SENTENCED TO LIFE

Protease inhibitors hold the promise of a way out of the AIDS nightmare, but they also represent a puzzle with all-new pieces

story by Richard Shumate ▼ photos by Linda Kliewer

Part 1: Edge of Hope, Edge of Fear

The crowd of about 100 was mostly male, mostly white, mostly gay. As these people walked into the slightly tattered auditorium of an inner-city high school, many stopped to greet and hug longtime friends, fellow warriors. Some faces showed the strain of battle, some bodies still bore the obvious traces of wasting.

But these were not, in either body or spirit, the walking dead.

As the night's program began and the conversation grew, a weathered but still handsome Latino man with more than a trace of an accent spoke up to ask a question, prefacing it with a simple, elegant statement of why he had come out to this forum on this November night. He was trying, he said, "to figure out what in the hell I'm supposed to do now."

The audience roared with a knowing laughter. These were people who have been living with HIV, or struggling against AIDS, or caring for and loving those who have been staring into the pit of a holocaust.

Sitting nearby, another man prefaced his own question with a succinct description of the dilemma he now sees for himself.

"I think there's life left in this old dog now," he said. "I just wonder if this old dog can learn new tricks."

Up on the stage, facing the questioners, were activists and lawyers and psychologists and people in the insurance business—learned men and women all—who had gathered here to offer their best advice as to what in the hell these people were supposed to do now. But as the night drew on, it became obvious that they would only be able to provide advice, not answers.

This gathering took place in Atlanta's gay Midtown neighborhood, but it could just as easily have taken place in Portland or Boston or Austin or any other place where AIDS has taken its toll over the past 15 long years. Because as the lesbian and gay community enters 1997, we are entering a new reality, a place where AIDS may no longer be the death sentence it once was. And we have begun to gather in forums such as this to sort out what that might mean.

At July's International Conference on AIDS in Vancouver, B.C., scientists reported a major breakthrough. Medical studies on a new class of drugs, called protease inhibitors, showed that when used in conjunction with existing AIDS drugs they can give many—but not all—people with HIV a dramatic new lease on life. In some patients' blood, the amount of virus has dropped to undetectable levels, leading to a still-unproven hypothesis that this treatment could even eradicate HIV altogether.

Estimates are that 100,000 people in the United States are now taking protease inhibitors, and the number is climbing. The mainstream media has given this breakthrough big play. The man who presented the good news in Vancouver, Dr. David Ho, was even named *Time* magazine's Man of the Year.

Because of the cost and complexity of treatment with protease inhibitors, this is far from a final panacea. The drug regimen can cost from $10,000 to $25,000 a year, putting it out of reach for uninsured people without sufficient financial resources or access to government-funded drug programs. The demanding regimen requires taking dozens of pills a day at certain times under specific conditions—difficult for people who are homeless or addicts or poorly educated. And in people in the later stages of AIDS who have undergone numerous other treatments, protease inhibitors seem to be less effective.

But for people like those who came to that auditorium in Atlanta—part of a gay community that is organized, with financial resources and established networks for disseminating treatment information and supporting people living with HIV—protease inhibitors are the edge of a world of hope.

They have also ushered in a world of change—and a world of fear.

On the West Coast, AIDS medical practices and hospices have begun to close. Viatical companies have stopped buying up life insurance policies. AIDS service organizations have started thinking about how to change programming to meet new needs—and how they'll pay for it if all this hope puts a damper on fund raising.

Safer-sex educators are scrambling to come up with a new message that will keep people from engaging in risky behavior based on the mistaken belief that HIV can now be cured easily with a few pills. Those who have seen dramatic improvements in their health because of protease inhibitors now have to decide whether, or when, to go back to work. They have been left to wonder how all of this will affect their medical insurance and finances.

People who live with death in full view live differently—and make different decisions—than do people who live with death as an abstract, distant concept. Decisions about careers, relationships, friendships and finances that seemed logical and constructive while dying can look downright illogical and destructive when there are 20 or 30 or 40 more years to go.

Many of these people find themselves alone at the edge of hope. The lament of that man who asked what in the hell he was supposed to do took on an even more poignant tone as he went on to tell the audience that most of the people in his gay family were dead.

"I find myself in the unehviable position of being friendless," he said.

The media has dubbed this "the Lazarus syndrome." But after explaining how Jesus brought Lazarus up from his deathbed, the Bible doesn't go on to give us detailed information about how Lazarus went about piecing his world back together after being sentenced to life.

"To people not intimately familiar with AIDS, this must seem like the most selfish, self-absorbed behavior they've ever witnessed. I'm sure they're saying, 'You know, you should be grateful just to be alive,' " says Mark King, an Atlanta AIDS educator who has lived with HIV for more than a decade. "But it is the same kind of shock to the system that you have when you believe you are going to live as long as everybody else and then find out that you won't."

Of course, in the years since the first cases of AIDS were reported among gay men in San Francisco and New York in 1981, the gay community has often been at the edge of hope, only to find that hope dashed. Those fighting the disease had become skeptical, perhaps even a bit cynical, when headlines trumpeted yet another breakthrough. But the reaction to this news has been different. Even in the HIV community, the sense of promise is palpable.

"It has produced this emotional change that's different than anything else I think we've seen," says King. "I think part of it is because we haven't hit the morning after yet. With those other drugs, the morning after came rather quickly."

To understand the promise of protease inhibitors—and why the morning after may not soon loom on the horizon—it is important to understand a little bit about how HIV works and how these drugs help the body fight back.

To multiply itself, a strand of HIV enters a white blood cell. Through a series of biochemical reactions helped along by specific enzymes, it turns the cell into a mini factory churning out more and more HIV. But this process can be disrupted by inhibiting production of the enzymes needed to make those reactions go.

Scientists have identified three of these enzymes, known as reverse transcriptase (RT), protease and integrase. The first wave of AIDS drugs, such as AZT, ddI, ddC and 3TC, inhibited production of RT. But they weren't 100 percent effective in shutting down production of HIV, and these newly produced strands adapted to the drug and became resistant to its effects. That's why within two years, AZT, when used by itself, becomes virtually worthless.

Protease inhibitors (the three now on the market are Invirase, Crixivan and Norvir) attack the second enzyme, protease. So, combined in a "cocktail" with AZT and other RT inhibitors, they put up a second line of defense. To reproduce, HIV has to overcome the suppression of both enzymes, making it much harder for the virus to survive, adapt and develop resistance.

However, initial treatment trials have shown that protease inhibitors are less effective for people who have already been taking RT inhibitors and have developed partial or complete resistance to them. In essence, their HIV still only has to go through one hoop instead of two, making it easier for HIV to survive and adapt.

What makes this multiple-drug regimen so promising is that new RT and protease inhibitors, stronger and more effective, are being developed, giving more options for people who have adverse reactions to existing drugs or show signs of resistance to them. Also on the horizon are integrase inhibitors, which will attack the third enzyme. That could lead to the development of a third hoop through which HIV would have to jump in order to multiply.

But the euphoria now sweeping through the HIV/AIDS community does not come from scientific promise alone. It is being fueled, too, by the atmosphere into which this promising news about protease inhibitors has surfaced.

After more than 15 years of organizing and fund raising and fighting off the effects of the disease—and burying those who didn't make it through the fight—people were burned out, perhaps even resigned to the idea that AIDS was going to be there, killing us, for a very long time. So we have leapt at the hope.

Not surprisingly, no one inside that Atlanta auditorium was expressing remorse that the paradigm under which people with HIV/AIDS have lived since 1981 has now changed. Yet they were clearly not yet comfortable with all that that might mean.

Panelist Tony Braswell, who heads Atlanta's main AIDS service agency, AID Atlanta, and who has been fighting this fight for years, put it this way:

"Every part of this puzzle," he said, "has to be refigured."

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