find a solution to the AIDS problem ourselves, instead of appealing to the government and the AIDS research establishment, which have failed us so miserably. To argue about conservative and liberal at this juncture is a luxury we cannot afford, because it has become a matter of life and death. In fact, those terms are becoming increasingly meaningless.

Don Des Jarlais's fear that Duesberg is opportunistically playing on a general disaffection with the "established order" is nonsense. Most of us in the gay community know that those who have survived AIDS have done so by combining the best of orthodox and alternative medicine. Among responsible gay men there is no desire to overthrow the established order, in spite of ACT UP's often strident and often nonsensical outbursts. If the gay community had been dealt with in a straightforward manner from the beginning, we all could have been spared these outbursts.

Peter Duesberg has not been hurt by Cohen's article; he will be remembered in history for having been one of the most vocal opponents of AZT and, if for no other reason, a great humanitarian on that count alone.

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*Co-signers: **Michael Jones,** *Los Angeles;* **Dennis McKown,** *San Francisco;* **Dean McKown,** *San Francisco;* **Bryan Coyle,** long-term survivor, *Marin County;* **Roy Sather,** *Glen Ellen, CA;* **Jeremy F. Selvey and associates,** Project Aids, International, *Los Angeles;* **Ed Vargas,** *San Francisco;* **Jorge Martinez,** *Marin County;* **Jeff Allen,** *San Francisco;* **Greg Silvia,** *San Francisco;* **Phillip Gales,** *San Francisco.*

Cohen's series of articles reviewing the etiology of AIDS presents an interesting and thoughtful discussion of the issues. The weight of evidence clearly supports a causal link between HIV and AIDS. While I do not wish to dispute this link, I must disagree with the authors of the Concorde study, who are quoted as saying that Duesberg misrepresents their work by reporting a 25% increase in mortality in the group receiving early AZT intervention—they say that the increase is only 2.2%. However, both of these interpretations are valid. Duesberg is reporting the relative risk of death (10.9%/8.7%), while the Concorde group regards the risk difference (10.9% − 8.7%). Hence, it is inappropriate to say that any misrepresentation is occurring. Further, in reporting the impact on mortality in epidemiological studies, the relative risk (or odds ratio) is the most commonly used statistic. Thus, the characterization of the Concorde study by Duesberg is reasonable. While a nonsignificant relative risk of 1.25 would not generally be considered of great interest, given the context, further exploration of the impact of early administration of AZT might be warranted.

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Congratulations to *Science* and to Jon Cohen for the analysis of Peter Duesberg's views on the relationship between HIV and AIDS. Two additional counterarguments that might have been adduced are the demonstration that congenital HIV infection leading to pediatric AIDS, in which behavior of the patient is not an issue, and SIV, the simian analog of HIV, with which Koch's postulates have been fulfilled.

Be that as it may, Duesberg's rejoinders to all objections reminded me of the old story of the man who complained to a psychiatrist that he thought he was dead. The psychiatrist then asked whether dead men bleed, and on receiving a negative answer, took out a lancet and stuck the patient's finger. The man stared at his bleeding finger for a moment and then said, "Well, I guess dead men do bleed."

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Response: I find Peter Duesberg's letter confusing. The mainstream view of AIDS is that HIV debilitates the immune system, allowing pathogens that are usually quite feeble to cause severe disease and even death. I don't see how the finding that a newly discovered herpesvirus may cause KS challenges the mainstream view. The role of HIV is highlighted by the fact that KS, in the absence of immunosuppression, is almost always a benign disease, but in AIDS patients it is often fatal.

On a separate point, Nicholas Birkett correctly notes that the Concorde data, like any scientific data, can be interpreted in more than one way. But Birkett does not emphasize just how slight the differences were in the Concorde trial between the HIV-infected people who were treated early with AZT and those who were untreated or received deferred treatment. As shown in a table accompanying the story, the *P* values—a measure of statistical significance—were 0.13 for total deaths and 0.34 for HIV-related deaths. Those are far from the *P* value 0.05 that most researchers accept as the minimal cutoff point for statistical significance.

Therefore, while it is true to say—as Duesberg does—that there is a 25% difference between the total deaths in the two groups, how much significance can be imputed to that figure remains an open question. In my article, I reported the view of the chief French Concorde researcher, who argues that the Concorde data do not support Duesberg's contention that AZT causes AIDS. Instead, as the Concorde study team concluded, the data simply indicate that treatment with AZT does not benefit healthy, HIV-infected people.—***Jon Cohen***

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Chromosome Behavior in Mutants Defective in DNA Methylation: Correction

In our report describing the isolation of *Neurospora* mutants defective in DNA methylation, "Abnormal chromosome behavior in *Neurospora* mutants defective in DNA methylation" (10 Dec. 1993, p. 1737) (*1*), we reported evidence for aneuploidy in a mutant (*dim-2*) devoid of detectable methylation. We also reported that mutants with defects in the biosynthetic pathway leading to the methyl group donor *S*-adenosylmethionine can be manipulated to show reduced methylation, and we used one such mutant, *met-7*, to follow up the suggestion that reduction in methylation leads to the abnormal chromosome behavior. A large fraction of progeny from crosses between two *met-7* strains showed evidence of aneuploidy, supporting the notion that normal DNA methylation is required for proper chromosome behavior. Results of recent experiments in our laboratory indicate, however, that our source of the *met-7* mutation, FGSC strain 3915, contains a previously unrecognized recessive mutation, unrelated to *met-7*, that is responsible for the unusual chromosome behavior (*2*). In addition, attempts to quantify the effect of *dim-2* on aneuploidy did not show significant increases in aneuploidy attributable to *dim-2* (*3*). Thus, we wish to retract our interpretation that methylation deficiencies cause abnormal chromosome behavior. Finally, we wish to correct an error in the legend to figure 6: the *met-7* strain number should have read "N561 (FGSC 4143)" instead of "N556 (FGSC 3915)."

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References

1. H. M. Foss, C. J. Roberts, K. M. Claeys, E. U. Selker, *Science* **262**, 1737 (1993).
2. A. Hagemann, J. Irelan, H. Foss, C. Roberts, E. Selker, unpublished data.
3. A. Hagemann and E. Selker, unpublished data.

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Sequence Correction

We wish to note a correction of the *NPM-ALK* sequence (GenBank accession number U04946) described in our report "Fusion of a kinase gene, *ALK*, to a nucleolar protein gene, *NPM*, in non-Hodgkin's lymphoma" (4 March 1994, p. 1281) (*1*). After re-examination of our sequencing data, we identified an erroneous omission of two nucleotides in the codon of NPM-ALK amino acid residue 495 that was made because of a reading error. The frame-shift produced by this error led us to assign a premature termi-