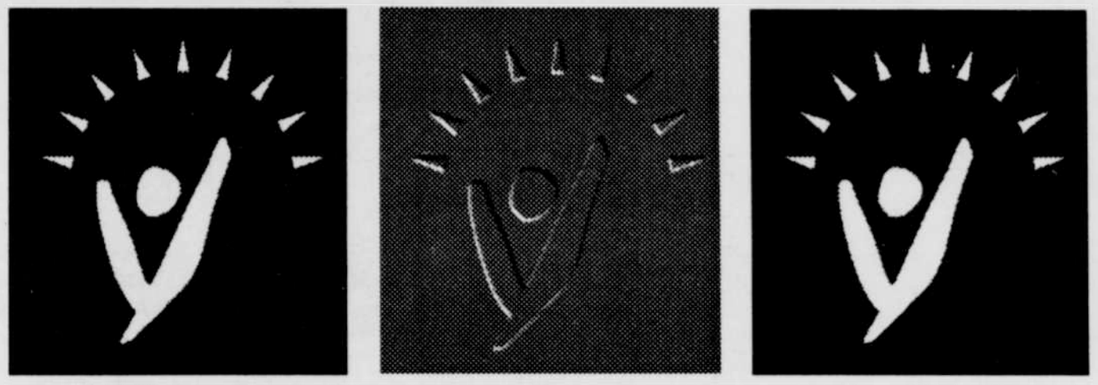

Look How Far We've Come

by The Boston AIDS Writers Group

The HIV-affected community filled with hope in anticipation of the International Conference on AIDS held in Vancouver this July. It is the first time since the pandemic began that there were reports on successful therapies to control HIV and even perhaps eliminate it in people living with the disease. Most importantly, people with AIDS who up until now felt that they were coping with a fatal illness, at last feel that they have a future with new hopes of managing HIV, feeling better and living longer. Let's take a look at how far we have come and what we can expect in the future.

In the Beginning

In 1983 the cause of AIDS was unknown, but it appeared that it took only two years to destroy the immune system. There was no treatment whatsoever for the disease, and assuming the disease was caused by a germ, there was no way to test if a person was infected. Back then doctors were reduced to fighting an odd and unpredictable list of infections to which afflicted people inevitably succumbed.

History

During the next decade the gay male community in the United States was hit especially hard, as were communities of color, hemophiliacs and intravenous drug users. But in so-called Third World countries, such as sections of Africa, the devastation was extraordinary. In some places entire villages were left with only babies and the elderly still living. The World Health Organization projected that by the mid-'90s, 20 million to 40 million people would be infected. For many years people got sick and died as scientists worked on what would prove to be the largest effort in world history to find what was causing this disease and a way to stop it.

By 1984, scientists discovered the virus that causes HIV disease and soon developed a test for it that revolutionized our ability to cope. Blood supplies could be screened to protect millions of people—especially hemophiliacs. The use of this test helped us to refine our understanding of how the disease was transmitted, so attention was focused on prevention, leading to the efforts to develop—with some success—"safer sex" as a cultural norm. The test also showed that the disease progressed much more slowly than was originally thought; it seemed to take many years before the onset of symptoms. This long period of infection without symptoms became known as the "latency" period.

Over the next few years, progress was made toward fighting the infections characteristic of AIDS (now known as opportunistic infections), especially pneumocystis pneumonia (PCP) which was the leading cause of AIDS-related death in the U.S. Gradually, people's lives were extended by the advent of prevention and early treatment of opportunistic infections.

Alphabet Soup

By 1987, AZT—the first of a series of antivirals which seemed to slow down the virus—was approved by the U.S. Food and Drug Administration. Other similar drugs, approved over the next eight years, became known by their acronyms, and soon we had an alphabet soup of antivirals—AZT, ddI, d4T, ddC, 3TC. None of these drugs seemed to work very well; all had side effects that were unpleasant, and by the early '90s there was a cloud of gloom around those people affected in any way by HIV disease. It seemed that HIV was able to mutate around any drug that science could throw at it, so that the treatments were only doing a little good for a limited amount of time. In fact many people preferred to just cope with the illness without therapy, or turned to alternative medicine because the limited benefit from the drugs was not worth the side effects that they caused.

Let There Be Light

As of last year the great mystery of the "latency" period has been solved. By using viral load tests (a new tool used to measure the number of viruses in the bloodstream), Dr. David Ho and his colleagues at Aaron Diamond AIDS Research Center in New York City have shown that the virus never rests; there is an ongoing war between the immune system and the virus from the moment of infection. The body replaces cells that HIV destroys, and without treatment virtually all immune systems will eventually lose that war. Dr. Ho helped to clarify two things that were not well understood: why T-cell levels continued to fall during the "latency" period, and why HIV becomes resistant to drugs. First, it has been discovered that HIV destroys slightly more T cells than are being produced, so that over time there is a gradual decline in the number of T cells in the body. Second, the virus reproduces so rapidly that drugs that do not drastically reduce HIV are overcome by viruses that are not affected by the drugs.

Despite the fact that the need to test different antivirals was hampered by ownership issues, concerns about profit, scientific secrecy inherent in the privatization of research and the lack of strong leadership at the federal level, scientists did make some progress toward fighting the virus. But until recently, no single antiviral was able to effectively control HIV. Then in 1994 the traditionally dour-faced scientists began to smile as antivirals used together in combination reduced the amount of virus (viral load) much more than when used alone, and this reduction seemed to allow for the redevelopment of a healthier immune system.

The first hint that progress was in the making was a study on a significant number of people with HIV which showed that AZT used in combination with 3TC reduced viral load by over 90 percent and kept it down for 18 months. T-cell counts rose as well, indicating that the immune system was less compromised, and it slowly became clear that indeed lowering the amount of virus was the key to controlling the illness.

There are now nine approved antiviral drugs, and we expect that by the end of the year there will be eleven. All of these drugs are important in the fight against HIV because people respond to therapy in different ways and need a variety of options from which to choose. For many, the days of suffering through severe side-effects or not using antivirals at all are past. For others, a safe and effective treatment regimen is yet to be found. However, most people can now choose the drugs that are best for them, and side-effects are now usually manageable, or at least tolerable, given the potential health benefits.

Another advantage inherent to the variety of antivirals available is that each works in a different way. One category of antivirals, called "nucleoside analogs," works by stopping the virus from infecting a cell; a second group, commonly referred to as "non-nucleoside reverse transcriptase inhibitors," works in the same place in the life cycle of the virus, but has different effects. A third group, called "protease inhibitors," has been made available most recently. These drugs work differently from the first two by stopping the virus from reproducing. Attacking the virus in different ways simultaneously will make it harder for HIV to fight back.

Finally, a major breakthrough occurred in 1995, when it was shown that many people with HIV who used protease inhibitors in combination with the other antivirals reduced their viral loads below the level that can be measured by the current technology, and they have kept them down for 18 months so far. There is even new evidence that people who have never used any antivirals can use certain combinations of three drugs to achieve the same effect without using protease inhibitors. This is exciting because now research can be directed toward finding the best triple combinations of antivirals to fight HIV.

Furthermore, the discovery and commercial manufacturing of viral load tests (the first was approved recently by the FDA) makes it possible to decide on a person-by-person basis when antiviral therapy is necessary, if it is working, and, if not, when to switch therapies. Viral load tests make it possible to decide which combinations of antivirals are working for an individual, making management of the illness on a case-by-case basis a realistic option.

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Revelations

This year we have confidence that HIV disease can be defined as a chronic rather than fatal illness—many scientists and doctors believe that the disease is manageable with the available antivirals. But there may be even more exciting news ahead. In some babies who have had viral load suppressed to below detectable levels there are indications that their immune systems might be returning to normal. This might well mean that there is simply no virus left.

Unfortunately, there has been less to report on other therapies that could directly rebuild damaged immune systems. This is due in part to the fact that these immune-based therapies have had a comparatively small amount of resources directed toward them and a far more difficult time on the regulatory level than drug company products. Immune-based therapies may be the only hope for repairing the damaged immune systems of people with more advanced HIV disease, and they offer a totally different approach for fighting the virus. For example, IL-2, a substance naturally produced by the body, when given as therapy can elevate T-cell levels of people with more advanced HIV back up to normal levels. However, this therapy, like other immune-based therapies, has not been studied with the aggression and the finances characteristic of the development of antivirals. As a result, there are no long-term studies that would determine whether this type of therapy actually rebuilds immune systems and lengthens lives.

Still, the most important news is that people with HIV disease now have a future.

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