AIDS: AN ALTERNATIVE SCENARIO

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INTRODUCTION

By the end of 1987, almost 50,000 cases of Acquired Immune Deficiency Syndrome (AIDS) had been reported to the Centers for Disease Control (CDC) in the United States.[1] The CDC estimated that between 945,000 and 1.4 million persons had a positive serum test (were *seropositive)* for human immunodeficiency virus (HIV) antibody.[2,3] These data have lead many authorities to view the future of AIDS with alarm.[4,5] In 1987, the Louis Harris organization published the results of a survey of 227 leading AIDS researchers.[6] The group jointly predicted that by the year 2000 about one million Americans will have developed AIDS. For the interim, the CDC is projecting a cumulative total of 270,000 AIDS cases by 1991.[7]

There are two suppositions underlying this prediction.[8] First, exposure to the virus beyond some certain (but unknown) minimum quantity and by the necessary (but not certain) route(s) will lead to infection among many of those so exposed. Second, infection will almost invariably lead to disease. A supplementary supposition is ascribed to by some in support of such predictions: AIDS will invariably become a heterosexually spread disease in this country, as it is in Africa.[5,9] Dr. Harold W. Jaffee of the CDC has stated: "You have to assume that tertiary spread will occur." Tertiary transmission of HIV is that which goes beyond the known high-risk groups and their regular sexual partners into the general population, even though, as he points out, "the evidence right now says that the extent to which it has occurred is remarkably small."[10]

If these predictions are correct, many U.S. citizens will suffer severely. The U.S. health care delivery system will be put under a severe strain. The national commitments to civil liberties and ethical behavior and to financing mechanisms will be severely burdened. If the predictions are correct, there are important policy decisions that must be made now.[11,12,13] However, before these decisions are made, there are questions about the conventional AIDS wisdom which should be raised and considered. There are important gaps in our epidemiological data base which should be filled in.

SOME REASONS TO PAUSE FOR REFLECTION

The predictions of 500,000 AIDS deaths and cases in the U.S. by 1992,[13] of one million AIDS cases in the U.S. by the year 2000,[20] and of the inevitability of heterosexual spread into the general population have a common weakness. They are based on an incomplete understanding of the epidemiology, virology, pathophysiology and natural history of this dreadful disease. Robert M. May and Roy M. Anderson have pointed out that:

> For public health planning, the dominant unknown is the...fraction infected who will eventually develop AIDS. Estimates of this parameter have been increasing in recent years, but on present evidence, the possibility cannot be ruled out that it is as low as 20% or as high as virtually 100%.[14]

There are other important gaps in our knowledge of the means of spread of this killer. For example, we know little about the infectiousness of any person for others at any given time. Our knowledge of the true state of health of individuals who test positive for HIV is also limited. We can determine if an individual has been exposed to HIV to the level that his/her immune system has been induced to manufacture the necessary antibody. However, we do not have a cheap, fast and convenient way to diagnose present, live, HIV infection. Therefore, we do not know whether HIV antibody-positivity means that the person has live virus in their system at the time of the test or has managed to fight off the infection with the antibody they have manufactured and are virus-free.

Virtually all of the print and visual media equate a positive test for antibody to HIV (seropositivity) with active HIV infection. Some medical and public health authorities do this as well.[15] Such an unqualified equation may be misleading, however. To date, it has been shown that many seropositive persons are infected with the virus at the time of testing. However, virology studies have demonstrated that this is not always the case.[16,17] And such studies have been limited. Among HIV-antibody positive persons, we certainly do not know just how many no longer have the virus in their system. In the absence of certain knowledge to the contrary, discussion of data on seropositivity ought to assume that seropositivity does not *necessarily* mean present infection. It also does not *necessarily* mean present infectiousness. But this kind of reporting does not often occur.

Certain available data appear to be ignored in discussions of the future course of AIDS. Perhaps it will sweep through the population without retreat. But then again, it may not. As the CDC's Curran *et al.* point out (footnote 1, page 613):

HIV data from prospectively followed cohorts of homosexual men consistently show lower HIV incidence rates for 1985 to 1987 than in the early 1980's.

The CDC's reported national HIV seropositivity numbers were stable from 1986 to 1987.[3] As of December, 1987, AIDS incidence reported in New York State was stable at 300 per month.[7] HIV seropositivity incidence among homosexual males in San Francisco has plummeted. In one group of 350, 21 percent became seropositive in 1982. There was one new finding of seropositivity each in 1986 and 1987.[7] During the first two years of HIV antibody testing among applicants for military service, the seropositivity level has remained constant.[1,18]

The changes in the HIV seropositivity and AIDS incidence patterns among male homosexuals could be due to changed sexual practices, as many claim. It could also be due simply to a decline in the number of susceptibles. Curran, *et al.*, have put it this way:

> *Some of the decline may be related to the early infection of highest risk persons in a closed group or to a 'study effect,' but the results are consistent with reports of substantial behavior changes in homosexual men....* (footnote 1, p. 613)

Presently, seropositivity is spreading rapidly among intravenous drug users. This spread could continue exponentially, as some predict. Alternatively, it could follow the pattern observed among male homosexuals in San Francisco, a pattern for which there is currently no complete explanation.

On the one hand, then, we have an incomplete, inadequate knowledge base. On the other hand, there are existing data which are not given adequate consideration. Nevertheless, perilous predictions and momentous decisions are being made. I suggest that it is time to pause and take stock. Are there any plausible alternative scenarios for the future of AIDS? Can the data and knowledge gaps be filled? Ought they to be filled before further policy decisions are made? Should certain existing data be given more credence, subjected to more analysis? I think that the correct answer to each of these questions is "yes."

HISTORICAL EVIDENCE

There have been other human plagues which were considered at first to be unstoppable, and then proved not to be. The Black Death killed one-third of the population of Europe in the 14th Century—A remarkable occurrence. At the same time, some thought that it was sweeping all life before it. Yet there was another remarkable occurrence. In the fact of the mighty onslaught of rats, lice and bacteria, two-thirds of Europe's population survived. This took place well before anyone knew anything about the epidemiology, biology, pathophysiology, laboratory diagnosis or effective treatment of the disease. There must have been a range of susceptibility.

Leprosy, cholera, syphilis, yellow fever and tuberculosis: all appeared, became epidemic, and then disappeared or became endemic but limited. And all demonstrated a range of susceptibility. In tuberculosis, for example, it is well-known that infection with the tubercle bacillus does not automatically mean that tuberculosis will follow. In fact, these days, conversion is rarely followed by disease. If HIV turns out to infect everyone who receives the necessary exposure and if in every infected person exposure leads to disease, the HIV will be a very unusual infectious agent indeed.

EVIDENCE ON THE DEVELOPMENT OF AIDS

A very important finding of a study by Grant, *et al.*, was that only a fraction of those exposed to HIV do become infected.[19] There is considerable variation in the rate of speed that an infected person becomes ill.[8,20] It is still not certain that every person infected with HIV will indeed come down with AIDS. In studies carried out by the San Francisco, California, Department of Health, of "6700 homosexual and bisexual men...enrolled in studies of hepatitis B virus infection between 1978 and 1980 [who] have been followed for AIDS since 1983," it was found that:

> *As of 30 September 1987, 804 cases of AIDS had been reported and 75% of all cohort members had HIV infection [presumably this meant seropositivity]; approximately 16% of infected men have developed AIDS. After 88 months of infection, 36% of the men had progressed to AIDS, while more than 40% had other signs or symptoms of infection; only 20% had remained completely asymptomatic.*[21]

This is quite a remarkable finding. This study group was at very high risk for HIV infection. Many of its members were not only homo- or bisexual, but also had, or had been exposed to, hepatitis B virus infection. Some had chronic, recurrent non-HIV sexually transmitted disease. Yet, after over seven years, only one-third had come down with AIDS, one-fifth of the seropositive men had no signs of it, and one-quarter of the original group was not even seropositive.

In one New York city study, 13 men infected

with HIV at least since 1978 had not developed AIDS by 1987.[22] In another study, conducted by the New York Blood Center, only one of 87 people known to have HIV infection since 1981 had developed AIDS by 1987.[22]

In the United States, many of the studies of seropositivity and AIDS development have been done in populations which first came to the attention of health authorities through their attendance at clinics for sexually transmitted diseases (STDs) other than AIDS[23] or because they had or had been exposed to hepatitis B. Most of the other studies have been done among intravenous drug users. Sexually transmitted diseases are found much more frequently among promiscuous gay men than among non-promiscuous gay men. In the former, there is also a high incidence of parasitic gastrointestinal infection.

AIDS is a disease of the *immune* system. It happens that most of the data on it come from populations which have immune systems compromised by chronic recurrent STD or hepatitis B or intravenous drug abuse. Generalizations to the whole population have been made from these data. Curran *et al.* state:

> *The data probably overestimate the true prevalence of HIV infection in most homosexual men since most surveys are conducted of persons seeking medical attention for STDs or because of concern that their past or present sexual behavior has placed them at risk.* (foomote 1, p. 612)

How true. But Dr. Curran and his colleagues fail to recognize the implications of their statement for our understanding of the true nature of AIDS and its potential for spread or lack therefor in the general population. Epidemiological study of the role of previous compromise of the immune system in the development of AIDS certainly seems to be indicated.

There are some other elementary epidemiological questions which should be asked and answered before further major policy decisions are made. for example, there appear to be few if any studies in the literature on the relationship between conventional risk factors and HIV seropositive/AIDS.[1,24] Perhaps there are personal or environmental risk factors which are important, such as cigarette smoking, drug and alcohol use, overweight, unbalanced nutrition, lack of exercise, abnormal blood chemistries, other diseases or exposure to toxic wastes.

Weight is a particularly interesting variable that might be profitably investigated. Persons with AIDS are invariably thin. But *pre-existing* obesity seems to be virtually non-existent among AIDS patients in the U.S. Is that a characteristic of the promiscuous homosexual population and infected IV drug users? Or is there something that excess body fat is good for other than protecting long-distance swimmers in cold water? A number of details of the epidemiology of AIDS in the United States are missing. They do not appear to be on the current AIDS epidemiological research agenda either.[24]

HIV INFECTION AND AIDS IN AFRICA

A population survey in Central Africa concluded that one factor accounting for the high frequency of heterosexual AIDS spread there is the commonality of heterosexual anal intercourse. The latter is frequent, it was said, among never-married women having sexual intercourse but not wanting to experience rupture of the hymen.[10,25] However, after reviewing much data, Plot and his colleagues from the World Health Organization have concluded that heterosexual anal intercourse is not a significant factor in HIV transmission in Africa.[26]

The CDC has postulated that another cause of heterosexual hIV infection spread in certain parts of Africa is the widespread practice of clitoral amputation.[10] This procedure often leaves the operative site subject to chronic infection and bleeding. Plot and his colleagues also cite genital ulcers, Chlamydia trachomatous, lack of circumcision in males, and the presence of chronic viral or tropical parasitic disease as important factors in the transmission of HIV in Africa. None of these are common risk factors in the U.S.

In a remote province of Zaire, HIV seropositivity was found to be endemic. However, over a ten-year period the prevalence was less than 1%.[27] During the ten years, three of the five persons in a 1976 sample died of illnesses that suggested AIDS. This population can hardly have a high level of natural resistance to disease in general. It is subject to endemic, major, chronic infectious diseases such as malaria, tuberculosis and parasitic gastrointestinal infection. HIV may have been present in the population for quite some time. But for at least ten years, neither HIV nor AIDS has been rampant.

In contrast, among female prostitutes in towns along the Zaire river and in the capital, Kinshasa, where the virus has been introduced relatively recently, the seropositivity rates range from 10 to 27%. One must wonder if it will eventually reach the same endemic rate as presently found in the hinterlands. In Africa as a whole, in 1988 the incidence of HIV infection was reported to be levelling off, even in the hardest hit areas of Central Africa.[28]

AIDS AT PRESENT

AIDS is a dreadful disease. In persons with AIDS death is an almost certain outcome. Even there, we

cannot be sure, however. There may be a few people who have contracted the disease and then spontaneously recovered.[22] Further, AIDS has much stigma and social and economic risk attached to it. It is possible that not everyone who has been stricken has sought medical attention. Perhaps then, there have been some spontaneous remissions that have not yet come to light. If that is the case, it would be very helpful to identify those cases. They should be thoroughly evaluated to determine, if possible, why they did not end in death.

The social stigma attached to AIDS itself has been accompanied by possible penalties for testing HIV seropositive alone. These include ostracism, loss of employment, exclusion from school, and physical isolation. Confidentiality in testing is not guaranteed in every jurisdiction. The President's Commission made a major point of this fact.[13(Chapter 6)] This situation may well have produced a skewed testing and data pattern in the population. It may be that the persons who are most likely to be come infected if exposed, and most likely to become diseased if infected, are differentially represented among those tested. Thus the data from the haphazard testing done to date could be misleading.

The standard AIDS scenario is: exposure means infection, infection means disease, disease means certain death, and AIDS will spread widely in the U.S. population. However, the findings from the literature that I have cited here must at least raise questions about the conventional wisdom. These findings indicate that additional data are needed before any final conclusions about the AIDS epidemic and its spread are drawn. Even without the needed additional data, it is possible to draw interim conclusions about HIV and AIDS that differ from those of the conventional wisdom.

In my view, the time has come to pause for a moment. We should look at our knowledge base. We should step back and decide if we are really seeing the whole picture that is presenting to us. We should make a determined effort to fill the gaps in our knowledge base before making further policy decisions.

AN ALTERNATIVE SCENARIO FOR THE OUTCOME OF HIV INFECTION

For virtually every other infectious disease that we are familiar with, there is a range of susceptibility in the population. Historically, infectious disease "wipeouts" have occurred only in populations that had absolutely no previous exposure to the new infectious agent. This occurred, for example, when Native Americans and Pacific Islanders encountered measles for the first time. But we already know[1,7] that at least in certain areas the spread of HIV infection and AIDS is abating among male homosexuals in the U.S. No significant tertiary heterosexual spread has occurred.[1,10]

It is certainly possible that this virus is infecting only the highly susceptible members of the population and then going on to kill only the most highly susceptible ones. This concept is only an hypothesis at present. But if it is true, the likely future scenario of AIDS would be rather different from the current conventional one.

The alternative future scenario uses existing data, much of which has been cited above. It also make some educated guesses about what additional research might show, based on our knowledge of the behavior of other infectious diseases.

There is variation in susceptibility to HIV infection given exposure.

The presence of antibody without infection means that the person is immune.

There is variation in the liability to develop the disease given HIV infection.

In many seropositive persons without clinical disease, seropositivity means that they have successfully overcome the HIV infection and are virus-free.

There are thus not just one, but at least four different possible responses to exposure to HIV (in the manner and amount that will produce infection in the least-susceptible person, both factors presently unknown): no infection; infection, but no diseases; infection, with a variety of disease states *other* than AIDS, but no subsequent progression to AIDS; and AIDS.

Many of the exposed susceptibles who will contract AIDS have already done so or will do so in the relatively near future. Most of them, but not all, will die.

As the pool of susceptibles dies, the disease prevalence will decline, both because the supply of virus and the number of point sources for it will decline. (Thus for this apparently obligatory human parasite, herd immunity will develop.)

In the United States, heterosexual spread, other than among susceptible IV drug users, will be limited.

The disease will not become epidemic to the general population. It will remain epidemic among potentially susceptible persons, as they reach the age at which they may engage in the sexual practices and/or contaminated needle use (and develop other co-risk factors presently known to be associated with HIV transmission and infection).

IN SUPPORT OF THE SCENARIO

Further research is needed to confirm or refute this hypothesis and scenario. It should be done, if for no reason other than to confirm the present majority view that AIDS is virtually unstoppable

without a vaccine or an effective anti-viral agent.[29] (Public health education[30] is treated by many as a palliative or stop gap for the epidemic.) However, even without further research, existing information raises enough questions about the present majority view to demonstrate that for now it too can be considered only an hypothesis.

To prove my hypothesis, first it would have to be shown that exposure to HIV does not necessarily lead to infection, and that infection with HIV does not necessarily lead to AIDS. Some of the necessary natural history studies are already underway.[22] Second, it would have to be found that HIV seropositivity without active infection does occur. (To do this a cheap, quick and accurate test for the virus needs to be developed. It is required both to correctly understand the natural history of the disease and how it is spread, and to deal appropriately with political and public hysteria.) Research along these lines is presently underway. Third, it would have to be shown that persons with previously compromised immune systems and other risk factors which have yet to be evaluated are more likely than the general population to become infected, (not just turn seropositive), and get the disease.

IMPLICATIONS FOR PUBLIC POLICY

What would a confirmation of the alternative scenario mean for public policy? The cost of caring for AIDS patients, already a significant figure even if the incidence and prevalence begin to fall, is only one of the major questions.[31] If my hypothesis were to prove correct, there certainly would be a call in certain quarters to let the disease run its course and die out, in both individuals and the population. However, that would be counter-productive, as well as immoral. There will always be new susceptibles coming of age. Virulence of the agent and susceptibility of the potential host can change over time. We could let the disease go now, thinking that it would just die out. But something might happen in the future to truly make it become the virtually unstoppable plague that many think it already is.

Those who have the disease certainly do not deserve to be abandoned to their fate. The United States is a wealthy country. We are supposed to be concerned about what happens to our fellow men and women. Thus we certainly should continue to search for effective treatments and a vaccine.

New research would not only show which scenario is the correct one. It might well identify currently unknown personal risk factors other than the broad categories of "homo- or bisexual male" or "intravenous drug user" for HIV infection given exposure and for AIDS given infection. This would be of great assistance in the control of disease spread. Hearst and Hulley suggest that the single best recommendation for preventing the spread of AIDS is to "avoid choosing a sexual partner who may be at high risk of carrying HIV."[32] Helpful in using that advice would be full knowledge of what the risk factors are.

Testing for HIV seropositivity is controversial.[13,Chap.6;33;34] If my alternative scenario is correct, any consideration of mandatory, broad-scale testing could be rationally abandoned as not only immoral and unconstitutionally intrusive, but also cost-ineffective. Testing would be indicated only among persons known to be at high risk. It should be done on a highly confidential basis, as recommended by the President's Commission. In this way, it would be focused on the control of spread and the understanding of the epidemiology of AIDS, rather than on potential punishment of the victim.

Naturally the question of isolation would arise. (Note that in the current debate, the term "quarantine" is often used when "isolation" is correct in context.) Some would say that I should not be setting out this hypothesis, just because certain quarters would turn automatically to isolation of high-risk persons as a solution to the problem, should the hypothesis prove to be correct. But if the science is correct, the questions about morality and civil liberties have to be dealt with on their own merits. As with tuberculosis, in terms of the public's health, it would be necessary to isolate only those infectious individuals, (knowing of course with certainty who they are), who prove themselves incapable of responsible health behaviors.

CONCLUSION

AIDS is a terrible disease. Nevertheless, before extremely ominous predictions of its future course are made, all, not just some, of the existing data should be examined carefully. Further, every effort should be made to fill critical gaps in our knowledge of the epidemiology, the virology and the natural history of HIV infection and AIDS. These steps should be taken before scientists as well as the prejudiced and ignorant among us[35] become agents of fear. We should not make policy and spending decisions that we need not and ought not to make.

What might further research show? It might show for example that chronic recurrent sexually transmitted disease (CRSTD) is a major risk factor for HIV infection and AIDS, that it is not the "promiscuous homosexual lifestyle" but what it can produce in the way of CRSTD that is primary. If that were true, then one approach to controlling the spread of AIDS would be a national campaign to eradicate STD, something that has been often discussed but never

implemented.[36,37]

Perhaps it is Hepatitis B that is the culprit. Or perhaps it is several different chronic diseases or conditions, each of which compromises the immune system in a way that allows HIV to gain a foothold. After all, the Acquired *Immune-Deficiency* Syndrome affects the *immune* system. It allows other diseases to establish themselves in the body. People don't die of the direct effects of the virus, but rather of the intercurrent infections and unusual malignancies that follow the establishment of the Syndrome, the severe damaging of the immune system.

Isn't it logical that we should be paying close attention to the role that previous compromise of the syndrome plays in the establishment of HIV infection and AIDS? Isn't it logical that we should stand back and question the real meaning of our epidemiologic data on AIDS itself, not HIV seropositivity, so much of which comes from populations that have either CRSTD or hepatitis B, chronic lower bowel infection or chronic intravenous drug abuse? This would not be the first time in history what we have stared a culprit in the face and failed to recognize him. Nevertheless, a recent review of "Needs and Priorities for Epidemiologic Research" which has a long list of recommended studies fails to mention what appears to be a central question.[24]

1. Epidemiology

a. The role of the compromised immune system in the development of HIV infection and AIDS.

b. The role of "conventional" risk factors, *e.g.*, cigarette smoking, alcohol abuse, nutrition, weight, environmental toxins, in the development of HIV infection and AIDS.

2. Virology

a. Development of a quick, simple, and cheap test for the presence of active HIV infection in the body.

3. Natural History

a. Investigation of possible spontaneous recoveries from AIDS and in persons with HIV seropositivity or infection who do not come down with AIDS; investigation of the factors which might account for that outcome.

FINAL THOUGHTS

It is possible that the AIDS epidemic will prove to be self-limited. It is possible that there is a range of susceptibility in the population, possibly mediated by the state of the immune system itself. It *is* possible that the Human Immunodeficiency Virus does not produce disease in all who are infected with it. It *is* possible that HIV does not produce infection in all who are exposed. It *is* possible that the immune systems of many people are able to cope with HIV. It *is* possible that general heterosexual spread will be minimal in the U.S. population, (and that of the other industrialized countries), because of the generally healthy state of the immune systems in that population.

Let us learn more. Let us focus better. Let us look at what we know from the history of other great infectious plagues. In regard to this new affliction, nature may be doing something for us as well as against us. If so, let us work with her, and use what tools she may give us. *If* we look, we can find them.

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