Introduction to Long-Term Survival with AIDS/HIV
by Dr. Joseph Sonnabend

AIDS is a new disease — entirely new or newly recognized. This means that we have had the opportunity to study it for only 13 years, and although we have made many advances there is, of course, much to be learned. As is to be expected when there are huge gaps in understanding, many speculations are put forward and sometimes these are presented as if they were proven facts. The issue of survival is an example. Very early in the epidemic it was stated that HIV infection inevitably led to AIDS and death, but we did not and do not know if this is the case. Are those individuals who remain well despite being HIV seropositive for a prolonged period just at the far end of a distribution curve that describes the varying lengths of time it takes to develop AIDS? If enough time passes, will they develop AIDS, or do such individuals include those who will never develop AIDS? Whatever the situation, it is important to study these individuals to try to identify factors that might either prolong their disease-free period or protect them from developing AIDS.

There have been several studies using different definitions of long term survivors, however generally these studies focus either on patients who maintain a normal CD4+ cell count over a long period of time, or patients who have a low CD4+ cell count but who remain otherwise healthy for a long period of time.

In all known infectious diseases, not everyone exposed to the microorganism becomes infected, and amongst those infected I do not think that there is an example of a viral infection in which 100% of infected individuals become ill. Rabies is often given as an example of an invariably fatal infection. However, there are documented reports of sub-clinical infection in some animals, and even reports of recovery in a very few humans.

In the case of infectious diseases generally, some factors might be expected to more or less influence whether or not disease develops as well as the severity of the disease. These factors fall generally into three categories: firstly there are those connected with the infectious agent. Some examples include the organism’s efficiency in being able to infect the host, and its virulence once infection occurs. Secondly, many host factors, including genetic factors and immune response, could influence the course of infection. Lastly, environmental factors could also play a role and this category would include among other factors, the effects of concurrent infections with other agents, behavioral factors, and therapeutic drugs.

In addition to the infected individual who remains well with no clinical abnormality (in the case of AIDS this includes maintaining the CD4+ count) there are those infected individuals who do well despite showing some clinical signs of infection, and in HIV disease this would include individuals with low CD4+ counts for prolonged periods who remain well. Clearly such individuals exist and must also be studied.

For many people living with AIDS/HIV today, there is a hope that studies will indicate some behavioral factor correlated with long-term survival. Such a factor would enable individuals easily to influence disease progression by changing behavior. Unfortunately, no such factor has yet emerged. But ongoing studies of long-term survivors are nonetheless important. As we clarify our understanding of AIDS, and of biological factors that may influence progression, we may also develop new ways of treating the disease. For example, if we can correlate a certain kind of immune response to long-term survival, we may be able to duplicate this response in those who do not develop it naturally.

CRIA is proud to have worked together with the Treatment Action Group (TAG) and the Gay Men’s Health Crisis (GMHC) in presenting the Community Forum on Long-term survival with AIDS/HIV, to inform people with HIV about this vital research.

INSIDE...Presentations on Long-Term Survival with HIV/AIDS by:

Aldyn McKean
Long-Term Survivor..........................p. 2

David Ho, MD
Aaron Diamond AIDS Research Laboratory..........................p. 4

Susan Buchbinder, MD
San Francisco City Department of Health..........................p. 5

Joseph Margolick, MD
Multi-Center AIDS Cohort (MACS) Study..........................p.6

Jon Ende
Long-Term Survivor..........................p.7

immune-system Basics..........................p.3

Glossary..........................back page

SPECIAL ISSUE ON LONG TERM SURVIVAL 1993
Different studies of long-term survivors have used different definitions of long-term survival. For example, normally in HIV-infected people, the CD4+ cell count is expected to gradually decline like this:

![CD4 cell count over time](image)

When this decline is averaged, it has a smooth, negative (downward) slope, like this:

![CD4 cell count over time](image)

One definition of long-term survival, therefore, is a positive (upward) CD4+ slope, like this:

![CD4 cell count over time](image)

In other words, after a significant time period, the patient has more CD4+ cells than when he or she started.

Another definition of long-term survival looks at the relation between CD4+ cell count and the development of disease. The patient may have a very low CD4+ count, but has remained free of disease symptoms for longer than would be expected:

![Symptom-free patients over time](image)

Finally, researchers may look at people whose CD4+ count declines much slower or faster than the statistically average patient:

![CD4 cell count over time](image)

Aldyn McKean
Long-Term Survivor

Because I think it’s important for you to get a sense of who we long-term survivors are, I’m going to talk mostly about my personal experiences living with HIV and AIDS. I believe that, based on my personal sexual history, I was infected in 1978. In 1980 I first began to show signs of compromised immunity, experiencing recurrent warts and herpes simplex that did not respond well to treatment.

My first T-cell tests were in 1983; my count was 162 in February of that year and 102 in August of the same year. When I asked my doctor what this meant, and he said, "Well, you might want to think about putting your affairs in order." In essence he was telling me that I was going to die soon. Unfortunately, that’s a common experience among people who’ve lived a long time with HIV/AIDS.

I can tell you that the first step I took to put my affairs in order was to find a new doctor. That also, interestingly enough, is something that one finds with people who’ve lived with the virus for a long time. Dr. Robert Remien has been studying extra-long-term AIDS survivors, (defined as people who were initially interviewed by Remien three to nine years after an AIDS diagnosis under the pre-1993 definition and who survived until a second interview one year later). He found that this group of long-term survivors is distinguished from other people with AIDS by being what Remien calls "superb medical consumers." He noticed that they were actively involved in their own medical care, finding out as much as they could about the disease, and participating in decision-making with their doctors regarding treatment strategies. He also found that this group of survivors "were not reluctant to change doctors because of dissatisfaction...or to get second and third opinions."

So one of the things that I think has contributed to my own long-term survival is that very early on I searched for and found a doctor who
(1) is knowledgeable about HIV, (2) attends the major AIDS medical conferences, (3) has a large number of HIV + patients, and (4) -- perhaps most important of all -- is someone with whom I have a good relationship and can communicate with easily.

As far as a regimen is concerned, I make it a habit not to tell other people what to do, but I'm happy to share with you what I do. I prophylax against PCP (Pneumocystis carinii Pneumonia). I also take 400 milligrams of acyclovir twice a day. I do not take any of the anti-HIV drugs -- AZT, ddI, ddC, d4T, etc. I briefly took AZT in 1989 and found that my white blood cell count went through the floor. I later took ddC but developed mild peripheral neuropathy -- a tingling in my fingers and toes -- and so had to stop that drug as well. As a result, I have come to the opinion that, for me, these drugs do more harm than good.

I do concern myself with nutrition: I eat a good, balanced diet, and take vitamin and micro-nutrient supplements. I exercise regularly and usually get plenty of sleep. I don't obsess about any of these things, but I do think they're helpful. I wish that there were definitive studies out there that could show whether or not these behavioral factors are associated with longer survival. Sadly, we really do not have such studies at this point, so most of what I do is based on common sense and guess work.

It's clear from some of the psychosocial studies that have been done that people who do well with the virus are people who have good support networks -- both organizational and social. Long-term survivors are more likely than others to have good solid relationships in their lives, and I therefore think it's important to nurture one's relationships to lovers, family and friends.

I'm a member of ACT UP/New York, and I think that being an activist is therapeutic in some ways. It puts me in a situation in which I'm constantly surrounded by people who have access to the latest treatment information -- people with whom I feel comfortable talking about my health, and who empathize with my situation, because many of them are also HIV +. Being an activist also contributes to my own empowerment; I feel that I'm engaged in activities that are of direct benefit to my health.

What has mostly been addressed tonight has been healthy long-term positives -- i.e., people with high T-cell counts. There are at least two other groups that I think are important to study: (1) people, like myself, whose T-cell counts have been below 200 for many years and (2) the first group of long-term survivors that was ever identified, which consists of people who continue to live for many years despite having an AIDS-defining condition. The usual definition of this latter group was proposed many years ago by the US Centers for Disease Control and stipulates that long-term AIDS survivors are those who have lived for at least twice the mean period of survival for the particular opportunistic diseases that they have.

I would like to close by pointing out that research on long-term survivors is expensive, and while there has recently been an explosion of interest in the subject, the necessary funding increases have not followed. It is essential that we translate this interest in long-term survivors into more resources devoted to their study.

---

SOME IMMUNE SYSTEM BASICS
(Excerpted from an article in Positively Aware)
By David Thomas

The immune system has two attack strategies. One, called "cell-mediated" immunity (CMI), uses T-cells for rapid, initial protection and to clear the body of infected cells. The other, called "antibody" (or "humoral") immunity, uses B-cells to produce antibodies that can prevent cells from becoming infected in the first place. One role of antibodies is to attach themselves like neon signs to pathogens, marking them for destruction by immune cells.

The two strategies may be somewhat exclusive of each other. The stronger the CMI, the weaker the antibody immunity, and vice-versa. A growing body of evidence shows that the CMI response is much more effective against HIV infection than antibodies. This may cause a problem as infection intensifies, antibody production is stepped up, and the CMI grows weaker.

All these players and battle plans are efficiently orchestrated by chemical messengers called cytokines. Different kinds of white blood cells secrete different cytokines, although CD4+ cells play a leadership role. Some cytokines step up CMI, some step up antibody production, and others stimulate or repress growth of certain kinds of white blood cells. HIV infection can disrupt the natural pattern of cytokines, wreaking havoc indirectly on the immune system.

This is an exaggerated, simplified account of how parts of the immune system work -- which no one understands perfectly anyway. But what should be apparent from this discussion is that more "basic" research into how immunity works must be conducted.
In order to study the predictors of long-term survival, we’ve got several scientists looking very closely at a few patients. We’ve defined long-term survivors as people who have measurable HIV antibodies, are asymptomatic with normal, stable CD4+ cell counts, and who have documented infection lasting more than ten years (generally documented through stored serum samples). As Dr. Sonnabend pointed out, there are three key things to investigate in order to determine why some people become long-term survivors of HIV infection: host factors, virus factors and immunological factors.

First, we asked if long-term survivors had CD4+ cells that were partially or completely resistant to HIV infection. Although results aren’t in on this yet, my gut instinct is that we will not find that the cells are completely resistant. It is likely that the CD4+ cells of long-term survivors will be slightly more resistant than those of other HIV-infected people, however we do not expect a major difference. We are now doing these tests.

There are basically two kinds of immune response (see related story on page three): we are studying both.

We are now studying levels of neutralizing antibodies in long-term survivors. Neutralizing antibodies bind to antigens and, in the case of viruses, prevent them from infecting new cells. So far, we haven’t found major differences in neutralizing antibody response between long-term survivors and other HIV-infected people, however this study is ongoing.

We’re also looking at the cell-mediated immune response, by measuring levels of cell-killing immune cells. When a person is first infected with HIV, they have a huge burst of viral activity, which is then controlled by the cell-mediated immune response. Results from this work are not yet complete, however it is possible that we will find that long-term survivors are able to mount a CMI response that targets a portion of the virus that is required for infection, and that is conserved (does not mutate).

Doctors at the University of Massachusetts have studied one long-term survivor, and found that his CMI response is actually lower than normal, however we don’t know what this means.

We’re also looking at virological factors, such as levels of virus in the blood. The five long-term survivors we’re studying so far seem to have very low levels of HIV in their blood. In 3/5 patients, we could not culture virus from their blood. We haven’t yet tried to culture lymph nodes. In one of these patients, several labs have unsuccessfully tried to culture virus from his blood.

In the other two patients, we consistently find only very low levels of HIV in the blood. One of these two patients is sometimes negative for viral culture, but sometimes has low levels of virus.

Therefore, we are looking to see if there is something unusual about these viruses in long-term survivors. Obviously, these kinds of tests can only be done on patients with culturable virus.

So far we’ve found that all these patients are infected with one type of virus, known as "non-scycntia inducing" or "NSI" virus. Scycntia are giant clumps of immune cells that form in the presence of some strains of HIV. Long-term survivors’ viruses do not seem to cause scycntia formation.

We’re also looking to see if these viruses are naturally attenuated. This would not be unusual -- some strains of poliovirus, for example, do not cause disease.

We’re looking at specific genes on the viruses to determine whether or not these genes are functional. Specifically, we’re looking at a set of genes that “turn on” HIV's reproductive mechanism. These genes are called "tat" and "LTR." Also, since we know that the envelope protein surrounding HIV is necessary for the virus to infect cells, we’re looking at "ENV," the gene that makes this envelope protein.

Also, a group of scientists working with monkeys have shown that, when they remove the "NEF" gene from the monkey version of HIV, the virus ceases to cause disease in the monkeys. Instead, it produces a syndrome that looks very much like what we see in long-term survivors: low levels of viral replication, no CD4+ decline, and no clinical disease. These monkeys also become protected against infection with more virulent strains of virus.

We have an early finding of a defective NEF gene in a long-term survivor.

If these are actually naturally attenuated viruses, they might serve effectively as vaccines, however it is probably not possible to test this hypothesis at this time.

Finally, I think that I should share my frustration with you. Right now, we have lots of different labs working on lots of different long-term survivor cohorts. But to ensure that we produce meaningful information, we need a coordinated, multi-pronged approach that studies many different factors in one cohort. I’d like to encourage people to share their research materials, and their sera and tissue samples, and to ask that we all work together.

We also need research volunteers. I’d like to ask people who think that they fit our definition of long-term survivors to call my office at (212) 725-0018.
Susan Buchbinder, MD  
Chief, Research Branch, AIDS Office  
San Francisco, City Department of Health  
Investigator, San Francisco City Clinic Study

Our cohort of patients derives from a study on hepatitis B conducted between 1978 and 1980 by the San Francisco Department of Health and the Centers for Disease Control. We recruited 6,704 gay and bisexual men from the sexually transmitted disease clinic in San Francisco, and we stored samples of their sera for future testing.

In 1983, we contacted the men from our earlier study and asked them for permission to test their stored blood for HIV antibodies.

Approximately 3/4 of the men from the original study are now HIV infected. We are currently studying HIV-infected men for whom we were able to establish the date of their seroconversion plus or minus twelve months. We get information regularly on their sexual practices and recreational drug use, and we do regular blood work and clinical evaluations.

First we tried to find out how long it took on average to progress from HIV infection to CDC-defined AIDS. We used the 1987 CDC definition, and therefore did not count patients who were without AIDS-defining infections or malignancies who had less than 200 CD4+ cells. On average, these patients developed AIDS within ten years after infection.

After ten to fifteen years, 64% of men infected with HIV have AIDS. Another 6% without AIDS have <200 CD4+ cells/mm³. 11% have 200-500 CD4+ cells/mm³. Another 11% were lost to follow-up, and 8% have CD4+ cells counts of >500 cells/mm³ (see pie chart).

Then we tried to determine why those 8% remain healthy. We looked at behavioral factors, such as sexual activities, recreational drug use and life-enhancing activities such as exercise and diet. To date we haven't found any correlation between these behaviors and long-term survival.

We also looked at CTL response, antibody response, viral factors and host genetic factors. This is work-in-progress, and very preliminary.

So far we've found several subgroups of long-term survivors, implying several different factors influencing rates of progression. My personal bias is that we will not, ultimately, find that there is only one factor.

I suspect that we will find several factors, which may lead us to several different ways of treating HIV disease.

We're looking for unusual CTL responses in long-term survivors. This could be a CTL response to many parts of the virus, a response to a part of the virus that can't mutate and remain functional, or it could be a response that is remarkably effective in killing infected cells.

We're also looking at suppressor cells. These cells function by stopping viruses from reproducing inside infected cells. We are working with Dr. Jay Levy, from the University of California in San Francisco, who thinks that he has found a factor secreted by suppressor cells that stops HIV from replicating. If this works out, it might lead to new treatments to boost this factor in people who don't produce it naturally, and thereby control HIV reproduction.

We're also looking at patients' genes, to see if people with some genetic types progress more slowly than people with other genetic types. We're looking at lots of genes, but mostly at the genes called the Human Leukocyte Antigen (HLA) genes. These are the genes that allow the body to distinguish between self and non-self, and to mount an immune response to non-self objects. This system protects against autoimmune diseases.

We have begun to find some correlation between HLA subtypes and long-term survival. This correlation is not 100% -- some patients with the special HLA subtype get sick, and some patients that don't have it are long-term survivors. But the correlation is much stronger than you would expect to happen randomly. While our work on this is preliminary, there has been some confirmation from other laboratories.

If we can find such a correlation, it would suggest that long-term survival is not random. It would suggest that long-term survivors aren't just on the lucky end of the bell curve -- that something is making them live longer. Again, this might lead us to new treatments for HIV disease.

Finally, we are looking at some viral characteristics of long-term survival. Some long-term survivors have a lot of virus. We are investigating whether these patients are actually infected with a weakened or non-disease causing strain of HIV.

Again, it is important to emphasize that we're probably looking at several factors that influence long-term survival in people with AIDS/HIV.
Joseph Margolick, MD
Chair, Immunology Committee
Multi-Center AIDS Cohort (MACS) Study

I’m an investigator with the Multi-Center AIDS Cohort Study (MACS), which studies the natural history of HIV disease in a group of 4,954 gay men.

When the study began in 1983, there was no HIV test, but serum specimens were saved, and we were eventually able to find out that about 1/3 of our participants were HIV seropositive when they entered the study. We set out to ask which participants who were seropositive at entry were the most successful in controlling the disease. I’m going to describe the types of designs that we’ve used to approach the phenomenon of long-term survival. I’ll also describe our populations of long-term survivors, and tell you what kinds of tests we’re doing on them.

Participants are seen semi-annually, and we began the study at visits 3 & 4 (1.5 - 2 years after study entry). We started by trying to identify those individuals who had no CD4+ decline since entry (positive slope), and had never taken antiretroviral treatment. Out of 493 HIV+ participants who had not taken treatment and who met our follow-up requirements, we found 67 who had experienced no decline. We stratified the 493 participants according to their rate of CD4+ decline. 163 participants were labeled average decliners, and those participants had an average decline of 10 CD4+ cells per year. Participants in the lower 25th percentile were categorized as fast decliners, and those participants had an average decline of <53 CD4+ cells/year.

We then matched slow, average and rapid decliners according to their baseline CD4+ count. We also matched participants according to research site, in order to ensure that any differences we saw weren’t based on laboratory variations. Participants CD4+ counts fell between 400-1200 CD4+ cells.

We found groups within the study who stabilized at any given CD4+ count. The mechanisms for stabilization may differ according to the stage of disease at which the patient stabilizes. There were no laboratory or behavioral differences at baseline that would distinguish the groups. There were slight CD4+ differences at baseline: the no decline group had the highest CD4+ count at baseline, the average group had slightly fewer cells, and the fastest declining group had the lowest CD4+ at baseline.

There were no significant differences in history of sexually transmitted diseases, serum immunoglobulin levels, immune activation markers, behavioral characteristics, history of viral infections, or antibody titers. We had to borrow Dr. Sonnabend’s phraseology, a well-controlled study, but it didn’t tell us very much. But we hadn’t done studies of changing immune system function, antibody levels, or viral replication studies. Therefore, we designed a prospective study to find out more about our long-term survivors.

Many of same participants from the earlier study enrolled; however, because the fastest progressors had often been diagnosed with AIDS, or had died, we studied only two groups: those who had average CD4+ cell declines, and those who had no declines. We only counted participants who had more than 800 CD4+ cells. This group consisted of 43 participants in the MACS -- 2% of those who were initially seropositive. Of those 43 participants, 19 had positive CD4+ slopes.

We measured many of the same parameters that Dr. Ho and Dr. Buchbinder have mentioned, including CD4+ cells, CD8+ cells, viral load (both DNA & RNA, in order to measure cells with latent HIV and cells that are replicating HIV), neutralizing antibody levels, and we did lymph node biopsies in a subset of participants to determine levels of HIV in the node even when virus levels are low in peripheral blood.

We may have found lower levels of infected cells in the nodes of long-term survivors than in other participants. This is still a preliminary finding.

Like other studies that you may have heard about, we found different immunological patterns in the lymph node than in the blood. There was a higher percentage of CD8+ cells in the blood than in the node. However, we found a lower percentage of CD4+ cells in the node than in the blood. We also found that CD4+ cells in the lymph nodes of long-term survivors are more likely to have positive activation markers than those in the blood; however, we don’t know if this is different in long-term survivors than it is in participants with average CD4+ decline.

Levels of viral DNA in the blood were not different between the groups.

I’d like to end by thanking all of the participants in our studies, including the researchers and lab workers.

Future Community Informational Meetings

This special issue of CRIA Update grew out of a community forum that was co-sponsored by CRIA, the Gay Men’s Health Crisis (GMHC) and the Treatment Action Group (TAG). We are now holding a community forum each month to share information about AIDS research and treatment. We have tentatively planned for the following topics to be addressed in upcoming meetings: Opportunistic Infections: PCP & MAC, Opportunistic Infections: CMV & Fungal Infections, Perspectives on Alternative Therapies, Management of Early HIV Infection. For more information on upcoming meetings, contact Gary Bonasorte at (212) 924-3934.
JON ENDE
Long-Term Survivor

In a recent issue of the Journal of the Acquired Immune Deficiency Syndrome, a leading light in the field of psychoimmunology, UCLA’s Dr. George Solomon, reports that of nine healthy men with a mean T-cell count of 15.6 and a mean time since last symptom of 19.2 months, all had natural killer (NK) T-cell function within the same range as healthy HIV-people. A control group of four men with similar T-cell counts and symptomatic disease had abnormally low NK function. Dr. Solomon associates this with attitudinal differences, reporting that the healthier men had good relationships with their mothers, were most likely to describe themselves as responsible, conscientious, alert, aggressive, etc. and least likely to describe themselves as meek, bitter, or guilty. It is proposed that AIDS patients be prescribed assertiveness training and exercise.

In the same issue of this journal, two British researchers quite snappishly insist that smoking must cause a more rapid progression to AIDS, and are rather smartly put in their place by Margolick and Munoz from the Multi-Center AIDS Cohort Study (MACS). On the contrary, though the differences are not statistically significant, it would appear that heavy smokers are less likely to progress to AIDS, and also less likely to develop PCP. Questions of the effect of attitude and behavior on survival and progression are vexatious, especially subject to pre-existing biases. Received wisdom may or may not apply.

I mention these instances as reminders that puritanism renews itself unshakably, and Cotton Mather is always with us. As for myself, bitterness and humility seem part of the range of appropriate response to this incessant devastation in which one lives. It isn't necessary to be cheerful to have a fercious will to live. It may even be that meanness and self-involvement also serve very well. There is a hidden theological agenda in much talk of living with AIDS that may not be useful. Let's attend as closely as we can to particular acts: nutrition, self-education, choice of medication, obtaining first-rate primary care, and prophylaxis...things we might know and teach. And anyone lucky enough not to be living in California should have a vice.

Let me say very briefly that I've had no opportunistic infections, that my T-cells have been pretty consistently below 200 for pushing six years now, and that I've taken all drugs, but in a snobbish and selective manner (as I do everything), including 1200mg of AZT for two years or more. I think this makes me statistically unusual, and also very tired. I suspect that some of my treatment choices have been wise or lucky, but like any one, there is only uncertainty, intuition, and a persistent curiosity.

AIDS has become routine, even banal. This was announced by the ready willingness of absolutely everyone to wear red ribbons. Americans love emergencies, love blood and gore on the highways, but are impatient with the persistently disabling, the totalities of melancholy and incompleteness. Living with AIDS or something near to AIDS for a very long time now has the air of participation in a ghostly secret society whose members recognize each other by a few key words, but whose real existence goes unknown.

If you want advice, follow the literature, take many pills, visit doctors, follow your favorite surrogate markers of disease progression, and from time to time treat yourself to a new treatment or a new study protocol. And worry about sex and whether to have the bedroom wall replastered.

I remember the first MACS meeting I attended, and my surprise at how unfamiliar the epidemiologists were with the existence of apparently healthy people with under 50 T-cells. Presently people who exist as long-term survivors, however defined, are fashionable objects of study in the hope that mechanisms of disease will be elucidated and better therapeutic interventions obtained. This is of upmost importance, but equally important in the real world of people living with HIV would be rigorous, controlled studies of multiple minor interventions with possibly additive effects that occur in sophisticated primary-care settings, and that might contribute significantly to improved survival overall.

And should there ever be developed a tissue repository, let me encourage people to volunteer their flesh.

Dedication to Michael Callen (1954-1993)

Michael Callen, one of the first AIDS activists, died on December 27, 1993. This issue of the CRIA Update is dedicated to him. Michael's work has inspired so many of us, that we thought it best to leave you with his own thoughts on long-term survival: "After months of beating the bushes of the PWA grapevine, I found 20 gay men who have survived full-blown, CDC-defined AIDS for three or more years. I discovered patterns, but no one pattern. The best that I can surmise is that hope – a passionate commitment to fighting for one's life -- is a necessary, but not a sufficient ingredient for survival. It won't guarantee that you'll beat AIDS, but you've gotta have it to even be in the running. I'm convinced that it's as rational to have hope as it is to give up. If 85% of people diagnosed with AIDS are dead after five years, then 15% are still alive."
GLOSSARY of SCIENTIFIC TERMS

Antibodies: Molecules in the blood or secretory fluids that tag, destroy or neutralize bacteria, viruses or other harmful toxins. They are members of a class of proteins known as immunoglobulins, which are produced and secreted by B-Lymphocytes in response to stimulation by antigens.

Antigen: A substance which, when introduced into the body, is capable of inducing the production of a specific antibody.

Attenuated Virus: A weakened virus whose ability to infect or produce disease is potentially reduced.

B-Cells: A type of white blood cell (lymphocyte) that comes from the bone marrow. It is one of the two lymphocytes that play a major role in the body's immune response. B-cells work are precursors of plasma cells, which secrete antibodies into the body's fluids.

Cell-mediated Immunity (CMI): One of two fundamental but overlapping branches of the immune system (Humoral Immunity is the other). The cell-mediated immune response relies on cells that bind to, digest and break down invaders.

Cytokines: Molecules released by immune cells that regulate the immune response.

Humoral Immunity: One of two fundamental but overlapping branches of the immune system (cell-mediated is the other). The term “humor” refers to body fluids, primarily serum and lymph. Molecules of the humoral immune system are proteins collectively called immunoglobulins, a single such molecule is called an antibody.

Immunoglobulin: See antibodies.

Lymphocytes: One of two kinds of small white blood cells (leukocytes) responsible for much of the immune response. Lymphocytes normally include 25% of the total white blood cell count but increase in number in response to infection. They occur in two forms: B cells and T cells.

Macrophage: Any large cell that can surround and digest foreign substances in the body, such as protozoa or bacteria. Macrophages are found in the liver, spleen, and in the loose connective tissue.

Pathogen: Any virus, microorganism or substance causing disease.

T-Cells: One of two types of white blood cells that are primarily responsible for immune response. T-cells are mainly responsible for cell-mediated immunity.