RECORD OF SOCIETY OF ACTUARIES
1995 VOL. 21 NO. 4A

THE GREAT HIV/AIDS CONTROVERSY

Moderator: PETER W. PLUMLEY
Panelist: ROBERT S. ROOT-BERNSTEIN*

There is considerable controversy regarding the role, if any, of HIV in causing AIDS. This panel will update attendees on the issues involved in examining this matter.

MR. PETER W. PLUMLEY: With me is Dr. Robert Root-Bernstein, who will be our principal speaker. I'll tell you more about him in a few minutes, but first I want to give you a little background about the AIDS epidemic and the role of HIV in it.

As I'm sure most of you know, AIDS was first identified in the early 1980s. Soon after that, it was announced that it had been determined that AIDS was, in fact, caused by a virus. This virus was given the name of HIV. It was determined that it was a blood-borne virus and therefore could be transmitted when it came in contact with blood. This generally occurred through sexual contact or by infected needles inserted in the body for various reasons. Since the early 1980s, the AIDS epidemic has been the subject of tens of thousands of articles, papers, TV talk shows, and AIDS education campaigns of various types. In the process, millions of people have been terrorized, many of them unnecessarily.

Actuaries deal in risk. As an actuary, I first took a look at the AIDS epidemic about ten years ago. I examined it from the point of view of the risks involved, particularly as it related to the group that makes up the great majority of the U.S. population, namely, heterosexuals not using recreational drugs. As the years passed, it became clear that in spite of dire warnings to the contrary, the epidemic would remain largely confined to major risk groups, namely, homosexual men and intravenous drug users. Of those whose AIDS was attributed to heterosexual contact, nearly all were either regular sexual partners of intravenous drug users or bisexual men or were, in fact, drug users themselves. I might add that those comments apply to the U.S. AIDS epidemic. As we will hear a little later, the African situation is very different.

To summarize, a serious problem existed for homosexual men and drug users, but for the vast majority of the population in the U.S., the likelihood of contracting AIDS was about as great as winning the lottery.

Why is there such an enormous discrepancy in risk between those who are in the high-risk groups and those who are not? This phenomenon does not occur with most other diseases. The original explanation was that HIV just happened to start its infectious path with homosexual men and that it then spread to the drug users through drug-using homosexuals. Some believed that it was only a matter of time before the heterosexual community would have a serious problem as well. Others recognized that HIV can be transmitted by heterosexual intercourse, but the extremely low efficiency, combined

*Dr. Root-Bernstein, not a member of the sponsoring organizations, is an Associate Professor in the Department of Physiology at Michigan State University in East Lansing, MI.

with the relatively small amount of sexual contact between those in the drug community and the non-drug-using heterosexuals, would keep the epidemic from spreading.

It was possible to create a model of the AIDS epidemic based on various assumptions relating to the number of sexual contacts, the amount of intravenous drug use, and so forth. I did this in a paper, "An Actuarial Analysis of the AIDS Epidemic as It Affects Heterosexuals" in the *Transactions* [XLIV (1992): 333], and a number of other people around the country have done so as well. The modeling technique varied, but in nearly every instance the central assumption was that a person infected with HIV would in time become ill with clinical AIDS. In other words, HIV was *the* cause of AIDS.

As time went on, however, an increasingly large group of AIDS researchers began to realize that the AIDS epidemic wasn't quite that simple. They were disturbed about the explanations for the manner in which HIV supposedly worked its damage to the human body. Why did it take only a year or so for some HIV-positive people to develop the clinical symptoms of AIDS, while others could live in apparent perfect health for a decade or more? Considering that nearly all AIDS victims lived what might be characterized as an unhealthy lifestyle, what was the relationship of AIDS to other health factors besides the HIV?

As you can imagine, the answers to these and other related questions are important for a number of reasons. Perhaps the most important reason is that if we knew the answers, we would know what type of treatment to give those who test positive for HIV. Instead of merely telling them that they will die from AIDS in a few years, or prescribing treatment by such powerful and dangerous drugs as azidothymidine (AZT) in the hope that it will delay the onset of AIDS, we might be able instead to prescribe changes in such items as diet, vitamin intake, treatment for venereal disease, and the discontinuance of practices such as recreational drugs, smoking, excessive drinking, and anal sexual practices. In other words, we could be prescribing more of a holistic health treatment instead of relying so much on drugs.

In addition, it is my hope, perhaps unjustified, knowing human nature, that better knowledge will help put an end to the reign of terror that has swept the nation based largely on the concept that everyone is at risk for AIDS. Wouldn't it be great if there could be general agreement that only certain specific conditions create a risk of contracting AIDS, and that unless you had one or more of these conditions, you were totally safe from AIDS?

To analyze the relationship of HIV to AIDS and to discuss the various cofactors that are involved in the epidemic, we are fortunate to have with us Dr. Robert Root-Bernstein. Dr. Root-Bernstein is an associate professor in the department of physiology at Michigan State University. He received an A.B. degree in biochemistry from Princeton in 1975 and obtained his Ph.D. from Princeton in 1980, majoring in the history of biology and minoring in the history of modern Europe and the history of chemistry. Prior to coming to Michigan State, Dr. Root-Bernstein was a research assistant at the Jonas Salk Institute for Biological Studies and later a research assistant at the Veterans' Administration in Los Angeles. He was a MacArthur prize fellow from 1981 to 1986. At the present time, he has an active laboratory research program under way looking at the causes of autoimmune diseases in AIDS.

Dr. Root-Bernstein is a very prolific author. He's written two books, contributed chapters to several others, and has had 60 peer-reviewed articles published in various research publications. His first book, *Discovering*, is not related directly to AIDS, but nevertheless is insightful in its analysis of the way to approach research.

His second book, *Rethinking AIDS: The Tragic Cost of Premature Consensus*, is the one that caught my attention as well as the attention of many others working in the field of AIDS. It is only one of a growing number of books and articles that in one way or another has questioned the relationship of HIV to AIDS, but it is probably the best reasoned and documented. It contains more than 100 pages of references in addition to several hundred pages of text. At this time, I'd like to introduce Dr. Robert Root-Bernstein who will present his views of the relationship of HIV to AIDS.

DR. ROBERT S. ROOT-BERNSTEIN: I want to simply explain a few things that I will and will not do. I will not question what we know about HIV. I'm going to assume that researchers have done a good job in the same way that I've done a good job in my research and that other people in other biomedical areas are doing a good job in their research. But that doesn't mean that they have the whole story. So much of what I will do is point out that there are other facts that need to be factored into what is a very complex equation before we can understand AIDS. In other words, I'm going to argue that we have oversimplified the case.

Here it's worth remembering something that Albert Einstein said about science in general. He said, "Make it as simple as possible, but no simpler." Here I think we have oversimplified. I'll try to make the case that we've oversimplified and therefore a case for what else we need to do.

To set the tone for this, I want to tell you about a letter that I received a couple days ago from a person in Toronto who got HIV infection. She knows whom she got it from. She knows how she got it. She is a heterosexual. She wrote to say the first thing she picked up was my book. Did I still agree with what I had written in the book, which I do, and did that mean the following things? Among them were, "Will I die within ten years of AIDS?" She contracted HIV in 1993. She has gone to three different doctors, and they are literally telling her to make her will and take care of her business because she'll be dead five to eight years from now. Second, she asked, "Is there any chance that I won't develop AIDS at all? In other words, will I necessarily die of this disease?"

The Centers for Disease Control (CDC) or almost all "experts" in this field would say that what her doctors told her is absolutely correct. The average latency period from infection to AIDS is about ten years. She could live a year or two after that with full-blown AIDS but then she will die. According to the CDC, we're all at equal risk. If you get nothing else out of what I'm going to tell you, please get the following points: (1) we are not all at the same risk for getting AIDS—it depends on a whole series of factors I will demonstrate to you; (2) we are not all at equal risk of developing AIDS after an HIV infection; (3) nor will we all necessarily die from AIDS if we get an HIV infection. None of those things is theoretical. There is a large body of evidence to back every single one of those statements up. How people can make the opposite statement, given what's already in the literature, makes me very angry, and that's why I give these talks.

Let me start with just a basic introduction to what everybody thinks we know. We start with the human immunodeficiency virus, the retrovirus. It's an unusual type of virus in that most viruses of this class don't actually produce overt disease. A few animal models are fairly similar to AIDS, but they are very acute. The animal gets the disease and either dies or survives. It doesn't last for ten years the way humans with AIDS do.

HIV uses what are called receptors on the outside of cells, particularly something called T-helper cells, part of the white blood cell system. There are literally like walking T-interactions, which allow into those cells, macrophages, a few other types of cells in the immune system, and almost nothing else; it's very specific in its target. If we look at the immune system, it's very easy to describe why this type of infection could be imagined to destroy immune function.

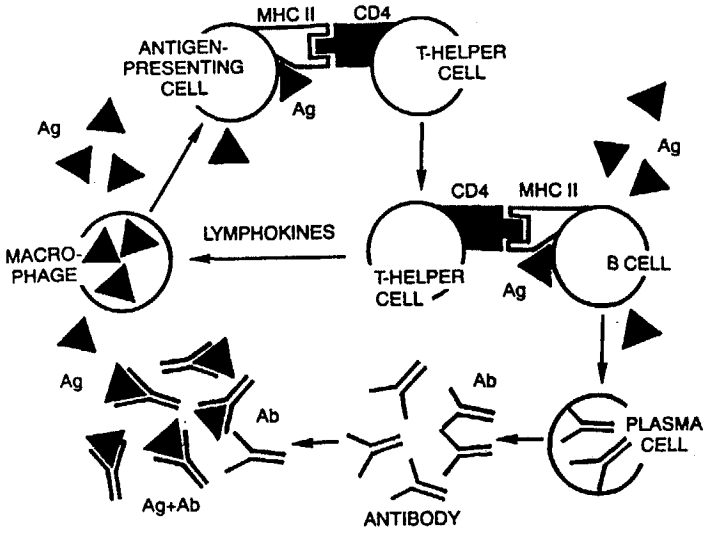
Let me explain to you what's in all the textbooks right now and what you would find if you talked to most experts in the field. Let's start in the upper left corner of Chart 1 where it says "Ag." That stands for antigen. Antigen is an immunological term, and it's simply anything that will provoke an immune response. It's anything foreign to your body. What happens is that something called macrophages, literally "big eaters," will eat this antigen—they take it up inside. They present it on the outside of the cell in the form of antigen-presenting cells. They interact with these T-helper cells, which are the same things that HIV likes to infect. Now these T-helper cells have a whole series of functions in your immune system. One is (lower left on Chart 1) that they clone themselves. They make many copies of themselves, turn themselves on, and produce something called lymphocytes, which are simply chemicals that regulate the immune system. It makes the immune system much more efficient. So you get more macrophages, more antigen eating up more T-helper cells. It is a nice cycle that makes you more and more immune and more and more reactive to whatever is getting in your body.

Now at the same time, those T-helper cells (right side of Chart 1) interact with another part of your immune system called B cells. B cells produce what we call antibodies. An antibody is sort of a floating arsenal of proteins, which are produced at the bottom there, and they are made specifically against whatever that antigen is. This is what we do often when we give a vaccine. Flu vaccine, for example, makes antibodies against that flu. It takes the flu out of the system. There's now less antigen around for those macrophages to eat; therefore there's less activity of the T-helper cells, and now there is a regulating system. So these balance systems are going on.

Now imagine what happens if the HIV gets in here. Everything is mediated by those T-helper cells. If there aren't any T-helper cells, there isn't any macrophage activity. In fact, the HIV will also infect macrophages. They take HIV in and, instead of spewing it out and getting rid of it, they actually are killed by it. So T-helper cell activity goes down. Macrophage activity goes down. The system doesn't make the antibodies. Eventually the immune system literally collapses. A person can't respond to anything. This is what AIDS is clinically. Clinically, it is when the immune system doesn't respond to things. So AIDS patients die, not directly of an HIV infection, but of an inability to respond to other forms of infection. These are called opportunistic infections, essentially things we all run into: *Pneumocystis carinii* pneumonia, for example. Probably 80% of the people in this room ran into that before the age of two.

You probably got antibodies that you produced to protect you against it. It doesn't do anything to you. But if you happen to be an AIDS patient, or a transplant patient, or someone whose immune system isn't functioning properly, it can kill you. That's opportunistic. It takes advantage of the fact that your immune system isn't functioning.

CHART 1
REGULATION OF T AND B LYMPHOCYTE ACTIVITY
IN THE IMMUNE SYSTEM



Ag = antigen; MHC II = MHC class II proteins; CD4 = a protein characteristic of T-helper lymphocytes and macrophages that is used by HIV to recognize and invade these cells; Ab = antibody
Source: Root-Bernstein, Ph.D., Robert S. *Rethinking AIDS: The Tragic Cost of Premature Consensus* (New York: Free Pr., 1996).

So you can see theoretically that HIV is a beautiful model for what should happen. In test tubes, this is exactly what happens. If you put HIV into a test tube with the right kinds of white blood cells, it kills them off and there's no problem. I'll get back to this in a few minutes, because it's not quite that simple, but that's literally what the textbooks tell you.

What's actually happening in AIDS? The average person has about 1,000–1,200 T-helper cells per cubic millimeter of blood. There's a cut-off level that is now the point for AIDS. If you have HIV infection and a T-helper cell count of less than 200, you're automatically an AIDS patient these days.

When a person gets infected, there's a sudden drop in the number of those T-helper cells, and it bounces back up. Then HIV slowly erodes the immune system over a long period of time. Suddenly, at the very end of the disease, the number of cells drops off, and the immune system collapses. Now that break is very important because the

question is, how long is it and why is it occurring? It's about ten years on average, and I'll tell you how we know that and what that means in a couple minutes. Now at the same time, HIV bounces high and then goes down again fast. People who have just been infected suddenly produce a lot of HIV very quickly, and over a period of four weeks or so, it drops almost to zero. The antibody response is very good. The person produces many antibodies that drive HIV virtually into extinction and then the immune system starts collapsing; then it takes off again.

One of the questions is, why, when there is this very high amount of HIV in the system, doesn't it just kill off the immune system directly? This is literally what happens in most of the animal models that we have. Why does a person last for ten years with this infection, going up and down and not doing very much, and then suddenly it takes off at the end? A person produces many antibodies. Unlike the model, which said a person shouldn't be producing antibodies, there are many antibodies. In fact, one of the very strange things that I'll talk about later is that the antibody production doesn't die off during the disease. A person overproduces antibody to the extent that organ in the body is attacked. The person gets autoimmunity, which is what I study. This doesn't make sense from the model that we have at all.

So there are all sorts of little problems when you look at what's actually happening in AIDS. That's one of the reasons that you then have to say, do we understand what's going on?

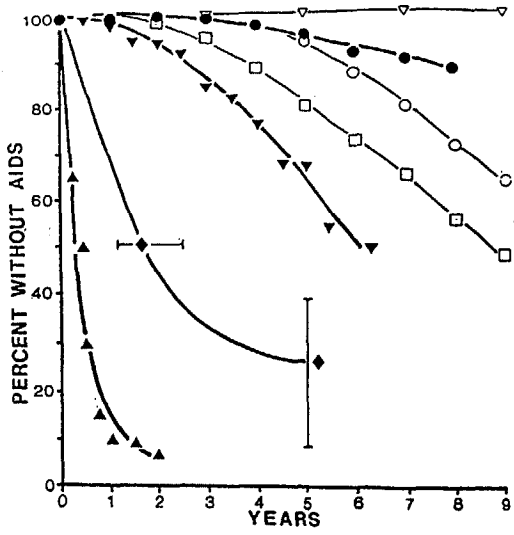
Well, what actually occurs over that period of time? How do we know it's ten years? "How Does HIV Cause AIDS?" is Robin Weiss's article from *Science* [Vol. 260 (1993): 127]. He actually cites my book and says it's the best case for cofactors of AIDS. "I want to test whether Root-Bernstein is right; do cofactors have any effect on the course of AIDS?" is what he said about the key graph, His conclusion is no. This is very important. This also shows the ten-year average latency period. Do they progress to AIDS over 12 years? The answer is no. There are actually 200 known exceptions to this idiopathic CD4 T-cell lymphopenia. I think they really are exceptions, but we can talk about that later if you're interested. A few people develop symptoms of AIDS, but percentage-wise they're so small they probably are real exceptions in my view. Other people take other views of them.

In certain data, they actually know when gay men and hemophiliacs were infected, and they look at how long it takes for them to develop overt AIDS symptoms. The average is about nine to ten years, or 50%. They notice also that their weight is basically a straight line. Once they start, it goes down at a predetermined rate, so it looks as if it's a stochastic process. The only exceptions that Weiss mentions in the article are the triangles that are pointing up, and those are young hemophiliacs. They seem to live a couple years longer than the older group. The explanation isn't known, and he and several other people suggested that maybe just young hemophiliacs start out with more T-cells. There's no evidence for this, but that's the conjecture at this point.

He points out that the slope is the same. Once you start the process, you go down, and it's a random shot as to how long you last, but it will happen. That's where you get that number from. Clearly, if this graph is correct, there goes the case for cofactors. So I checked it (Chart 2). Basically, I agree with the data on the top there. The very top line shows people not infected with HIV and certainly in the studies they don't go

on to get AIDS. This is good evidence that HIV is certainly a part of what's going on in AIDS.

CHART 2
PROPORTION OF INDIVIDUALS SURVIVING WITHOUT AIDS



Proportion of individuals surviving without AIDS plotted with data combined from various European and North American studies detailed in the text:

▽ HIV− homosexual men and hemophiliacs (Weiss, 1993)
□ HIV+ homosexual men and hemophiliacs over the age of 25 (Weiss, 1993)
○ HIV+ hemophiliacs under the age of 25 (Weiss, 1993)
● HIV+ hemophiliacs under the age of 25 (this study)
▼ HIV+ blood transfusion patients (this study)
◆ HIV+ transplant patients (this study)
▲ HIV+ pediatric patients (this study)

Note that no study of HIV+ transplant patients larger than 25 has been performed so that statistical variation in reported AIDS-free survival times vary much more widely than in studies of other risk groups. In order to indicate the variation, bars have been added to the transplant patient points indicating the range of reported data, and the points themselves are drawn from a single large study of 22 patients by Lang et al. (1991). Note the tailing off of AIDS risk with increasing length of AIDS-free time in infants and transplant patients. I predict that a similar tailing off will cause all other risk groups to have rates of AIDS that become sigmoidal.

Source: Root-Bernstein, Ph.D., Robert S. "Five myths about AIDS that have misdirected research and treatment," *Genetica*, (1995): 111–32.

When I look at young hemophiliacs, however, I get a very different curve. The open circles are Weiss's data; the solid circles are mine. I did an entire worldwide literature search. Weiss took data from two or three hemophilia treatment centers. There's a major difference which, in fact, I didn't find. There are a half dozen different articles on the difference between looking at hemophiliacs in treatment centers versus the entire population of hemophiliacs. People in hemophilia treatment centers are the most severe hemophiliacs. They get the most factor treatments. They have HIV, but they also have the highest incidence of hepatitis B and hepatitis A. They use the most opiate and steroid drugs to control the pain and the problems they have with their joints. In other words, they have a whole series of medical problems as part of their hemophilia, which mild hemophiliacs, for example, do not.

In countries where they look at the entire population of hemophiliacs, a graph would look like the solid circles do, and the average latency period for these people now turns out to be not 12 or 13 years, as Weiss says in his studies, but rather somewhere around 20–22 years. That's a rather large difference and, again, note that the slope is quite different. So we don't have something that's occurring at a given rate.

In terms of the gay men and the older hemophiliacs, I more or less agree, so I just left the open boxes, which are Weiss' data; those are good data. I can't find anything that contradicts them. Weiss didn't mention several other groups for which we know actual date of infection, often down to the specific hour, which aren't on there. There's no excuse for them not to be on there. The triangles pointing down are people who got HIV infections during blood transfusions. The average time from infection to overt AIDS is about six years. This is very well documented in dozens of studies. Here we have a group of people who are clearly much more ill than the average person. They're not getting just blood transfusions; they are also getting anesthetics, opiates, and analgesics afterward. Along with HIV, they get in their blood, they also get a whole series of other viruses, which I'll talk about in a few moments and which were not screened for before 1987–88 and so forth. Again, notice that the slope is different from what Weiss has.

Perhaps the most striking group is the one with the diamonds. Those people had organ transplants. So they had blood transfusions along with an organ transplant. They could have gotten the HIV either from the organ or from the blood or from both. They tend to develop AIDS within 2.2 years of their infection. In this case, we have, in a sense, definite proof that cofactors can play a role in the onset of AIDS because they are given immune-suppressant drugs to prevent them from rejecting their organ. I'll come back to that because people are doing many immune-suppressant things in high-risk groups. We know in this case that those immune-suppressant drugs certainly speed up the rate. Think about drug addicts and many other things that I'll talk about as we go forward.

The final group that Weiss doesn't really talk about are represented by the triangles pointing up. Those represent infants who were infected with HIV from their mothers. The average time to onset of AIDS is six months. Now this makes sense from many different perspectives, but I don't know why the people in HIV research don't make more of it. If you think about it, an infant is born without an immune system. The immune system develops during the first three months after birth. These infants literally have an HIV infection in place at the time their immune system is starting to grow. But, again, I also have to point out that all the different cofactors that I'm going to talk about are also in place at the same time; it becomes a very complex issue.

Let's get back to that woman in terms of how long she is going to live. She's a heterosexual. Which group does she fall in? That ten-year average latency period applies specifically to gay men and older hemophiliacs. There are no studies of heterosexuals per se. This is the closest I can come. When you look at Cox Proportional Hazard Regression Analysis, homosexual men had increased risk over heterosexuals in progressing to AIDS in all the different studies that have been looked at. Now they all define things slightly differently and use different ways of looking at the data. But they all say the same thing: homosexual men progress to AIDS at the highest rate, and intravenous drug users progress at a slower rate. Heterosexuals progress at the

slowest rate of all. I would tell this woman she probably is going to be around for 15 or 20 years. Probabilistically, that's what you would predict.

Why the differences? I'll get to that soon. Do we therefore need to explain the differences of rate of progression? I think so. Furthermore, there are people who say that we can't even explain the AIDS epidemic without drawing on cofactors. Jurgen Weyer and H.J. Eggers, German biomathematicians, have modeled the AIDS epidemic. They find that they cannot get anything that looks like a proper set of data for how fast the epidemic is progressing if they don't throw in a cofactor with no cofactor, an epidemic either goes out the roof instantly or just disappears, but that is not what we see in AIDS. They are now collaborating with Luc Montagnier, the man who discovered HIV, who has been saying that HIV needs a cofactor. He has been saying this since 1990.

Steve Merrill, a biomathematician at Marquette, is a person I'm working with. He has an immune system model of how the immune system works, and uses it rather than looking at the epidemic. Again, he finds that he cannot model HIV getting into the immune system and taking over the immune system by itself. To get into the immune system and actually become part of your immune system and eventually do damage to it, Merrill finds that several cofactors need to be in place at the time of infection. This is very important. Pete Plumley has looked at the epidemic. Gordon Stewart in England has looked at the epidemic. All these people who look at it say that we can't explain it without bringing in other factors.

If you talk to people off the record, whether they're working on HIV or anything else, they'll tell you, "We really don't understand how HIV does the dirty work it does." This may sound shocking because the public just hasn't heard this at all, but it isn't very shocking. Peter Duesberg, probably the most outspoken critic, a retrovirologist from Berkeley, has been claiming that HIV has no role in AIDS. For my taste, he's gone slightly overboard when he says that HIV is irrelevant. But nonetheless, he has made a large number of very well-targeted criticisms of the research, some of which I will incorporate in the talk I'm giving here. He's the first person to really point out that there are huge flaws in the research that we need to correct. So he's been claiming that we missed the boat altogether. I should point out that there is one person who still claims that HIV is the entire cause. David Ho in "Was HIV Present in 1959?" [*Nature*, Vol. 374, April 6, 1995] did that. He still claims that HIV explains everything about AIDS and we don't need to think about anything else. He's about the only person with that position anymore.

About two years ago, the cover of *Science* magazine said, "AIDS, The Unanswered Question." This was the first public recognition in the science community that there were things we really didn't understand that might interfere with our ability to control the epidemic or to bring about cures. In one article after another, people said that these are the things we don't know. This was crystallized last year by Bernard Fields, who is head of immunology at Harvard. He wrote a very influential piece for *Nature*, an editorial that essentially said, "Look, the holes are so big that we literally have to start over," which was basically Peter Duesberg's argument, but it was coming from somebody who was within HIV community rather than outside it. If you haven't heard, the National Institute of Health (NIH) actually has a panel, and it's having open hearings with AIDS experts, activists, and many other people looking at how it should

redirect research. So it's no longer even particularly radical to say there's something we don't know that's going on here.

What are some of the things we don't know? Let me show you how basic our ignorance is here. First of all, Koch's postulates, which we've used in medicine literally for 100 years, determine whether we know the cause of a disease. There are many versions of them. The HIV doesn't satisfy any of them. But they all have this basic logic. Allow me to go through the logic because it's important.

First you find the correlation. There's no doubt that there's a correlation between HIV and AIDS. Every person developing AIDS, with only a couple exceptions that I mentioned earlier, has HIV. A large proportion of the people infected with HIV go on to develop AIDS. This is the same for every disease. So that's fine. Second is purification. We need to purify HIV, and that's simply because we want to control it. We want to inoculate it into a healthy animal, which is step three. And we want to know what it is we are inoculating, otherwise, we don't know whether it's the mixture or which part of the mixture it is, and so forth. So we want to get the pure thing. We can do that. We can get HIV, and it's pure enough. No problem there. We then inoculate it into a healthy animal. Note "healthy." It has to be a healthy animal because if it's not healthy, then we don't know if it's an interaction between what we just put in and what's already there or if we have triggered some new phase of whatever is already present. So it has to be a healthy animal. We now should get the disease symptoms. Finally, step four is resolution. Presumably, whatever we put in there is growing as the disease progresses. We should be able to resolute that disease organism, reinoculate new animals, and now have an animal model. Classically, this is how we develop all our drugs and vaccines.

There are chimpanzees and macaques that have been infected with HIV since 1983. This is 1995. We're told that the average latency period is about ten years. Yet none of these chimpanzees or macaques has any symptoms of AIDS at all. They have been infected. Their T-cells produce HIV. They have produced antibodies, but they do not lose immune function. They do not develop opportunistic infections or anything else. They're just sitting there, happily being taken care of in their little cages. They've been that way for 12 or more years.

Interestingly, the same thing seems to happen with people. Many people say we're going to have an AIDS epidemic because the HIV will eventually get into everybody. The infectors will be female prostitutes. Very simply, the predictions looked like this in 1984–85. One HIV-infected female prostitute, given the literally 100 partners that she would have during the year, would end up infecting approximately 61 people over a five-year period, most of them men, some of whom would transmit it to more women and some children. We only need a few of these and we would have a heterosexual AIDS epidemic. I'm sure you're all aware this hasn't happened. In fact, about 60 or 70 studies have been done on female prostitutes. Except for what's going on in Africa and Thailand, which we can talk about later, there are no large-scale HIV infections in female prostitutes (in the West) unless they use intravenous drugs. The highest rate in women who don't use intravenous drugs is about 2% in New York City. Many cities are reporting 0%. So healthy women, the higher-class hookers, the ones who are call girls who don't work on the street, tend to have virtually no risk of getting HIV.

They're picking up everything else—hepatitis and many other things—but not HIV; that's very striking.

You can't find any tertiary cases of HIV transmission. What do I mean by that? To begin with, we have primary cases: high risk to high risk; gay men to gay men; intravenous drug users sharing needles; blood from a blood transfusion. We know the source, we know the high risk, and there is direct cause.

Secondary cases include people who are at high risk transmitting to people who are at low risk. For example, a hemophiliac goes home to his girlfriend, makes love to her, and transmits it. A small number of cases are like that; it's nowhere near the number you would expect, but there are cases like that. However, what is not in the literature anywhere in the Western world is a single case of one of these girlfriends or wives running off and saying, "I can't hack this. You're getting AIDS. I'm leaving," not knowing that she is HIV-infected, sleeping with someone else, and passing HIV on to another person. It stops at the secondary case. I'm not willing to say that absolutely, but I've been challenging people at every AIDS conference I've gone to to find a single case of a tertiary transmission. So far, no one has ever published one, so if it's out there, it's extremely rare.

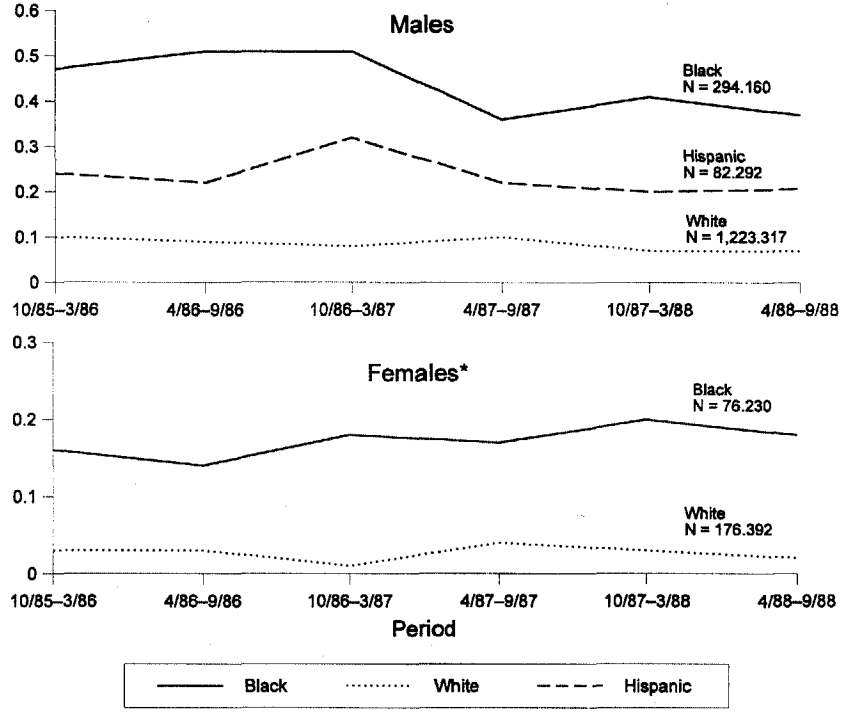
That's striking because what we just discovered about tertiary cases is something that could occur and does occur all the time with syphilis, with genital urinary disease, with ulcerative disease, and things such as that. With syphilis, the U.S. Department of Health would have tracked every one of these people and tested them; that's law. However, we don't do it with HIV because we don't need to; it doesn't happen.

Another interesting anomaly is that many people, such as Arthur Ashe and Magic Johnson, have HIV or had HIV for long periods of time, sometimes ten years, without knowing it. Many of these people are HIV-infected. Their wives have kids by them during the period that they're HIV-infected. The wife doesn't get HIV and the kids don't get HIV; this is the majority. Heterosexual studies show that transmission of HIV occurs about one in 1,000 unprotected vaginal intercourses with infected partners. The exception almost always involves bleeding, anal intercourse, or use of immune-suppressant drugs, such as when people have multiple sclerosis and are on steroids, which makes them very susceptible to infection.

There is no evidence anywhere that the rate of HIV in the general population—first-time blood donors, applicants for military service, and so on—is increasing. Yet the CDC keeps telling us, "We're all at risk; it's growing, we have this terrible threat." Interestingly, Chart 3 shows CDC data. It stopped publishing these data in 1989. The only reason I can think of is that it simply became too embarrassing. Nothing was happening and nothing is happening.

Two years ago, the National Research Council, made up of members of the National Academy of Sciences, put together its report. It said that AIDS is staying within high-risk groups. It's even staying within locales within specific parts of cities—it's not moving. It said we're not all at risk. This isn't my conclusion. This is the conclusion of the National Research Council. If you read the reports at the time, the newspapers were just shocked. How could this be true?

CHART 3
HIV-ANTIBODY PREVALENCE IN CIVILIAN APPLICANTS FOR MILITARY SERVICE, RACE, AND SEX
OCTOBER 1985–SEPTEMBER 1988
Percent Antibody Positive



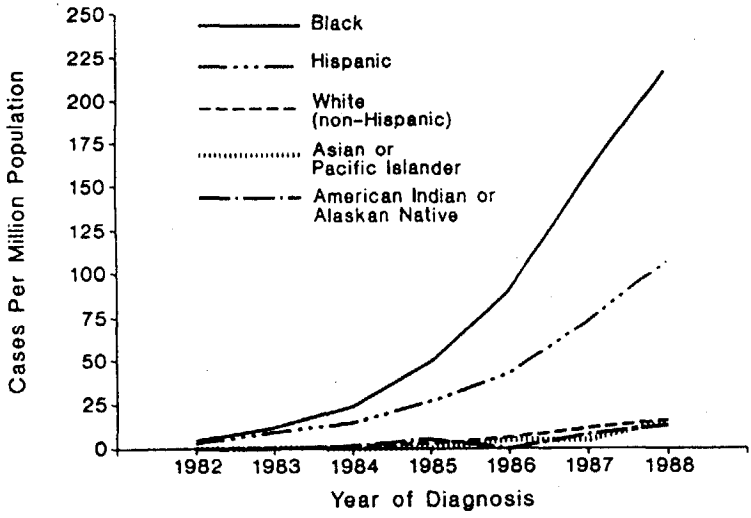
*Too few Hispanic women were tested for trends to be analyzed.
Source: Data from Centers for Disease Control.

The CDC people would say, well, we are not giving you the straight story. There is one exception. Let me show you the one exception so you know what it is (Chart 4). AIDS in 20–29-year-old women, supposedly from heterosexual contact, has overtaken intravenous drug use as the major cause of HIV transmission. This news was in all the newspapers and on all the TV shows. However, you're all sophisticated enough in statistics to know that you can't just take numbers without looking into them a littler further. So let's break all this down by race. The blacks have always had the highest rates of HIV infection. Hispanics are next. Whites, Asians, American Indians and so forth have had virtually no risk during the first few years of the AIDS epidemic.

The top line on Chart 4 continues the data that I just showed you. The Black curve continues up. In fact, it's starting to go exponential. The Hispanic curve has leveled off. The risk for everybody else has stayed virtually negligible across the entire epidemic. There are the CDC's own data. In other words, when the CDC says

heterosexual contact has finally overtaken intravenous drug use, that's solely due to a problem in the Black community.

CHART 4
ANNUAL INCIDENCE (ADJUSTED FOR REPORTING DELAYS) OF AIDS
AMONG WOMEN 15–44 YEARS OF AGE,
BY RACE AND YEAR OF DIAGNOSIS
UNITED STATES 1982–1988



Source: Data from Centers for Disease Control

Now we have to ask Why the Black community? Rates of syphilis in white men dropped drastically during the period of the AIDS epidemic, from about 25 per 100,000 down to somewhere around 5 per 100,000. White women have been somewhere around 4 or 5 cases per 100,000 for the entire epidemic; that's quite stable. This mirrors what's happening with HIV. Black men are not at 20, 25, 5, or numbers such as those, but are at 330 to 350 cases per 100,000; many times higher. For Black women, the number of cases is rising exponentially along with HIV. It has gone from about 100–150 up to 350 per 100,000. For Hispanic men and Hispanic women, the number has stayed stable or is dropping; it's around 100 for the men and 30 for the women. These numbers exactly mirror what's going on with HIV.

This isn't surprising to anybody who looks at AIDS in places such as Africa. We know that in Third World countries, HIV follows other sexually transmitted diseases. If a person has open sores, HIV can be transmitted much more easily. In the U.S., we find that genital ulcer disease is growing almost solely in people who use crack cocaine and who are having sex for drugs. HIV, again, is following the sex-for-drugs problem. Syphilis, genital ulcer disease, and others go hand in hand. If you interfere with the sexually transmitted diseases in general, in Africa rates of HIV transmission go down to the same rate that the other diseases go down to.

We don't just have an HIV epidemic, we have an HIV epidemic on top of other things. One of my other points that I'd like you to carry away is that we aren't going to control the HIV until we control all these other problems—the drug use, the sex for drugs, and so forth.

Let's get back to science. Louis Pasteur, one of the formulators of the germ theory of disease, points out that the terrain is as important as the germ. It isn't just that a germ is present, but it's what you are growing it in or on. In this case, we're talking about human beings. What's the status of the human being when the germ is put in there? How susceptible is the person?

The person who tied this first to the AIDS epidemic is a guy named Joe Sonnabend. I think when we look at the history 20, 30, or 50 years from now, Joe Sonnabend will be seen to be the most important member of the AIDS community to be working on this problem. He looked at people who were infected with HIV, looked back through his records (because he's both a clinician and an immunologist), and he said that no people who were getting HIV (whom he looked at in New York City) were healthy at the time they got their HIV infection. In other words, the terrain was set—they were susceptible. If we get back to why there isn't a heterosexual epidemic, he says quite frankly that there isn't one because most heterosexuals are just much healthier than the intravenous drug users or the very sexually active homosexual men.

This isn't a surprise to anybody who looks at the AIDS literature. A textbook on AIDS from 1984 and 1985 simply describes what you would see in somebody who is at risk for HIV infection. At that time, it was basically homosexuals or bisexuals. Of course, we now know there are other risk groups, with many different sexual partners. The average number of sexual partners in the first 1,000 AIDS cases was 1,200 lifetime partners each. Think about sexual transmission of syphilis, gonorrhea, and so on. Almost every one of these people had multiple cases of sexually transmitted diseases, some of them uncontrolled. Regarding the use of recreational drugs, 100% of the first 5,000 people used them. Parasitic diseases, which are very common, include something called gay bowel syndrome, which consists of a whole series of things that infect the lower intestines, often associated with receptive anal intercourse, and so forth. What we're talking about here is diarrhea for six months; these people have uncontrolled diarrhea for months at a time. That's very debilitating for the immune system because literally over half your immune system is in your intestines and you simply strip your immune system away. It also means that you don't absorb nutrients. Another problem: virtually every single AIDS patient is grossly malnourished.

It used to be thought there was a genetic predisposition to AIDS. That didn't hold up. But there are certain antibodies, Epstein-Barr virus, mononucleosis, cytomegalovirus, hepatitis A, hepatitis B—there's a whole list I'll get into in a moment. Humeral immunity refers to antibodies. This gets back to that problem I talked about before in which a person overproduces. That's hyperglobulinemia. Antibodies are overproduced, which nobody has explained. Also, antibodies go against T-lymphocytes. Those lymphocytes that are supposed to be being killed by HIV are actually being attacked by the antibodies. We know that the antibodies are killing off a certain fraction of the T-cells. That is typical of all AIDS patients. We know that antibodies in semen and sperm are present, and they have that same ability to kill off T-cells. This is typical of almost all AIDS patients.

I mentioned malnutrition. The number of things associated with malnutrition is extremely high. Zinc and selenium are depleted, along with iron and vitamin A. Almost anything that's necessary for immune function is depleted in AIDS patients. This is very important and was grossly ignored until very recently.

What Sonnabend pointed out, and what I ended up essentially reinventing later, was that there is a long list of immune-suppressive agents in high-risk groups. They don't have all these, but every person in high-risk groups had some subset of these: immunological exposure to semen, which I just mentioned, use of recreational drugs, and use of high-dosage antibiotics, which are associated with all these sexually transmitted diseases. It turns out that antibiotics can't be taken for more than a couple weeks without damaging the immune system. I talked to a large number of gay men who said that they would go off to the gay bathhouses, pop a few antibiotics so they wouldn't get any sexually transmitted diseases, take some nitrites, and get themselves high. That leaves the next problem: mixing those ingredients produces carcinogens. Gay men, unlike any other group, had extremely high rates of Kaposi's sarcoma, lymphomas, and other types of cancers. As soon as they found out there was a problem, the gay community responded very fast. They stopped doing nitrites, a number of them refused the antibiotics, and this problem disappeared. The cancer rates are now down. Something was going on here.

There's also a problem with intravenous drug abusers. Most people don't know this, but there is an underground market in antibiotics in the intravenous drug community. Basically, they know that they're using dirty needles. They know that they're getting infected all the time. So every time they buy drugs for intravenous use, they also buy antibiotics illicitly. We have no idea how much they take or how long they take them. Antidepressants can be a problem. Opiate abuse is a problem; any kind of opiate taken in any way is a problem. It suppresses the immune system. The more you take, the more suppressed you get; anesthetics work the same way. For blood transfusions, we actually use them in people who don't need them who are getting organ transplants because they will suppress the immune system far enough so that they will accept organs they wouldn't otherwise take. This is standard practice now in organ transplantation. Yet, we're talking about people who give blood transfusions as if the only risk they had of AIDS was the HIV. Not true—they're getting anesthetics, blood transfusions, opiates, analgesics, and so forth.

As for frequent-factors therapy, the more factors a hemophiliac takes, the more immune-suppressed he or she is. Most hemophiliacs have half the T-cells this audience probably has. That was just their baseline before they ever got the HIV.

I've already mentioned malnutrition as being the oldest and best known cause of immune suppression. We've talked about the multiple concurrent infection. I want to simply point out a fact that's very important here. All the viruses and bacteria appear. Adenovirus, cytomegalovirus, Epstein-Barr, hepatitis B, HIV, herpes simplex, microbacteria, and all similar illnesses, each infect immune system cells; every one of them. I can't find a single person in the AIDS community who doesn't have several of these at the same time. We know, in fact, that they work synergistically with HIV in test tubes, and there's no reason to suspect they don't do the same thing in people. Every single one of these things is known to increase the rate at which AIDS develops in any

given risk group, both from in vitro evidence and from epidemiological evidence. We don't even have to surmise that this is going on.

To give you a quick idea of what the risk group profiles look like in terms of these various infectious agents, I've put together many charts. These are from my book. About 250 different studies were put together. Don't look at these as real numbers, because no particular study will say that exactly 65% of the heterosexual population has the antibodies in herpes simplex. But it's in that basic range. Consider these as general profiles.

If a group of people were to walk into a clinic and you were to do a series of antibody studies and virus isolation or bacteria isolation, this is what would you find (Chart 5). On the left-hand side is HIV; the other side has cytomegalovirus, Epstein-Barr, two types of herpes simplex, hepatitis A, and hepatitis B viruses. Human T-cell lymphotropic virus (HTLV) is a virus discovered by Bob Gallo that affects T-cells and was thought to be the cause of AIDS initially. Entamoeba, giardiasis, and toxoplasmosis are related to those lower-intestinal infections. Chlamydia, syphilis, and gonorrhea are the basic sexually transmitted diseases. Then there is mycobacteria, general bacteria, and infections of the blood. Protozoa, malaria, and helminth, a general term for worms that infect people, are not major problems for the Western countries but a major problem in Thailand and Africa, and similar areas.

You can see that this is heterosexual. These would be people basically 20–45 years of age living in the Western world, Canada, the U.S., and Britain. These are all data from the peak period for HIV infection. We have a healthy population in general. By the way, the solid grey bars are active infections at any given time. So 5% of the population within this particular case have active Epstein-Barr virus. The white bars show antibodies; that means the people have been exposed at some point.

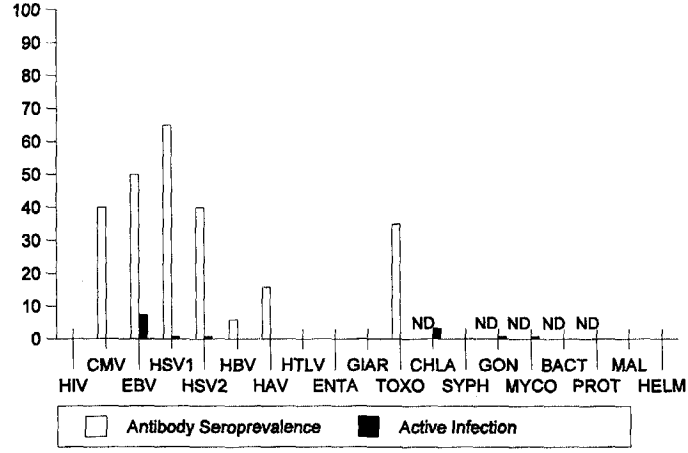
Chart 6 shows the general profile of the hemophiliac. Hemophiliacs don't get the sexually transmitted diseases and so forth at any higher rate than the general population does, but they get a whole series of blood-borne diseases, including HIV, cytomegalovirus, Epstein-Barr, the herpes simplex viruses, and so forth, at much higher rates than the rest of the population.

Chart 7 shows intravenous drug abusers. They have many sexually transmitted diseases. They have hundreds of thousands of times the rate as the rest of the population, and 60% of them walking into clinics will have active bacterial infections in their bloodstreams, which is why they're taking those antibiotics.

Chart 8 shows the same information for the North American and European HIV-negative gay men during this period. During the height of the AIDS epidemic, gay men were extremely unhealthy, particularly the ones who were visiting bathhouses and who had many partners. They had many active infections, even without HIV being present.

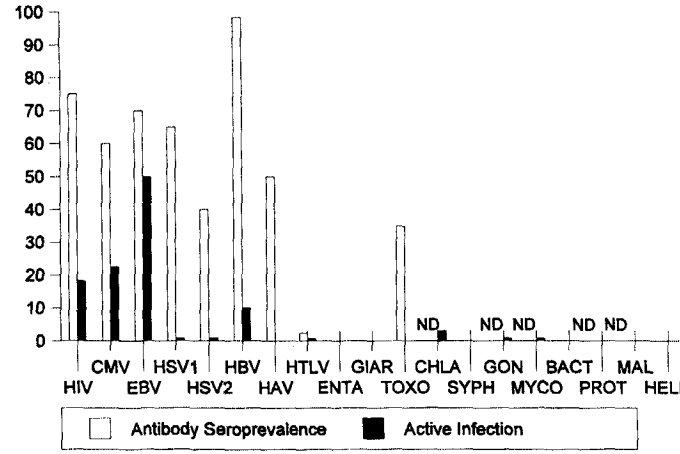
Chart 9 shows what's going on in Africa. It is a disaster zone. Chart 9 reflects typical heterosexuals in Africa. These people have a higher rate of infection than almost any population. I want to read you a report from the National Institutes of Health that was made by Tony Fauci, who was head of AIDS research in the U.S. up until this year.

CHART 5
INFECTIONS AMONG NORTH AMERICANS AND EUROPEANS



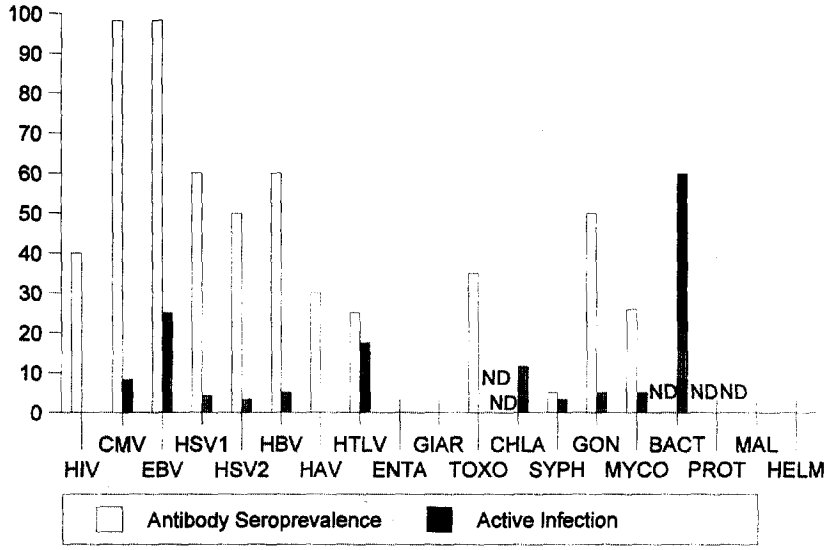
Source: Root-Bernstein, Ph.D., Robert S. *Rethinking AIDS: The Tragic Cost of Premature Consensus* (New York: Free Pr., 1996).

CHART 6
INFECTIONS AMONG NORTH AMERICAN AND EUROPEAN HEMOPHILIACS



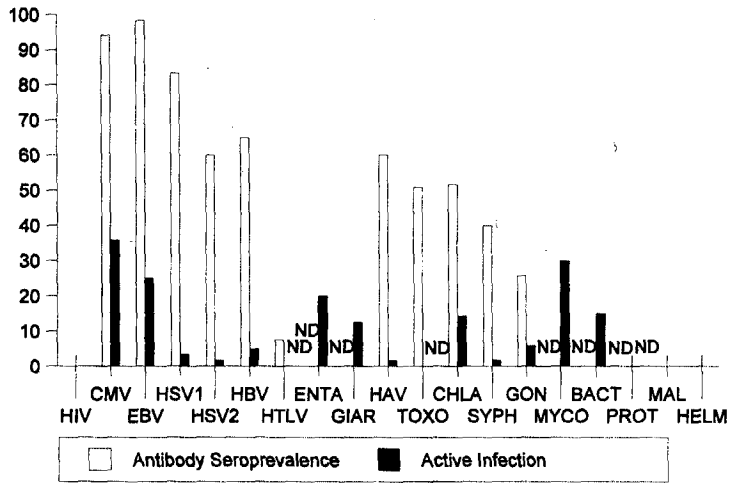
Source: Root-Bernstein, Ph.D., Robert S. *Rethinking AIDS: The Tragic Cost of Premature Consensus* (New York: Free Pr., 1996).

CHART 7
INFECTIONS AMONG NORTH AMERICAN AND EUROPEAN
INTRAVENOUS DRUG ABUSERS



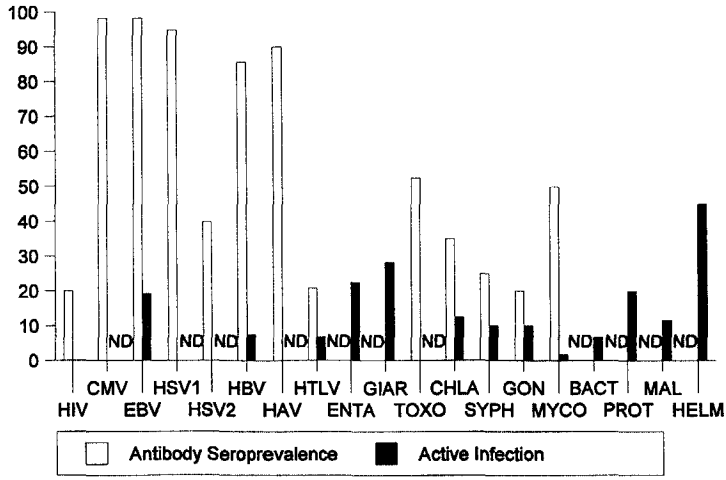
Source: Root-Bernstein, Ph.D., Robert S. *Rethinking AIDS: The Tragic Cost of Premature Consensus* (New York: Free Pr., 1996).

CHART 8
INFECTIONS AMONG NORTH AMERICAN AND EUROPEAN
HIV-SERONEGATIVE HOMOSEXUAL MEN



Source: Root-Bernstein, Ph.D., Robert S. *Rethinking AIDS: The Tragic Cost of Premature Consensus* (New York: Free Pr., 1996).

CHART 9
INFECTIONS AMONG HETEROSEXUALS IN SUB-SAHARAN AFRICA



Source: Root-Bernstein, Ph.D., Robert S. *Rethinking AIDS: The Tragic Cost of Premature Consensus* (New York: Free Pr., 1996).

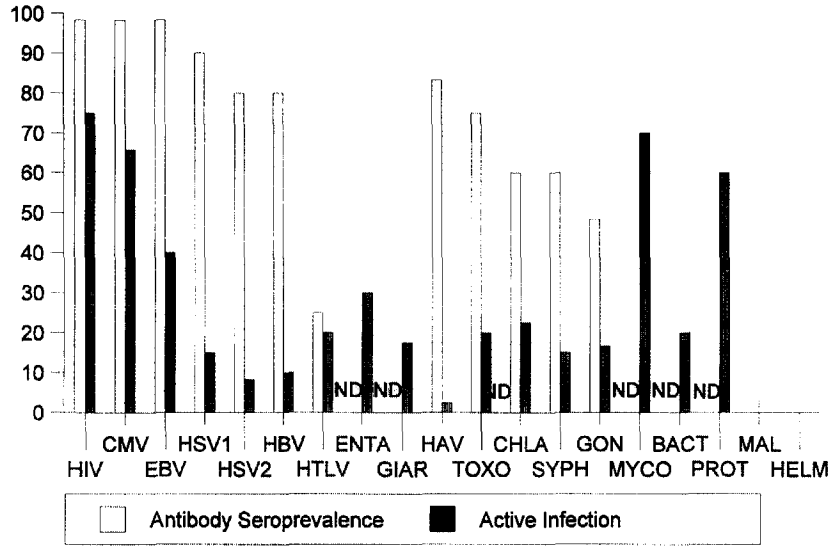
It specifically compares the situation in Africa with the situation in North America. It says that our serological study as well as others demonstrates that heterosexual Africans are frequently exposed, due to hygienic conditions and other factors, to a wide variety of viruses, including cytomegalovirus, Epstein-Barr virus, hepatitis B virus, and herpes simplex virus, all of which are known to modulate the immune system; they recognize it. Exposure to these infections was also observed in the present study and in other studies among American homosexual men. In contrast, the prevalence rates of these infections was much less frequent among American heterosexual controls within this study.

Furthermore, the Africans in the present study are at an additional risk for immunological alterations because they are frequently afflicted with a wide variety of diseases, such as malaria, trypanosomiasis, and filariasis, which is a type of worm causing problems with the immune system and often causes heart disease. These are also known to have a major effect on the immune system. The frequent exposure to these multiple microbial agents could collectively or individually result in immunological modulations rendering the host more susceptible to HIV infection by influencing disease progression and by increased bioreplication of HIV and the killing of T-positive cells. Our immunological data on the Africans in this study support these latter concepts.

What they're saying in layman's terms is that poor African heterosexuals have so many diseases and they are so immune-suppressed that they are much more susceptible to HIV and its effects. If it's true of the Africans, it's also true of all the other groups I showed you, because their statistics look alike. The American, British, and Canadian heterosexuals have a totally different disease profile. Just for comparison, Chart 10

represents AIDS patients. By the time a person has full-blown AIDS, he or she has several concurrent infections; it's very difficult to treat.

CHART 10
INFECTIONS AMONG NORTH AMERICAN AND EUROPEAN PEOPLE WITH AIDS



Source: Root-Bernstein, Ph.D., Robert S. *Rethinking AIDS: The Tragic Cost of Premature Consensus* (New York: Free Pr., 1996).

What do we know about some of these viruses? Well, if you go back to the literature, you'll find out that in 1985, when we didn't know that HIV was definitely the cause, as everybody now says, people such as Jay Levy, who was one of the big AIDS experts at ACT UP in San Francisco, were saying, "We think that cytomegalovirus may actually be necessary for HIV to be triggered. It has to come first." Many people were saying the same thing.

We now know from studies done this year that Epstein-Barr seems always to be present and activated when HIV gets turned on; they always go hand in hand. We even know, and this is very frightening, that giving HIV-positive people a flu vaccination will activate their HIV. It can be quiescent—they are given the vaccine, and all of a sudden they start producing HIV at 100 or 1,000 times the rate they were before. A concurrent infection hyping up the immune system isn't good.

Many people recognize this. Why the public hasn't heard about it is probably due to politics. Luc Montagnier, the discoverer of HIV, has been saying since 1990, "HIV cannot cause AIDS by itself." That's a direct quote. It must have a cofactor. He thinks it's something called a microplasma, which is a new type of very unusual bacteria. There are strains found in AIDS patients, but in no other group. Essentially, he's verified work done by a guy named Shyh-Ching Lo with the Armed Forces

Institute of Pathology in Washington, D.C. Lo has been arguing since 1985 that these new microplasma, which are associated only with AIDS patients, are pathogenic, cause disease, and work with HIV to cause AIDS. That research is still going on.

Bob Gallo, the other discoverer of HIV, is now saying, "Guess what? Herpes simplex type 6 and HTLV work with the HIV and speed the rate at which AIDS develops in HIV-infected people." Tony Fauci last year wrote an article titled, "Multifactorial Nature of HIV Infection."

Harold Jaffe, two weeks ago in a publication called *The Scientist,* made the statement, "It is almost certain that cofactors play a role in the course of HIV infection." I'll be honest—I was glad I was sitting down when I read this. I'm not sure we have anything to argue about on this particular issue anymore, but it's taken an awful long time to get here.

Is AIDS an autoimmune disease? I mentioned part of your immune system attacking you. One part is killing off the other part. This is why many people start questioning whether autoimmunity is a major part of the AIDS epidemic. There is a major problem here. We don't understand what triggers any autoimmune disease in a human being. I can say that flatly. We don't know what causes multiple sclerosis, Lou Gehrig's Disease, or what triggers arthritis; we can't tell you what goes on in any of these things. Now we're talking about AIDS perhaps being an autoimmune disease.

We know that HIV mimics a whole series of blood proteins on white blood cells in the blood system. That's how it hides from the immune system. All pathogens do this. There is a selection process in which molecular camouflage is selected for those things that survive the immune attacker, the things that most like you. It is the same thing that we do when we put on a camouflage uniform and crawl in the jungle. If you look like a jungle, they can't find you. If you look like your own immune system, then the bacteria disappear. The problem is that when you do find them and attack them, you attack your own body. Half the time you're shooting yourself, and half the time you're shooting the other thing. We're actually finding that if we inject these AIDS vaccines that we're making into a human being, we get rid of HIV, but in time we start making antibodies against the white blood cells. The untold story behind this that you probably never see in the newspapers or on the news is that most of these vaccines have had their trials terminated because we think they may actually be killing off the people we're giving them to. That's very frightening because we're not going to get anywhere.

The other side to the story is that we know that we can trigger these same types of antibodies that kill off our own T-cells with things such as sperm antibodies. They are present in AIDS patients. This has been studied in animals for over 100 years. This isn't anything new. We also know that we get the same type of antibodies even in HIV-negative hemophiliacs. Something in those factor concentrates that they're getting can trigger these lymphocytotoxic antibodies, as they're called. This is particularly frightening because it now means that there is a whole series of things that may be triggering these autoimmune disease conditions and adding to the AIDS problem.

I have to say that when we look at Koch's postulates, none of those chimpanzees or macaques that were infected developed any autoimmune problems. Again, this may be

a key that autoimmunity is crucial. If we can get the autoimmunity started in them, maybe we will get a better clue to what's going on. But as I say, we don't know how to do that.

One other thing you should be aware of, which may be important from an actuarial standpoint, is that all AIDS patients get multiple autoimmune diseases. They get every known autoimmune disease that human beings get, whether it's systemic lupus, polymyositis, Sjogren's syndrome, or multiple sclerosis, and so forth. Every single AIDS patient will get a multitude of these. That's very difficult to take from my perspective because even if we can stop HIV in people, a large proportion of them will go on and develop these autoimmune conditions, which we cannot control, and they will wind up dying of those conditions. That's one of the reasons why I'm doing the research I'm doing. I'm afraid that by focusing on HIV we've missed many other things regardless of what the role of HIV is in this epidemic.

Let's go back and look at those earlier charts. What's going on in this 10-, 12-, 15-year lag period? Is this just HIV slowly working away at the immune system? This answer is, I think, too simplistic. I've shown you that there are many other things. People are getting multiple infections. They're getting reinfected with HIV plus many other viruses and sexually transmitted diseases. They're continuing to use drugs, engage in receptive anal intercourse, and are getting the semen to make the antibodies, which will attack the T-cells. They continue to have to use blood products if they're hemophiliacs, and so forth and so on. In other words, it isn't just a simple thing, "Oh, I have HIV. I wait a number of years and I die." Many other immune-suppressive things go on continuously.

I'm arguing that AIDS is multifactorial. Yes, there's HIV; but all the other things I talked about—autoimmune conditions, multiple infections, drug use, problems with blood factoring in semen, and problems in the immune system—have essentially the same effect on the immune system. They're all going to end up being additives or maybe even multiplicatives.

What does this mean? Let me give you several of the possible implications of this. One is we're going to have to look at AIDS in a different way. We're going to have to end up isolating more than one agent. Neither of the agents will be sufficient in and of themselves to cause the disease. We'll have to have them together. We're going to have to go through Koch's postulates, but with multiple things together. Those experiments haven't been done. I'm the first person to be trying them, and those are just being set up now. It's going to be a while before we know the results. I can tell you this isn't anything new. I'm only codifying things that people have done since 1930. Again, it's simply that nobody has sat down and said, "This is another way we can get infectious diseases that is more complex than what we're used to thinking about."

More importantly, we can actually look at many other things in AIDS progression, rather than looking at HIV. In fact, autoimmune markers are just as good. Many studies say that if a person has an autoimmune marker in which all of a sudden the person is making lupus antibodies, its own T-cells are being attacked with antibodies, and you are in big trouble. If you don't develop these, you have a very good prognosis.

What are the markers? Cytomegalovirus and Epstein-Barr virus. As I said earlier, there's some evidence they may actually have to precede the HIV. There's also evidence that they grow at the same rate as HIV. We can measure them just as easily as you can measure the HIV, and they're just as good a predictor of the course of AIDS.

Over the last couple of years, a whole series of studies finally came out on malnutrition being directly predictive of the time course. The more malnourished a person is, the shorter he or she will live. There's some evidence that if we interfere with the malnutrition, we can extend life expectancy.

A number of people, such as my friend Arthur Gottlieb at Tulane University who has been doing AIDS research since the beginning, are beginning to come out and say, "We have to stop looking only at HIV. There are other ways of going about targeting this disease. We can't stop HIV. We can stop some of the other things." Some of the nonretroviral interventions for AIDS are, in fact, out there and have already been tried by somebody somewhere and have seemed to work. There are things such as treating or preventing cofactor infections, eliminating drug use, giving nutritional support, purifying blood and blood-clotting factors to get out whatever is causing those problems for the hemophiliacs and other people, having immune reconstitutions, and giving a number of drugs that are fairly cheap and apparently effective. They are very good not only for AIDS patients, but also for autoimmune diseases and cancers. They seem to help AIDS patients survive longer and help in treating autoimmune complications.

Many of these things are out there that say, we can increase survival simply by targeting cytomegalovirus, by targeting drug use, or by eliminating it in people. Simply giving AIDS patients vitamin A increases their probability of survival. In Africa, this is a very cheap and simple way to start intervening. This has already been tested and was summarized in the *American Journal of Public Health* a couple months ago and it turned out to be very effective. There is increasing general literature on nutritional support, something that most physicians just don't even think about. As long as they're treating HIV, they don't think they have to treat the rest of the patient. It's a shocking state of affairs in this day and age, but true.

The greatest and most interesting data that we have in terms of being able to interfere with the progress of AIDS comes from hemophiliac research. I mentioned that clotting factors seem to cause immune suppression, even in HIV-negative people. On the average, hemophiliacs will have 700 T-cells rather than the 1,200 that most of us have, even being HIV-negative. A number of different drug companies have developed ultrapure or recombatant DNA-produced factors. They have nothing else in them; they are pure factors. When these are given to HIV-positive people, their immune system always stabilizes, and 30% of the time it starts to go back up toward normal. This is so simple. All we're doing is getting rid of the viruses and the antibodies and all the other junk that's in the factor concentrate. If we want proof that there has to be something besides just HIV in there to have immune system activation, this is it. This says that there's much we can do for people that we're not doing.

Imreg-1 is another thing that's being used and also is very effective and one of the very few things that is on the market. It got approval from the Food and Drug Administration (FDA) for full clinical trial, but because of the political climate and the climate in

the AIDS research establishment that we should only be targeting HIV, no one warmed up to it. They have not been able to raise the capital to actually do the final study. Its preliminary data say it's effective. All the data say it's perfectly safe. But they can't do the final clinical trial. I find that a terrible shame.

At the same time, all these data say we can intervene without targeting HIV—maybe the immune system can actually take care of itself for some people. More and more people with HIV are surviving longer and longer beyond the average time that you would expect. They're staying perfectly healthy; many have no immune system dysfunction at all. But what's even more impressive is that there are seroreversions. There are people who have had HIV infection, people who had multiple positive enzyme-linked immunosorbent assay (ELISA) test results, multiple positive Western blot results, and either a polymerase chain reaction or a cold culture. In other words, they have had every test that we have that says they truly had a real HIV infection and it was proved multiple times. Then at some later date, they lost their HIV seropositivity. They lost evidence of having an HIV infection: they are healthy. It's not many people so far, but then it has been assumed that every person who becomes HIV-positive will remain HIV-positive forever and will never serorevert. So people never get retested after they're verified.

The most interesting groups are the hemophiliacs. I spoke to a group down at Tulane. After my talk, a graduate student got very excited and retested the 100 people in their study, and ten turned out to have seroreverted. They're all healthy. These are all severe hemophiliacs. They think that if they look at the general hemophilia population, they will find that 20–30% have seroreverted and remain healthy. This means there are people surviving HIV. It shouldn't be surprising that no disease is 100% fatal, but this is the only one that people have claimed is.

What does this mean in terms of prevention, prophylactics, and so forth? Do we throw out the condoms? Absolutely not. Many people immediately say, "You're saying we're never going to get it. Why bother?" Remember what I'm telling you is that many other things can set the stage; many of those are sexually transmitted diseases. In fact, one of the reasons that safer sex has worked so well with homosexuals is probably because we're not stopping just HIV but the cofactors as well. If you think about it, that's a multiplicative effect, it's not a simple additive one. If both things must cause the disease and if we can stop both of them or all of them, we'll be in very good shape.

The Gay Man's Health Crisis Center in San Francisco has continuous blood samples every few months for years. They know exactly when every one of these people seroconverted to HIV-positivity. The number of new infections by 1987 or so was close to zero. Most of the people in the gay community who are getting HIV infections now do it purposely by having risky sex. How many times can they have sex before they get HIV? It makes it exciting. Or, "My friends are all dying and I feel terrible that they're all dying and I have to join them." Also, some young men just don't believe there really is an AIDS epidemic. That's scary, but those account for almost all the new HIV infections in the gay community. They get HIV and then become diagnosed with AIDS. What we are seeing now is that AIDS today, especially in the gay community, is all a response to that very first high rate of infection. What we should be seeing is AIDS plateauing or going down.

I want to read you something that's really very interesting. A study by Max Essex, who is a gerontologist and head of AIDS research at Harvard, was presented in a talk, which is reported in *Science* [Vol. 270, page 31, October 6, 1995]. One of the slides he showed presented the fact that there were two types of epidemics going on. Epidemic one is in the U.S. Epidemic two is what's going on in the rest of the world. The rest of the world, he said, is going exponential, and there will be a major problem there. But interestingly, he made no comments about epidemic one whatsoever. The press didn't pick it up; there are no comments anywhere. Let me read you what he says: "Epidemic One: U.S. and Europe location. Cause: HIV type 1B. Number infected: somewhere around a million or a million and a half overall in the U.S. and western Europe." That's much lower than most of us expected that number to be. Epidemic status: plateaued or decreasing. Australia announced that the number of AIDS cases this year is down dramatically from last year. So did Britain. The U.S. has plateaued. Canada has plateaued. Nobody is telling you any of these things. But if you look at the data, that's exactly what we would expect to be happening. "Exposure risk: blood and rectal bleeding are the major routes." We're not all at risk because we don't all have exposure to blood or rectal bleeding. It's all right there, and nobody is making any comments; pretty strange.

Here's the risk (Chart 11). Every measure we have of drug use, and there are a lot of data, shows that drug use is still going exponential. Crack cocaine, intravenous use of cocaine, even now opiates again, are growing so fast that we can't even keep up with it. If AIDS continues, it's going to be because we can't control what's going on. Here's the problem: we must stop drugs. We must stop the malnutrition that goes along with it, the social conditions, all sorts of things. That's a much harder problem to solve than stopping HIV.

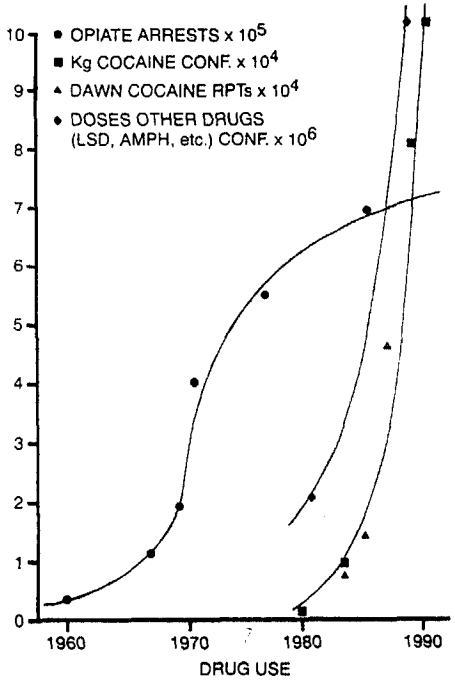
Let me end with a couple things I hope will be of direct interest to you as actuaries. I don't know exactly what data you can get hold of. Here are some critical studies I think need to be done. One is hemophiliacs. More than 90% of hemophiliacs in the U.S. are thought to have been infected with HIV by 1984 or 1985. Fifty percent should now have AIDS if we use the standard data from Robin Weiss and all the other people. As I said, I don't think that's true. However, there are no long-term studies on large groups in the U.S., Canada, Britain, and similar countries. We don't know how many hemophiliacs are alive from that period, but half should be dead or have overt AIDS right now. This is a critical study to read in order to know what's going on.With regard to hemophiliacs retesting, there are no large-scale studies of seroreversions in hemophiliacs or anybody else.

As for heterosexual AIDS, as asked earlier in the talk, Are there tertiary cases? This is critical for understanding the spread of AIDS. Nobody is looking. Either they aren't there, and I think we should simply say we looked at as many as we could and they're not there, or nobody will look. Are there any no-risk heterosexual AIDS cases? New York City supposedly reports there are only about eight no-risk people in the entire epidemic. It has probably one of the best groups to track down everybody and follow up and say, What are you really doing? They actually go in and interview people.

Many people say they are at no risk, but then there are problems that have to do with some guys who are having sex with other men and don't say that they're homosexuals. It all depends on which question you ask. They ask them if they ever use drugs, and

they say, "No." The questioners will say they have to use the bathroom and open up the medicine cabinet and find the drug paraphernalia. People lie, and we need to know that.

CHART 11
USE OF ADDICTIVE DRUGS IN THE UNITED STATES
1960–90



- Opiate arrests in hundreds of thousands
- Kilograms of cocaine confiscated in tens of thousands
- Drug Awareness Warning Network (DAWN) cocaine reports in tens of thousands
- Doses of other drugs (LSD, amphetamines, barbiturates, etc.) confiscated in millions.

Source: Root-Bernstein, Ph.D., Robert S. *Rethinking AIDS: The Tragic Cost of Premature Consensus* (New York: Free Pr., 1996).

What's the rate of seroreversion in heterosexuals? There isn't a single study. We don't even know the rate at which they develop AIDS, for that matter. Is the rate of HIV in the first-time blood donors changing? Just look at the standard rate of HIV in the population—we don't have any general study. Every one that the NIH has tried to set up has been stopped, so we have no data. For all groups, is the rate of HIV in people entering the armed forces, the Peace Corps, etc., changing? Everybody gets an HIV test when they go into these things. What happens to these data? As I said, the CDC stopped making it available in 1989; that should be public information. Also for all groups: Is the rate of HIV on new requests for life and medical insurance

changing? That's something you should have direct information on. I know when I moved to a new university, I had to have an HIV test for my life insurance because I have a large policy. A stable group of people are getting new insurance over the years. They're probably a fairly stable group in terms of income and other things. This should at least give us some measure of what's going on.

Everyone needs to know if we can track and predict the future of AIDS and other epidemics by means of surrogate markers. It would be interesting to go back and look at the data we have on HIV-positive people and ask what their health status was prior to HIV infection. Were they making many insurance requests to pay for syphilis tests and treatment, general ulcers, and so on? Again, nobody has ever bothered to do this. This could be interesting because we might not only be able to look retrospectively to see if we could have predicted the epidemic, but we might also be able to track what's going to happen in the future. This may be a general way of looking at many new diseases and how they're going to emerge. New diseases tend to emerge on top of other diseases. They don't emerge totally by themselves anytime, anywhere.

Do prior common diagnoses or cofactor exposures predict a poor prognosis? That is, when people are diagnosed with HIV, what else were they diagnosed with, either at the same time, immediately before, or immediately afterward? Can we use this to say they will die in the next 5 years, or will they survive for the next 20 years?

Here's what it comes down to: there are all those facts out there and I have simply given you a different selection than you would have gotten from somebody from the NIH and CDC. Who are you going to believe? I don't think you should believe any of us. I think you should go out and check for yourself; that's what science is all about. But the only way you can do that kind of checking is to make sure you have an open mind—but one that will accept data that don't fit your preconception. The reason I keep giving talks such as this is because I want to open up people's minds. I don't care whether I'm right; that's not the point here. The point is that we're not controlling HIV or AIDS by anything we're doing medically. That means we have to look at it in different ways if we're going to succeed in stopping people from dying here and in the rest of the world.

MR. DAVID M. WELSH: I found your biological explanation to be fascinating. While listening to you, it occurred to me that maybe this is as much a political problem as anything else. As long as AIDS can be presented as a general threat to the population, that supports research funding; that's one aspect of it. A second is that if it's a general threat, then nobody is responsible. It's not a consequence of choices people have made in the way they manage their lives. I'd be interested in your reactions to those ideas.

DR. ROOT-BERNSTEIN: Let me start with the latter first. One of the things I was told when I came out with my book a couple years ago was that I should change my phone number, change my address, and do everything else because all the people who were in various risk groups were going to send me hate mail, bombs, and so on. None of that happened. ACT UP New York, for example, reviewed the book and said, "We can't believe nobody is actually implementing this research program." If any group was going to go after me with a hatchet, it would have been ACT UP New York. The gay community, the hemophiliacs, and now all people are at the point where they don't

care what the cause is anymore. They would just like to have something they can do about it. It's clear that the medical community isn't doing anything for them right now.

Part of the politics has changed dramatically. If you mentioned receptive anal intercourse in 1985 or 1986, the gays would go after you. You weren't supposed to talk about specific sexual practices. Now it's fine. They want to know what the risk factors are so that they can avoid them. That's the only way you're not going to get AIDS in this day and age. You can see from those graphs that education made a huge difference in the gay community. They know more about AIDS than most of the caregivers know about AIDS; it's absolutely amazing.

Part of the politics is misrepresentation or misthinking about what the risk groups are worried about and so forth and so on. We haven't caught up with the changing times. There are certainly politics. One of the most interesting things that's happening with the people in AIDS research is that they're all leaving their positions. You want to track what's going to happen with AIDS research, look at the following. Bob Gallo just resigned from the NIH and got his own separate research institute at the University of Maryland. Tony Fauci stepped down as head of NIH research on AIDS. Harold Jaffe just stepped down; he's going to go to Emory University as head of its epidemiology department. James Curran has just resigned and he's going to Emory also.

Why are they all leaving now? I want to make a prediction. This may be totally wrong, but my guess is they know that they can't finagle the numbers anymore. There's something I didn't throw in here—all the AIDS data you get are finagled in some way. The AIDS definition has changed formally five times since 1984; each time the number of people included in the AIDS definition is larger. If you say in 1984 there will be so many hundreds of thousands of people by such and such a date, and you're not there and you increase the number of people you include in the definition, and you keep doing that, you keep getting close to your prediction, even though you're not really playing fair.

In 1993 they enlarged it as far as they could. They literally doubled the number of AIDS cases overnight. Almost nobody picked this up. Some of the papers actually reported it, but that's what happened. They're still grossly under the number that they were predicting. I think they see there's no way that they can now enlarge the group anymore. That means the phenomena I showed you at the end with the numbers of cases in gay men and everything else going down has plateaued no matter how you look at it, even with all the AIDS definition changes. It's going to start going down. So, yes, funding will start dropping off. There hasn't been a heterosexual epidemic. Congress will start catching on and there's no way to push this anymore.

What scares me is that people are still dying. Moreover, this is becoming a bigger and bigger problem in the Third World because it's piggybacking on the malnutrition and all the diseases that are out there. It would scare me to death if we turn our backs on the rest of the world just because it's not our problem anymore. It will become our problem again when all those people start dying. I don't know if we're bright enough in this country to see it that way. Who knows? We'll see.

MR. MARK ALAN CHESNER: How do you respond to the assertion that for some people the disease has disappeared simply because they had a very weak form of the virus?

DR. ROOT-BERNSTEIN: My first response is, What does that mean? There are people who have written that. What's a weak form of a virus? There is no evidence at this point that there are more or less pathogenic strains. If the virologist can actually publish a paper and say he or she found one that's more viral than the other, great, I could accept that maybe that's actually true. They have looked at people who have seroreverted from the type of HIV that was present. All these people have different types of HIV, and there isn't one type that everybody who seroreverted has. Every single one has a different type. I don't think that your assertion makes sense.

Other things are going on that have not been looked at formally so far except for a couple studies. All the people I talked to who have seroreverted and all the small studies that have been done on seroreversion say that the people who seroreverted changed their lifestyles dramatically. That doesn't mean that they were gay and suddenly didn't become gay. What it means is they were gay and instead of going to bathhouses every week, they got a single sexual partner and started using safer sex practices. They stopped using drugs, antibiotics, and so forth. Or if they're heterosexual, they immediately said they would not go out there and have sex with anyone at the bar at night; that's not a good idea, obviously. Almost everybody reported going on a high-nutrition diet, but that's one of the reasons nutrition needs to be looked into.

My answer is, I don't think it's right, but I would really like to see a formal study that checks into it. As I say, I don't care what the answer is here, as long as we get it. What scares me is that people come up with these pseudoanswers for which there's no evidence, they write it off and then don't bother finding out whether they're right or wrong or bother to look at anything else.

MR. MICHAEL J. COWELL: You said that one of the studies that you recommended would be the relationship between HIV seroprevalence found in blood testing by insurance companies and the presence of the disease. Those studies have been done, and they do show a very high correlation of HIV seroprevalence by state, according to where the insurance was applied for, with the estimate of HIV prevalence in that state. They are leveling off. They are showing the same tendency to decline as is the amount of insurance claims reported to be AIDS-related or HIV-related in our industry studies. So this is consistent.

As a life insurance risk manager, our current tests are for HIV; those are the ELISA, the Western blots, and so forth. Given the situation you described, what alternatives do we have in our testing protocol going forward until we can absolutely determine what the other cofactors are?

DR. ROOT-BERNSTEIN: Several are very highly suspected to be cofactors and always turn on at the same time or before. There are things such as cytomegalovirus for which there is a simple test already available. Again, there are simple blood tests available for Epstein-Barr virus. There are some general tests available for the microplasmas, which are the things that Lo and Montagnier are claiming are cofactors. Those are three things that are already on the forms that the physicians have. They

could literally just check a box when doing the blood work and add those on. I don't even remember what the cost is, but I think it's actually less than the ELISA and Western blots for HIV.

Other fairly simple things can be done, such as screens for lymphocytotoxic antibodies. Those cost more, but you will pick up people not only at risk for HIV, but also for many autoimmune diseases; it's nonspecific. This is something that may give you a much better handle on general autoimmunity periods, and those are going to be expensive cases no matter what. Those are the simplest, direct things that are already available.

Malnutrition is another thing you might want to look at. I don't suspect that's a major problem for most people you're going to be insuring. But interestingly, regardless of risk group, this is a problem. There are gay men who are eating right and doing everything else. Apparently, it's the number of times they've been ill that depletes the immune system. There are hemophiliacs who are having malnutrition problems and so forth. Again, the tests are available, but physicians almost never order them. In this case, they're correctable, which is even nicer. Do something about it when you tell them to go take care of this problem so we don't have to deal with it in a more severe form a couple years from now. That doesn't mean to not do HIV tests, by the way. You can add these on to HIV and probably get a much better picture.

MR. ROBERT G. PLUMB: As a member of the Health & Care Committee of the Institute of Actuaries, I studied this problem for a good number of years, partly in long-term disability as well as in the medical field. As far as the United Kingdom is concerned, mercifully, we have seen a gradual drop-off on AIDS cases, and a few years ago, the Department of Health started to reduce funding for AIDS as such. It caused a tremendous outcry until it was explained why. Some of the specialist units have found it very difficult to be filled.

My question must come to you on the Epstein-Barr virus. You stated that this comes up with HIV. There is an underwriting concern in the U.K. over some meat products about some of the viruses. Will we see, if Epstein-Barr becomes a problem for us, that this will produce HIV and AIDS through that field? Or is that just something totally unrelated?

DR. ROOT-BERNSTEIN: I don't think that will be a problem. There are several possibilities. One is that the Epstein-Barr types that we're seeing related to meat products and so forth may actually end up protecting human beings against natural strains that are out there. We may have a case such as what we had with cowpox and smallpox: cowpox protecting people against the smallpox. There may actually be a benefit; that's one way of looking at it.

Another is it may simply spread Epstein-Barr more generally through the population. But if you're healthy, Epstein-Barr gives you at most mononucleosis and you get over it after a few weeks and you're fine. Most of the people in this room have probably been exposed. A few of us are probably even carrying Epstein-Barr right now. That's not a huge problem, I don't think.

It will be a problem if, in fact, we're reintroducing Epstein-Barr at higher rates into people who are already HIV-positive. That may trigger their latent HIV or fairly quiescent HIV or work with the other things such as cytomegalovirus and so forth, instead of just take away the speed, or the rate at which they end up developing AIDS. That would be definitely unfortunate.