

Side Effects: The New Age of AIDS in America

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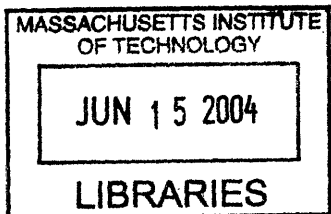
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ABSTRACT

When the cocktail of AIDS drugs called highly active antiretroviral therapy (HAART) was introduced in 1997, it radically changed the picture of HIV and AIDS in the U.S. Deaths from AIDS plummeted by two-thirds. Now, far fewer people are progressing along the once-inevitable path to illness and death. The impact of new therapy has been both dramatic and double-edged: it has spared tens of thousands from death, but has complicated their lives in countless ways. This newspaper series in five parts examines the new landscape of AIDS in the aftermath of success – a success that is still incomplete as there is still no cure. The new therapies carry literal side effects – the toxicities of drugs that infected individuals must take everyday for the rest of their lives. But the drugs have also created social and political side effects as AIDS is transformed to an increasingly chronic disease. The series relays the stories of HIV-infected individuals, clinicians, social workers, and AIDS service and prevention workers in Boston and examines how their lives and work have changed now that AIDS is no longer seen as a “crisis” in the U.S.

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Part I - Borrowed Time

A GAY MAN NEARING FIFTY, whom we will call Bill Dudley, lives with his partner in a restored farmhouse in the western suburbs of Boston. Though they had always lived in the city, a couple of years ago Dudley and his partner saw a classified listing for the farmhouse and decided to give rural life a try. Dudley works a few hours a week writing grant applications for a hospice organization, but most of his time is devoted to their farm and its collection of chickens, sheep, llamas, goats, geese, and ducks.

Like many other refugees from the city, Dudley and his partner are gradually restoring their home, living a quiet and in many ways idyllic life.

Less than a decade ago, all of this would have been unimaginable. Not because Bill Dudley has been leading an openly gay life in a bucolic suburb, but because Dudley has been living on borrowed time. Since 1980, he has been infected with HIV, the virus that causes AIDS.

Dudley is not sick. Fit and trim, with cropped black hair flecked with gray, he shows no outward signs of an infection that he has carried for nearly half his life. But his health depends on the daily regimens of HIV medications he has taken since they first came to market in 1987.

Not only is his infection a silent one, but Dudley does not suffer from any side effects of the medications that many other people infected with HIV experience. "I've had this iron stomach," he said. "I don't know what plans God has for me but I've never had problems with any of the drugs." There is the hassle of taking the drugs everyday, of making sure they are covered by his insurance, but for the most part HIV plays a small role in his life. "To be honest with you, even though I take a lot of pills everyday, I don't think about it much," he said.

Welcome to the world of AIDS as a chronic disease. When the cocktail of AIDS drugs called highly active antiretroviral therapy (HAART) was introduced in 1997, it radically changed the picture of HIV and AIDS in the U.S. Deaths from AIDS plummeted by two-thirds. Though the rate of new infections has held steady since, far fewer people are progressing along the once-inevitable path to illness and death.

In 1996 Dudley was featured in an article in *Time* magazine about hope for AIDS patients. Basketball star Ervin "Magic" Johnson's smile lit up the cover. The hopeful news that new treatments were on the way could not even foreshadow the reality that AIDS, though still an incurable disease, would for many people become something to live with, rather than die of.

The impact of new therapy has been both dramatic and double-edged: it has spared tens of thousands from death, but it has complicated their lives in countless ways. As America's attention turns to the devastation that HIV is causing in parts of the developing world, the problem of HIV and AIDS within its own borders is largely

forgotten. In Boston, HIV-infected individuals and those who work in HIV prevention and treatment continue to adapt to changes brought about by HAART.

This series examines this new landscape of AIDS in the aftermath of success – a success that is still incomplete as there is still no cure. Those who inhabit this new landscape may lack the sense of crisis that permeated the early years of AIDS, but their lives are no less complex. With more and more people living with HIV infection, the disease is every bit as much a reality in the U.S today as it was a decade ago. But the new age of AIDS is fraught with uncertainty as well as optimism.

Howard Heller, a primary care physician specializing in the treatment of HIV/AIDS, began taking care of AIDS patients at Massachusetts General Hospital in the mid-1980s, when the work was both frustrating and tragic. In the early years of AIDS, Heller explained, patients “would get one infection and [a treatment] would bring it under control, but they would get another one, and they would have to be on dozens of medications just to try to keep everything under control.”

Human Immune Deficiency Virus (HIV) attacks cells of the body’s immune system called CD4+ T cells. As the immune system weakens over time, the infection leads to the disease known as AIDS, in which infections by normally harmless viruses and bacteria invade the body.

Progress in treatment was at first painfully slow and incremental. Azidothymidine, widely known as AZT and the first treatment to directly block HIV, was approved in 1987 and prolonged life a few months, but it had major toxic side effects. Then came other drugs that prolonged life a little more. Eventually physicians learned that by combining drugs they could slow the virus’ propensity to quickly developing resistance to the medications. Treatments for the myriad opportunistic infections also improved, but it was still a constant battle for physicians to keep these infections in check.

When a new class of drugs called protease inhibitors emerged from the lab in 1996, everything changed for HIV-infected individuals in the U.S. The following year, studies found that a triple-drug combination reduced the levels of virus in the blood to the point where they were often undetectable. “All of a sudden [patients] just weren’t getting sick,” Heller said. “And the management of HIV, from the perspective of a doctor taking care of patients, it sort of – I don’t want to say became less challenging – but it became more rote.”

Heller’s patients have simply stopped dying. “I’m trying to think of the last time I saw somebody dying of AIDS,” he said, and paused for half-a-minute to think. “I guess it must have been five years ago, at least a patient of mine.” And five years ago such a statement would be unthinkable for a physician caring for HIV-infected patients.

Harvey Makadon, a primary care doctor at Beth Israel Deaconess Medical Center specializing in HIV/AIDS, also has not lost a patient to AIDS in four or five years. Not only are his patients living longer, the opportunistic infections that used to plague AIDS patients are now far more rare. “I haven’t seen a person with an opportunistic infection in probably three or four years,” said Makadon.

For those with access to care, these new medicines have changed the face of AIDS and they have done it far more dramatically than many people in the field would have thought possible. Vastly more people are living with HIV infection than are dying of AIDS. The Centers for Disease Control and Prevention (CDC) estimates that between 800,000 and 900,000 people are living with HIV infection in the U.S., and nearly 400,000 of those are living with AIDS. In 2002, 16,371 people died of AIDS.

Just as insulin treatment changed diabetes from a fatal disease to a chronic one, so HAART has changed the meaning of testing positive for HIV infection in the U.S. In the 1980s and early 1990s, finding out you were infected with HIV often meant dramatic

HIV/AIDS

The disease that came to be called AIDS was first reported in the June 4, 1981 edition of a then obscure publication of the Centers for Disease Control and Prevention (CDC) called *The Morbidity and Mortality Weekly Report*. The article reported a cluster of cases of an unusual pneumonia in gay men in San Francisco. Similar cases emerged of men with the formerly rare skin cancer Kaposi's sarcoma, and a host of illnesses caused by infections that were normally seen only in people with compromised immune system, such as transplant patients and people with cancer.

Eventually these illnesses were recognized as a single entity – called Acquired Immune Deficiency Syndrome because it is an amalgam of infections and malignancies caused by the devastation of the immune system. When a virus called human immunodeficiency virus (HIV) was discovered in 1983 and recognized as the cause of AIDS, scientists realized that what was known as “full-blown AIDS” was the final stage of a viral infection that progresses gradually for years with few symptoms.

Nowadays, physicians largely view AIDS as a clinically useless term and an historical artifact, and often refer to it as “HIV disease” in medical literature. “I think looking at the spectrum of HIV-related diseases would make more sense, but there is twenty years of history to change,” said Harvey Makadon, a primary care physician specializing in HIV at Beth Israel Deaconess Medical Center. To try to standardize the meaning of AIDS, the Centers for Disease Control and Prevention (CDC) has established a definition for it based on the levels of CD4+ T cells detected in the blood of an HIV-infected person, or by the presence of any of 26 conditions and infections associated with the disease. The CDC's definition is useful for tracking the disease, but it does not define a clinical change. And the meaning of an AIDS diagnosis is complicated now that HIV infection is not a gradual but steady decline in the immune system. With therapy, a patient who meets the criteria for AIDS might regain healthy T cell numbers and maintain them for years, though the patient is still considered to have AIDS.

life changes and coming to grips with impending mortality. Some quit jobs and abandoned long-term plans.

But some of these patients, resigned to certain death, received newer treatments and “suddenly it was, ‘Here is your life back. You’re not going to die,’” said Heller. “And a lot of these people who had put their careers on hold, and their lives on hold, and had not gone into relationships, and had sold their life insurance policies, and didn’t bother building up their 401Ks” suddenly were given back their lives, but they had already abandoned the things they needed to have a life.

Psychologists dubbed this phenomenon the Lazarus Syndrome, because these patients, if not awakening from death, were returning to their lives after acclimating to the idea that death was at hand. But their new reality was far more complicated than simply waking up to restored health. They suddenly faced the complex financial and medical issues of someone living with a chronic disease. Many had gone on disability insurance during their illness, and now found themselves able and willing to work but afraid to lose their disability by looking for jobs.

From a medical standpoint, the man we call Bill Dudley is leading a life very similar to that of a patient taking medication for high blood pressure, and he represents the ideal in the medical treatment of HIV/AIDS. In the natural course of AIDS, symptoms of illness appear after a mean of eight to ten years. Dudley was fortunate in that he managed to stay healthy for many years until better medications came along.

In the early days of his infection, he was meticulous about his health, regularly working out and meditating. “Back then you were always prepared for the worst,” he said. Now he is less vigilant. “But I think part of that has to do with age. I never thought that I would actually see 50.”

He has been sick only once, an excruciating period of time when he was hit with a bacterial infection that gave him severe night sweats for days before the problem was diagnosed and treated. But other than that episode, he does not feel his illness. He knows that if he did not take his medications he would face inevitable disease and early death. But with them he is able to get on with his life, his medications keep his illness at bay, and his borrowed time is indefinite.

“I take my drugs everyday, but it’s not something that I dwell on,” Dudley said. “Now, if I started getting sick I’m sure I would.” Like other HIV-positive people, he still lives in uncertainty, never sure whether the success of the treatments will continue or resistance to the medications will develop.

Over the years, he saw many others die of the same infection that he carried. His partner was among the first ten men in Massachusetts to be diagnosed with Kaposi’s sarcoma, the formerly rare skin cancer that served as a surrogate indicator for the disease that did not then even have a name. Dudley took care of his partner when his health failed, nursing him for the seven years before his partner died of AIDS.

At that time, AIDS was such a frightening and fatal disease that it dominated life for the gay community. All of Dudley’s friends and activities revolved around taking care of his partner. “It wasn’t until after he died that I had time to think about myself,”

he said. "My whole personality and my whole life revolved around him, so when he was gone I had to refocus."

"Anyone who has taken care of someone, anyone who's really honest would say when their partner who they've had for a long time finally died of AIDS, it was always a relief," he added. "For one thing, they were always so sick. But there was also a relief that it's finally over. And then you sort of have to redefine your whole life."

Even after that time, Dudley spent years taking care of other dying friends and going through therapy to overcome the emotional numbness he had developed after years of watching others suffer. In the past few years, he has had little contact with friends from the old days. He recently was invited to attend the 20th anniversary party of AIDS Action, Boston's oldest and largest AIDS advocacy group, but did not want to go. "That was such a bad period of my life that I don't want to go back there," he said. Which in part explains why is no longer willing to have his name used in this story, though he allowed it to be used when he was interviewed by *Time* eight years ago.

As he sat on a Victorian-style couch in his sitting room, rising occasionally to stoke the fire in the woodstove, it was apparent that Dudley's move away from Boston was in many ways a step away from his past. "I haven't had this conversation in so long," he said. "I used to [participate in medical] studies, and I used to talk to medical students at Harvard, and I just pushed away from that because I didn't want that to be such a part of my life." Now, he said, "I see [my physician] three or four times a year, I have my blood work done, nothing seems to be changing. And so I just keep doing it, and I'm more concerned these days about the price of hay than other things."

Not everyone has been so lucky. The hunt for HIV medications went on for years before effective therapies were found. Even now, though medicines can keep many people infected with HIV healthy for long periods of time, the therapy comes with a price.

Tomorrow: New drugs, new challenges

Disappearing infections

When the AIDS epidemic began, it presented numerous medical conundrums for physicians and medical researchers. Because HIV works by debilitating the body's immune system, leaving it prey to unusual infections that had rarely caused health problems in humans before, managing these opportunistic infections became medical specialties in themselves.

Among the most common and vicious of these illnesses was cytomegalovirus (CMV) retinitis, a condition in which an AIDS patient would begin to lose peripheral vision in one or both eyes, and eventually went completely blind. Most people are infected with CMV, but the virus usually does not cause disease. In people whose immune systems are compromised by HIV, however, CMV infection can lead to several diseases throughout the body; retinal infection and blindness can be the most devastating. Treatment for the disease would involve spending hours receiving antiviral medications intravenously. The goal of treatment was to keep patients from going blind before they died, which, because CMV retinitis usually struck late in the natural course of AIDS, was at most a matter of months.

Michael Pinnolis, a specialist in retinal surgery and disease, became one of the ophthalmologists in Boston to get intensely involved in treating this emerging problem in the late 1980s. By the early 90s, Pinnolis, who practiced at Harvard Vanguard Medical Associates, was a leader in the treatment of CMV retinitis, also heading a clinic for AIDS-related eye disease at Massachusetts Eye and Ear Infirmary.

For Pinnolis, the complicated management of the disease posed an intellectual puzzle. "It was my academic interest," he said. He was often asked to give talks to the ophthalmology community, many of whom were wary of the complicated treatment and, in the early days, were wary of treating AIDS at all because of the intense fear and stigma attached to the disease.

But when HAART therapy became widespread in 1997, it not only drastically curtailed the levels of HIV in the body of patients – it nearly eliminated opportunistic infections like CMV retinitis. "It really just evaporated," Pinnolis said. Not only could the drugs prevent new infections from emerging, but many people who were sick were rapidly brought back to health. "You would be looking to see where the CMV went and it was gone."

Though he insists there was plenty of work to still be done in his field, the disappearance of his academic specialty helped Pinnolis make the decision to leave MEEI and take up administrative work along with his clinical practice at Harvard Vanguard, where he has been ever since. He hasn't seen a new case of CMV retinitis in a year or two. "I think I may have four patients I still follow from the old days," he said, but the disease is long since gone in their eyes. "What a dramatic difference," he marveled.

Side effects: The new age of AIDS in America

Part II – The piecemeal war

AT THE BEGINNING OF THE AIDS EPIDEMIC, people talked hopefully of a “cure” for the disease. But in reality, treatment has always been piecemeal, and probably will be for the foreseeable future. Physicians have never had a perfect weapon to completely suppress the virus, but they have over time managed to collect enough imperfect tools to keep the virus at bay until something new comes along.

Most people have heard that AIDS drugs are working well, making it possible for people with HIV infection live longer and healthier lives. But as time has passed, reports of side effects have increased, patients have developed other life-threatening conditions, and viral resistance to the drugs is constant problem. The current “cocktail” therapy has been a breakthrough because it is the first strategy to really hold the virus off for an indefinite period of time. Unfortunately, however, it does not eradicate infection.

HIV works by attacking the very cells that are designed to fight it, a type of white blood cell called CD4+ T cells, which normally help coordinate immune system responses. In a person with AIDS, CD4+ cells are slowly decimated over time, leaving the body vulnerable to other infections that eventually cause disease and death.

When HIV was first discovered, there were few approved drugs to treat viral infections. Unlike bacteria, which are free-living cells, a virus is tiny and lies inside the cells of its host, so targeting a virus is difficult without also harming human cells. But over the course of several years, research into the workings of HIV led to new drugs that could interfere with the virus. For those people infected with HIV at the time, the saga of drug development was often a personal struggle to find information about the latest experimental therapies, navigate the ins and outs of the health care system, and fight for access to new medicines.

Kevin Koerner, who coordinates programs at Boston Living Center, a drop-in facility that serves people with HIV, was one of the patients who managed to weather the tortuous path of drug development for medications to treat HIV. “The medications? I’ve taken the gamut pretty much since I’ve been HIV positive,” he said.

Koerner was diagnosed with HIV infection in 1988 after his partner tested positive for the virus. At that time, an HIV diagnosis felt like a death sentence. “When I got diagnosed, I remember walking out of the clinic and thinking ‘my life is over,’” he said. “I just was numb over that news,” he said.

By that time one medication existed that directly attacked HIV, azidothymidine (AZT), though many people, including Koerner’s doctor at the time, knew little about it. “I’d heard that they had a drug out there that had been used for cancer and didn’t work [for that], and now they were trying it with people with HIV. I mean that’s all they had,” Koerner said. He quickly found a new doctor and began taking the medication.

In order to increase its numbers, a virus must infect a cell of its host, infiltrate the cell's DNA, and from there direct the cell to produce new virus particles. Each step in hijacking the cell offers a potential opportunity to thwart the virus with the right drug.

AZT works by throwing a wrench in the machinery of HIV replication. The virus uses an enzyme called reverse transcriptase to copy its genetic material into a double-strand of DNA so that it can slip into the DNA of its host cell. AZT prevents reverse transcriptase from adding new pieces of DNA onto the strand it is copying. But it has the same action in other human cells in which new DNA is being created, such as cells in the bone marrow – which means that it is highly toxic over time and can lead to anemia.

HIV is an enormously prolific virus. Even in the earlier stages of infection before the virus causes disease, tens of billions of viral particles are produced in the body every day, each with a unique version of the virus' genetic material. While HIV is prolific in making copies of itself, it is also sloppy. It makes many errors in copying its genetic code, and this abundance of errors, called mutations, make it possible for the virus to change and adapt rapidly when faced with new challenges – such as a drug that fights against it. Within weeks of starting the medication, drug-resistant strains of the virus emerge.

Several drugs were developed after AZT was introduced that worked similarly to it, but were less toxic. Another class of drugs, called non-nucleoside reverse transcriptase inhibitors, directly mangle reverse transcriptase to keep it from functioning. None of these drugs was a breakthrough, but they could extend lives for at least a few months, sometimes long enough to hold people until a new drug appeared.

Koerner was one of those people for whom the early medications seemed to buy enough time. "More drugs came along, and more and more people were staying alive," said Koerner. "I thought, well, if I can hang out long enough maybe I'll be lucky and live long enough for more medication."

Two innovations allowed HIV treatments to move beyond extending life a few months or years. First, clinicians began using drugs in combination and learning more about how the virus develops resistance. Though HIV may develop resistance against one drug fairly easily, the likelihood of it developing resistance against two or three drugs together is vastly lower. That realization meant more complicated – but more effective – combinations of drugs for patients. "At one point in the early 90s I was probably taking 20 pills a day," said Koerner.

The second innovation was the development of protease inhibitors, which target the stage of production of new virus particles. Before protease inhibitors came out in 1996, Koerner was not dangerously ill, but he was developing infections in his mouth and on his skin that signaled that his immune system was losing ground.

Koerner, like many HIV-positive people at the time, sought access to new drugs before they were approved by enrolling in clinical trials. But in these trials, there was no guarantee that he would be in the group of people receiving treatment. When his numbers failed to improve, Koerner, who had heard through the patient grapevine that the new drug was effective, realized he was in fact receiving a placebo. With his viral load soaring, he left the trial and enrolled in another study for the protease inhibitor

Crixivan. This time he did get the drug. Like many people who switched to protease inhibitors after their infection had progressed, Koerner noticed a dramatic difference. "That saved my life, I think."

With three classes of drugs in their arsenal, clinicians could now mix up drug "cocktails" using different combinations from the three classes of drugs. This formula, called highly active antiretroviral therapy (HAART), made a dramatic debut in 1997. The effect was remarkable: AIDS deaths in the U.S. dropped nearly two-thirds following the introduction of the protease inhibitors and HAART.

Maura Fagan, medical director of the Center for Infectious Diseases at Boston Medical Center, first began taking care of AIDS patients as a medical student in the mid-1980s. "It's unbelievable how it's changed," she said. Patients would routinely come into the hospital already showing complications of AIDS. "Basically once the diagnosis was even made, patients had mean survivals of six months or less." Even as some therapies came out to treat HIV or AIDS-related infections, "everybody was sick," she said. "And no week went by when we didn't have at least one death, and it was usually more like two, three, four...more some weeks."

But when HAART came out, Fagan said, "People on the brink of death came back, went to work, got married, had children. The patients we were identifying as HIV-positive before they'd had a complication, we are preventing those complications out now seven, eight years, and allowing them to continue living a reasonably normal life."

For doctors like Fagan, taking care of HIV-infected patients is still complex, but the issues have changed. Treatment is no longer a matter of trying to stave off infection after infection until all that can be done is to make the patient comfortable in death. The infections, for the most part, never come. Instead, managing HIV is a juggling act of choosing the right drugs to keep the virus in check while limiting drug resistance and toxicities from the medications.

The combinations of drugs have been refined and honed over the past few years. Some drugs have been combined into one pill, while others have been found to be effective at much lower doses. Most patients need only take a few pills once or twice a day.

Even the kinds of combinations that physicians use has been simplified, from an overwhelming menu of options to a more standardized set of recommendations issued by the U.S. Department of Health and Human Services.

Because antiretroviral drugs are highly toxic, there is only a slight difference between an effective dose and a harmful one. Even a mutation that helps the virus resist a drug slightly can upset this balance. Patients often develop resistance to a particular medication and need to change combinations periodically. But there is always a trade-off: whether to jump to another weapon or spare the big guns for later use. "Every time you change a drug regimen, it's not something you do lightly, because of drug resistance and possibly taking those drugs out of the mix later on down the road," said Koerner. "There's only a finite number of medications out there." Often clinicians will try to spare certain classes, like the powerful protease inhibitors, until absolutely necessary.

The growing problem of hepatitis C

"It's very rare now that somebody dies from a complication of AIDS itself," said Maura Fagan, medical director at the Center for Infectious Diseases at Boston Medical Center. "Probably the biggest killer now is hepatitis-C related liver disease."

About one-quarter of HIV-positive people in the country are also infected with the hepatitis C virus. But among intravenous drug users, the rate is much higher, up to 90 percent in some areas.

Although there is little concrete data on co-infection with hepatitis C and HIV, clinicians report that it is a huge problem that accounts for many of the serious health problems that HIV-infected people undergoing therapy still experience.

Hepatitis C virus is transmitted through the blood, usually through sharing needles. The infection leads to scarring of the liver, or cirrhosis, in about 20 percent of infected people. In people with HIV, the hepatitis C infection progresses much more rapidly, over the course of seven to ten years rather than twenty or thirty. "They're dying a lot more rapidly now," said Dan Church, an epidemiologist at the Massachusetts Department of Public Health.

Now that antiretroviral medications are keeping HIV in check for most people, the threat of hepatitis C is far more pressing. Unfortunately, treatment for hepatitis C is very difficult, and it's particularly hard with people who have HIV.

The treatment for hepatitis C involves injections of one or two antiviral drugs over the course of several months. The success rate ranges from 40 to 80 percent, depending on the variant of the virus that a patient carries. Treatment is an arduous process, with patients often experiencing ongoing flu-like symptoms and malaise.

Some HIV medications also cause inflammation of the liver, which creates problems with hepatitis C. "It's not a common problem unless you've got advance liver disease. Then it's a massive problem," said Fagan. "You can't treat the hepatitis C until you got the HIV under control, and you can't treat the HIV because they can't tolerate the medications because their liver is so bad."

In an ideal situation, a person diagnosed with HIV early in the course of the infection can undergo hepatitis C treatment before ever starting HIV medications. But in a population that often is diagnosed late, like intravenous drug users, that scenario does not always happen.

In addition, the treatment for hepatitis C exacerbates depression in susceptible individuals. Depression and other mental health problems are highly prevalent in the homeless and poorer populations, the same ones that are more likely to have HIV and hepatitis C co-infection. A recent study in San Francisco found that 70 percent of poor people who were infected with HIV were also infected with hepatitis C. While half of them received antiretroviral therapy for HIV, only four percent had been treated for hepatitis C.

Fortunately, new permutations of the three classes of drugs have steadily been developed that can sometimes circumvent resistance. "As you get to the point that you're like, 'oh my God, they've blown through this class of drugs,' something else has come up," said Fagan.

After protease inhibitors stabilized Kevin Koerner's infection, he was able to switch to a regimen without protease inhibitors, since they had begun to cause wasting in his face and limbs. Many patients eventually settle into a regimen that causes few side effects and can keep the infection stable for years. "It's just a chronic disease and you live with it, and it's part of your life, and you pay your bills like you're supposed to," he said.

For others, the drugs have created a situation in which many people experience the disease through the effects of the medications, rather than the effects of the virus itself. Short-term side effects can include severe diarrhea, fatigue, nausea. Protease inhibitors, the most effective drugs in terms of controlling viral replication, can cause the most severe side effects of all the HIV medications, and the effects can be especially severe in those who are the sickest when they begin treatment.

The response to the drugs is idiosyncratic. Some people, like Charlotte Johnson, suffer from a general fatigue and malaise that can make even getting out of bed a chore. Johnson is a 46-year-old woman who has been infected with HIV since 1997. With her children grown, she has now returned to college on a scholarship to pursue a bachelor's degree, and hopes to live long enough to get a PhD and become a psychologist. But her illness, she says, often makes it difficult for her to manage her studies.

"At my most exhausted and tired I start to imagine [that] my viral load shot up, my CD4 count must be low, because I feel like shit," said Johnson. "And that's when I get back the results that I'm undetectable, that my numbers are good. And I'm amazed but I'm also kind of scared, because if feeling good feels this way then what does feeling bad feel like?"

Long-term use of the medications has created even more complications. Many HIV medications were rushed through federal Food and Drug Administration (FDA) approvals on a fast-track system developed at the insistence of AIDS activists, so they have not undergone the same rigorous testing that most drugs have. Some of the medications raise cholesterol and blood glucose levels, putting patients at risk for coronary artery disease and diabetes. In some ways, it is a testament to the drugs' success that a long-term problem such as cholesterol is a concern. But now that the drugs are being used on a long-term, chronic basis, their lasting effects on the body will become more important.

Patients who are infected with both HIV and hepatitis C also find that liver disease is a greater threat than developing AIDS (see sidebar). Larry Day, who was diagnosed with HIV infection eight years ago, said, "I've got coronary artery disease now, I've got hepatitis C – that will probably kill me before anything else. Those things are more frightening to me than the HIV."

Physicians have also expressed concern that more and more patients are first diagnosed with strains of HIV that are already resistant to certain medications. Martin

Hirsch, a physician at Massachusetts General Hospital who helps evaluate the effectiveness of different combinations of drugs, said that the same concerns arise with long-term treatment of HIV as with the growing problem of antibiotic resistance in bacteria. "What we've learned so far is that these bugs will continue to evolve as we treat them, and resistance will always be with us," he said. "Our goal is to stay one step ahead of the organism."

It is theoretically possible to "cure" HIV infection if drugs could completely halt viral replication for long enough periods of time, but in reality the current drugs only suppress the virus, not stop its replication completely. "Undetectable" levels of the virus in a patient's bloodstream – a sign of success in treatment – do not mean the virus is eliminated, only that current tests are not sensitive enough to measure viral levels. The drugs are no cure. "We're looking for the perfect regimen that will last forever," said Hirsch, but that goal represents an ideal, not a reality.

Maura Fagan said that the long-term care of HIV-infected patients will probably depend on the continuing pipeline of new drugs to overcome resistance to older ones. The first of a new kind of drug called fusion inhibitors has generated excitement. It helps block the ability of the virus to fuse with host cells and infect them. "That's a whole new class," said Fagan. "You're hitting the virus at a unique point in its life cycle compared to other medications that we had before."

Just how much time are the new drugs buying? The answer to how long a person infected with HIV can expect to live is a complicated one. The newer drugs have only been on the market for a few years, so many doctors refer to life expectancy as a "moving target," meaning no one can predict how long the drugs will hold off illness and how many new drugs will emerge.

But many physicians are optimistic. Fagan said, "People who are now in their 40s and 50s, I really and truly think ... they can expect a normal lifespan."

Tomorrow – The burden of living with HIV

Side effects: The new age of AIDS in America

Part III – A shifting epidemic

WHEN ANTIRETROVIRAL COCKTAILS FOR HIV INFECTION debuted in the mid- to late-1990s, their startling success provided real hope to those suffering from what to that point had been an almost universally fatal disease. Since that time, the medications have continued to improve and to keep people with HIV in the U.S. alive and, for the most part, healthy. The sense of drama that helped to build and sustain early prevention and treatment movements has dissipated – and the infected have largely dropped from public view.

But living with HIV is still a daunting challenge. In addition to the constant side effects of the medications – some of which may cause life-threatening illnesses after years of use – HIV-infected people face the difficulties of living with a chronic, infectious disease.

“You know that there’s a battle going on in your body, and that drains you physically and emotionally and psychologically. Managing your HIV is like having a part time job,” said John Ruiz, consumer office coordinator at the Massachusetts Department of Public Health’s HIV/AIDS Bureau. Ruiz serves as a liaison between the Bureau and people infected with HIV. He tracks the needs of HIV-positive people and attempts to make sure those needs are addressed in policy and program development. And Ruiz has more than a professional knowledge of those needs: he has been HIV-positive since 1986.

“When I was first diagnosed, there was really no reason to find out your [HIV] status, because there was no place to turn to for treatments, there were no programs, there was no government funding for primary care or support services – you were pretty much on your own,” Ruiz said.

Now, many more services are in place, but the needs of people infected with HIV have become more complicated. Rather than simple medical services or preparation for dying, people require help living with their disease – adhering to difficult medication regimens, coping with depression and feelings of alienation, overcoming substance abuse problems, figuring out how and when to disclose their status, and reentering the workforce. “These are all emerging needs that our system is not really prepared to address because of lack of resources,” said Ruiz. “But I think it represents an evolution where our needs were very simple at one time and they’ve become more and more complex.”

Ruiz, who is 45 years old, has dealt with some of these issues in his own life. He takes antiretroviral medications twice a day, and also takes medications to manage the side effects of the HIV treatments, such as chronic diarrhea. He watches what he eats and works out regularly in the hopes of controlling his soaring cholesterol levels, another side effect of his medications. Sometimes it can be difficult to pull himself together in the morning because the medicines make him groggy.

“Every time you take your pills, it’s a reminder that not all is well and these pills are what’s keeping you alive,” he said. “So these pills are your best friend but they’re also your enemy because they make you feel like shit.”

The protease inhibitors that he takes to control the virus have changed the way the fat in his face and body are distributed, causing the skin around his cheeks and temples to dimple. Though the changes are not noticeable to people who do not know him, Ruiz knows that the facial wasting will continue to progress and make him less recognizable to himself in the mirror.

Like many people with HIV, Ruiz said, “depression is ever-present in my life.” Whether it is the psychological impact of living with HIV or an effect of the virus or the medications, Ruiz said that a large body of evidence has shown that most people with HIV experience depression and that the problem often goes untreated. “Often people don’t even know that they are depressed,” he said, and “there aren’t many mental health programs that people can access out there.”

And then there is simply the psychological impact of uncertainty; the drugs work wonders, but at any time they may fail. “I’m running out of options. I’ve used most of the pills that are out there,” Ruiz said. “I dread developing resistance to this current regimen, which is likely to happen eventually.”

Sandra McLaughlin, a social worker at Massachusetts General Hospital, said that the success of treatments for HIV has created a mistaken belief that the infection is easy to manage. “I think some people are not as vigilant as they need to be about protecting themselves, in part because we have better treatments,” McLaughlin said. When these people test positive, they initially feel like it’s not a problem, she said, “but they tend to crash at some point, because you don’t know the realities of what it’s like to take all these medicines and really live with this until you are dealing with it. I think some people are surprised about how hard it can be.”

McLaughlin often sees people when they have first learned of their infection and helps them on an ongoing basis to handle all of the emotional and social burdens the disease brings. “It’s a complicated illness. And now, even though we have much better treatments, we’re starting to see much more of the side effects that some of the treatments can cause,” she said. “It’s adding another whole set of issues that people need to deal with.”

She said that one of the most distressing side effects is a redistribution of fat in the body, like the changes Ruiz is experiencing. Limbs become thinner, the rear end flattens out, and the abdomen (and breasts in females) become fatter. At its most extreme, the condition causes a “buffalo hump” of fatty tissue on the patient’s back. McLaughlin said that this condition worries people not only because of the cosmetic unsightliness, but also because they fear being identified as having HIV because of it. “People [with HIV] tend to be much more isolated in their illness than any other diseases,” she said, and a visible marker of what is usually a private infection frightens them.

Though the stigma once associated with HIV and AIDS has lessened, it is still a reality. A survey conducted in 2002 by researchers at the University of California at

Davis found that negative feelings towards people with AIDS declined during the 1990s, but at the end of the decade, 20 percent of those surveyed still reported feeling fear of people with AIDS and 25 percent said they would avoid direct or indirect contact with them. Consequently, the decision to disclose HIV status at work and in personal relationships is still a difficult choice. "Once you've shared the diagnosis you can't take that back," McLaughlin said.

Unlike other chronic diseases like diabetes, HIV is infectious; it requires not only constant adherence to drug regimens, but also constant adherence to behaviors that minimize the possibility of transmitting the infection. And navigating those risks is not easy.

People with HIV "are living longer and healthier, and with that comes engagement in life and engagement in sexual activity," Ruiz said. HIV-positive people can now look forward to having long-term relationships, instead of relying on their partners as caretakers.

They can also have families. Treatments can prevent mother-to-child transmission of the virus during birth, and women are choosing to start families despite their HIV infections. In Massachusetts, less than three percent of babies born to mothers with HIV are infected with the virus, and most of those births are to women who have not received treatment.

With their lives returning to normal, people infected with HIV often need help in the lifelong effort to reduce the risk of transmitting their infection. HIV prevention has traditionally meant trying to keep people from getting infected, but in the complex landscape of HIV today its definition has broadened. Federal and state agencies are just beginning to shift the focus of HIV prevention programs to so-called "secondary prevention," helping HIV-positive people avoid infecting others.

"People with HIV make extraordinary efforts to not infect their partners," said Ruiz. "I'm a good example of that: my partner and I have been together for four years, he's negative. My ex-partner and I were together for 15 years and he remained negative. And like me, many others make those efforts, but we're doing so without much support from the system of care."

The Massachusetts HIV/AIDS Bureau receives federal and state money to fund programs that provide primary care and medications to anyone with HIV in the state. It also funds HIV testing and counseling, prevention and education, and support services for infected people and those at high risk of infection. But the support available to those infected with HIV is slowly being chipped away by state budget cuts. The state AIDS budget has been reduced 41 percent over the past four years, and the latest budget for fiscal year 2005 includes an additional \$1.7 million cut to the AIDS budget.

"We have done a really good job of shuffling the money around to mitigate the impact of these cuts on people's lives," Ruiz said, "but right now we are in a place where we can no longer do that, and if we get another budget cut people will experience real losses to services."

The cuts in state funding have been felt acutely by AIDS service organizations like the Boston Living Center, a drop-in facility that provides support services for people with HIV.

At the time the Center was founded in the late 1980s, its members were largely gay white men, and the center has always maintained close ties to the gay community of Boston. But times have changed. The membership of the Living Center reflects the shifting demographics of the AIDS epidemic. There are more women and minorities. The communal meals that the center offers have become more than just a social event to get sick people out of their houses: for many members, it is the only full meal they get in a day. Seventy-five percent of the center's members live at or below the poverty level. Increasing numbers of them are homeless. Many are struggling with mental health problems and substance abuse.

As better medications have curtailed the medical burden of the disease for patients who can easily access care, AIDS service organizations have increasingly found themselves serving the needs of infected people on the fringes of society.

"Nowadays you're really trying to determine [whether you are] serving people because they're HIV-positive or because they're poor," said Cathy Morales, executive director of the Boston Living Center. "And in some cases I think it's hard to tell."

Morales, a petite woman with a determined demeanor, said that in the early days of the epidemic the work of AIDS organizations "was very much related to the disease and...to the discrimination and the misperceptions about how it was spread. Today, yes, you still have some of that stigma too, but you're talking about people who were already facing huge obstacles and barriers – prolonged drug use, prolonged undiagnosed mental health issues, chronic poverty generation after generation. It's taken on a completely different spin these days."

And spin is something that people like Morales are acutely aware of, as AIDS service organizations increasingly feel a pressure to justify their existence. "We are very aware of the writing on the wall," she said, adding that many AIDS groups in the city have been collaborating and finding ways not to duplicate efforts. That way, she said, "you don't have this splintering off and people really competing for shrinking pools of money." For instance, the AIDS Action Committee of Massachusetts recently absorbed the center's development staff to combine their fundraising efforts into one office.

The current financial woes stem in part from the high level of support that AIDS received when it was still considered a crisis. Massachusetts has had one of the most generous AIDS programs in the country. As a consequence, said John Ruiz, "our budget line item looks really big in the eyes of state legislators."

The services available for HIV-positive people do raise questions of fairness. Should patients with HIV be reimbursed for all of the co-payments of their medications, if someone with diabetes is not? People who are homeless or otherwise struggling with poverty, addiction, or mental illness can sometimes access better services if they are HIV-positive than not. One staff member of the Boston Living Center said, "I've heard members that come in here and they are happy about being diagnosed as HIV-positive

because they have access to all of our services. Maybe we make life too good for people with HIV if that's happening, I don't know."

Those involved in AIDS services are acutely aware that treatments have turned AIDS into a largely chronic disease. And they are wary of the backlash against special services for people infected with HIV that the good news may cause, as the public associates "chronic disease" with "problem solved".

HIV treatment can be daunting for anyone with the infection. But it is even harder for those whose lives are already complicated by drug addiction, poverty, homelessness, and mental illness.

Tomorrow – The poorest AIDS patients

Side effects: The new age of AIDS in America

Part IV – The toughest cases

THE MAIN LOBBY OF BOSTON MEDICAL CENTER (BMC) is perpetually crowded. Clusters of patients sit in chairs along the wall and form lines at the pharmacy window, while others gather in the sitting area by the Dunkin Donuts counter, sipping coffee or just talking. For anyone accustomed to the Harvard teaching hospitals in Boston, which are more likely to have a Starbucks in their large, light-filled lobbies, the BMC feels more run-down.. It is also livelier. Perhaps because many people seem as if they are used to waiting here it takes on the feeling of a social hub, a respite from the bitter cold of the Boston winter.

The Boston University teaching hospital, located along the busy thoroughfare of Massachusetts Avenue in Boston's South End, sits in the middle of a diverse urban area and serves several of Boston's poorest neighborhoods. BMC is New England's largest safety net hospital. Half of the patients at BMC are uninsured or have Medicaid, and the hospital estimates that more than half have an annual income of \$17,000 or less.

Charles Riley was waiting in the lobby for an appointment with a physician one day in January. Riley had been in and out of homeless shelters and makeshift refuges for the past ten years, but had recently procured a room in the nearby suburb of Lynn through a friend. He is a small, pale man with bright black eyes, wears a brace on his right leg and walks around with the help of a crutch. He has a seizure disorder for which he is being treated. And he is also one of the 200 or so HIV-positive patients at BMC's Health Care for the Homeless Specialty Services clinic, which is dedicated specifically to helping homeless and poor people infected with HIV.

Riley acquired HIV while in prison. The prisoners were regularly tested for HIV, and Riley remembers being called back to get his results. "I automatically knew," he said. "Normally they just send you a piece of paper." When he found out he was positive, Riley tried to commit suicide. "My life is over, that's what I thought."

But it wasn't over. Riley has been on anti-HIV combination therapy for several years. Though he has been through a few different combinations of pills as certain ones failed, the current cocktail seems to be working and the virus has not developed resistance to the drugs yet.

Riley is not anyone's idea of an ideal patient. He is an admitted crack addict, and his life is chaotic. Gesturing with tobacco-stained fingers, he spoke bitterly about his past, being molested as a child, drifting in and out of prison, about the treatment he receives as a homeless person. Tears filled his eyes when he recounted the police destroying a makeshift shelter he and a friend had constructed under a nearby bridge, and having all his meager possessions confiscated. Even as he spoke he signaled to a man who was waiting outside the window of the lobby, and when the friend came inside, Riley stopped his story and asked the man to try to score some drugs from a woman whom he said owed him money.

Riley has made multiple unsuccessful passes through detox programs, but lacks the motivation to get clean since he feels he is already dying of AIDS. Even so, he admitted he was starting to realize that the drugs were working. "I'm dying of it, but I'm also living with it."

Even for someone living in a tenuous situation like Riley, staying healthy with HIV infection is possible in Massachusetts. The uninsured can access medications under one of several different free care programs. Anyone infected with HIV is covered for medical services under the state's MassHealth system. The state's HIV Drug Assistance Program also pays for HIV and AIDS-related medications for people whose annual income is below \$50,000; those who exceed that level can get drug co-payments reimbursed. A free-care pool covers undocumented immigrants who do not qualify for other programs. Programs like the Special Services clinic at BMC, which is funded by a federal grant from the Ryan White Comprehensive AIDS Resources Emergency Act, help reach populations that have the least access to care.

In an ideal world, all of these programs that make drugs and health services affordable would make HIV treatment equal for all. But treating HIV infection involves much more than just providing drugs.

For many of the patients at the clinic, HIV may be the least of their worries. In the cramped space where the clinic is housed, a team of nurses and case managers gets closely involved in helping patients stabilize their lives and their health. They encourage patients to drop in frequently, sometimes offering them used clothing, nutritional shakes, or just conversation. HIV may be the last thing they discuss during visits.

The nurses and case managers at the clinic cannot possibly hope to solve all their patients' problems. They look instead for the small successes. The first goal is a stable place to live. "Nothing is more pressing to a homeless person than getting housing, and health care definitely is second or even third to that," said Carole Hohl, director of the clinic. For many patients, getting into a detox program or getting treated for mental health problems may be necessary before they are stable enough to begin HIV medications.

Though they have been greatly simplified over the past few years, HIV treatment regimens are notoriously difficult to follow. Because HIV undergoes rapid genetic mutations that allow it to resist the actions of drugs, HIV medications require an adherence rate of 95 percent or more in order to maintain their effectiveness. And adherence translates into strict routines and organized schedules – something that many of the patients at the homeless clinic don't have.

Sandra Escalera is a case in point. One day in February, Escalera sat down with Georgia Thomas, her case manager, to talk about her life and treatment progress. She had been HIV positive since 1990, but had been unable to stay on antiretroviral treatment for more than six months at a time. Escalera had drifted in and out of addiction to heroin and cocaine. She had quit both but relapsed while pregnant with her fourth child, who is now four months old. "I figured if I used drugs maybe the baby would die," she explained.

Escalera, who is 38, was neatly dressed in a black dress and long blazer, and fidgeted with a nervous energy that spilled into her husky voice. She had no side effects from the HIV medications, but said she sometimes stops taking them when she begins to think about what they're for: treatment for a fatal disease. She is easily depressed, and said she spent the past four years mostly lying on the couch and spending little time with her children. "I'm just wasting my life, I realized."

Escalera receives regular visits from someone at the Massachusetts Department of Social Services, which had taken her children away temporarily in 1996. She listed all the steps she has taken to get her life stabilized, multiple support groups and one-on-one counseling, as well as parenting and early intervention programs. Despite her relapse, she said, "There are a lot of things that are in place"

Thomas advised Escalera to think about today instead of getting herself depressed worrying about her future. When Escalera admitted that she and her boyfriend have unprotected sex because he hates condoms, Thomas said, "The two of you don't need to both be sick. Think about the little one you have now." She made a note to provide Escalera with female condoms. The staff may privately express disappointment in their patients, but for now Thomas reserved judgment.

Escalera is an example of what lies behind the problem of treatment adherence in HIV. It is more than a matter of remembering to take pills at the right time every day. In order to avoid developing drug resistance, an HIV-infected person has to make a commitment to following a regimen as perfectly as possible for the rest of his or her life.

Carole Hohl said that adherence is by no means impossible in homeless and impoverished populations. "If you've got someone who's even living on the street, if they're willing and there isn't alcohol involved it's not a problem. As long as we can keep a close watch on them, they can do it."

HIV regimens are much simpler than they used to be. Some medications have been combined into one pill, and the patients now only have to take them once or twice a day. Though not glamorous medical innovations, these improvements are enormously important in making treatment accessible to patients who might not adhere to more complicated regimens.

HAART has been a huge success, but it is not successful in every patient. There are a number of reasons why treatment may fail:

- The drugs may cause side effects that are too unbearable;
- A patient may develop resistance to several drugs, making it difficult for a physician to concoct a regimen of drugs that is effective;
- Some patients metabolize drugs differently and have trouble reaching an effective dose.

But beyond these medical anomalies, the best predictor of treatment success is the patient's ability to adhere to the regimen. The experience of patients with other chronic diseases has shown that only about one-third of patients adhere to a chronic treatment 90 percent of the time. The majority are more erratic, taking medications intermittently. For patients with a disease such as diabetes, the consequence of missing a

dose of medication might be illness. HIV infection is more like high blood pressure – a missed dose has no effect the patient can immediately feel; the consequences come later.

The clinic staff members give out plastic pill cases and alarms to patients to help them remember to take pills regularly. But the regimen doesn't take into account the depression Escalera feels when she sees her pills and remembers that she has HIV and wants desperately to forget it. It doesn't consider her ambivalence about her pregnancy, her fear of transmitting the virus to her child, her addiction to drugs, the mental health problems, the self-destructive and sometimes irrational behavior.

"Disorganized" is a word that clinicians often use to describe the kind of lifestyle that makes adherence difficult. Even drug use does not necessarily make treatment impossible. Heroin addicts, Hohl noted, tend to have more organized lives than cocaine or alcohol abusers.

"To take medications when you're homeless, just keeping medications, trying to keep track of them – it's almost overwhelming," said Hohl. "I remember pills by putting them by my toothbrush. Well, they don't have a place like that."

BMC sees a disproportionate number of intravenous drugs users and their sexual partners, groups that tend to be poorer and have more difficulty accessing health services. Out of all the groups of people at risk for HIV infection, intravenous drug users have the shortest survival rates after an AIDS diagnosis, often because they are less likely to be diagnosed early in the infection and to access medical care.

Because of the challenges facing BMC's population, the success stories told by doctors here are less dramatic than those told by staff at hospitals such as Massachusetts General Hospital and Beth Israel Deaconess Medical Center, which serve more middle-class patients. Many BMC patients are being treated successfully and are living with HIV infection as a chronic disease. But the hospital also sees more patients who are diagnosed late in their infection, which makes treatment more difficult.

Edward Feinberg, ophthalmologist-in-chief at BMC, said that he still sees a few patients who have cytomegalovirus (CMV) retinitis, an opportunistic infection that appears in late stages of HIV infection and was an early hallmark of AIDS. The infection, he said, is much rarer among wealthier populations with better access to care.

But while many health care workers are trying to funnel services to the populations that need them most, those who are trying to prevent new infections are eyeing the rising number of new infections in gay and bisexual men.

Tomorrow – HIV prevention in the age of complacency

Side effects: The new age of AIDS in America

Part V – Updating the message

IT'S 11 PM ON A FRIDAY NIGHT, and the AIDS Action "Use Me" boys, Dusty Latimer and Diego Maldonado, have just arrived at a deli on Boylston Street, armed with duffel bags filled with condoms and personal lubricant. A few volunteers have already gathered there, recruits whom Latimer and Maldonado have assembled to help them distribute their wares to clubgoers next door at the Machine, one of Boston's most popular gay nightclubs. After chatting for a few minutes, they distribute uniforms, T-shirts and red-and-black bowling shirts, bearing stickers with the Use Me logo: the silhouette of a penis and testicles, outlined by a condom.

The Use Me boys, both 22 years old, are leading an AIDS Action Committee of Massachusetts outreach program that is designed to promote safer sex in young gay and bisexual men. Three nights a week, the two young men and their volunteers hit some of the popular venues for gay men. Their goal is to be a regular presence in clubs, and to be available to talk to people about safer sex.

Inside the Machine, the mostly male crowd is just starting to fill up the lowered dance floor. The team fills up bowls of condoms in each bathroom and at the bars. Then they split up to offer protection to each patron at the club; some take the crowded main dance floor, others go upstairs to Ramrod, a leather bar that attracts an older crowd. One of the other volunteers returns to pick up some female condoms for a woman he had promised to supply the week before.

Latimer makes his way around a quieter room with pool tables and a bar. He approaches each cluster of men, introducing himself and offering them free bags of condoms and lube. It helps that he is friendly and attractive, though he insists that the female volunteers sometimes have better luck connecting with patrons. Some of the men are happy to accept the free gifts, others shake their heads or say they already have enough of their own. Occasionally someone takes offense. A few couples exchange glances before deciding whether to accept. Some mention they are abstinent, others ruefully admit they haven't needed condoms for a while.

The Use Me program is part of AIDS Action's efforts to spread HIV prevention messages to young gay and bisexual men, one of the risk groups in which infection rates seem to be rising. Many people involved in HIV prevention complain about the complacency people feel towards HIV, especially younger people. Maldonado said that many younger gay and bisexual men feel they are going to get infected anyway, so are less vigilant about safety.

Latimer, who spent a year manning AIDS Action's HIV hotline, said that many callers had the impression that anti-HIV therapies so good that being infected is no problem. "[In] almost half of the calls, people would ask, 'so the medications are really good, right? and the medications can make you live your life normally?'" he said.

While better treatments have shifted public attention away from AIDS in the U.S., preventing new infections is still a challenge. Several indicators point to rising HIV

infection rates, particularly among gay and bisexual men. According to the CDC, during the period from 1999 to 2002, HIV diagnoses in the U.S. increased about five percent – but among gay and bisexual men, the increase was 17 percent.

Syphilis, once an infection that was nearly absent from the country, has reemerged in gay and bisexual men in several cities in the U.S. In Boston, syphilis rates doubled from an all-time low in 1999 to 2002.

“There is a huge increase in infection rates of syphilis, which is a proxy indicator of unprotected sex,” said Eric Rubenstein, an epidemiologist at the Massachusetts Department of Public Health. Epidemiologists worry that the rise in syphilis, which is generally treatable, will herald a further rise in incidence of HIV.

In the early days of AIDS, the new and mysterious illness led to hysteria and homophobia over the lifestyles of gay men, but also led to a reckoning over some practices, such as rampant unprotected sex in bathhouses, that clearly fueled the spread of the virus. Gay men drastically reduced unsafe sexual behavior during the height of the AIDS epidemic. With infection rates up, the spotlight has again turned to the gay men and their sexual practices.

Although they account for less than one-third of deaths among people with AIDS and have the longest rates of survival, gay and bisexual men account for half of new HIV infections in Massachusetts. Studies have found increases in unsafe sex among gay and bisexual men since the late 1990s when drug cocktails first began extending the lives of people infected with HIV. The rise in infection rates has been widely reported in the media, as have stories of disturbing trends of “bug-chasers” who actually seek out HIV infection, and “gift-givers” who are willing to infect others.

Prevention workers are eyeing two developments as causal factors in the resurgence of syphilis and rising rates of HIV infection. The first is the growing popularity of methamphetamine (crystal meth) among gay men in Boston.

“It’s definitely on the increase,” said Patricia Case, associate professor of social medicine at Harvard Medical School who is studying the links between use of club drugs and STDs among gay and bisexual men. “Gay men are just reflecting a general trend,” she said. “Over the last five years there’s been a pretty rapid diffusion from methamphetamine centers on the west coast across the country.”

Since crystal meth is not a direct carrier of the virus, unlike the needles used to shoot heroin, its relationship with HIV transmission is more complex. For one, the drug is used as an aphrodisiac. Jon Vincent, prevention coordinator for AIDS Action, said that under the influence of the drug, men are able to prolong erections and withstand sex for longer periods of time. Vincent said that, in the gay community, the drug has become part of a ritualistic culture of going to clubs, staying up all night, and having group sex.

Although the use of crystal meth in unsafe sexual practices is not exclusive to gay men, more people are paying attention to it because of its link with disease. “What we’ve seen, anecdotally speaking, is most long-term, habitual users of crystal meth who are [gay or bisexual men] turn up HIV-positive, and most have had syphilis at least once,” said Vincent.

The other development that has been linked to a resurgence of sexually transmitted disease is the use of Internet chat rooms to find sex. On AOL, Yahoo, Gay.com, and numerous other websites, users are able to log on anonymously and arrange sexual liaisons with strangers.

In San Francisco in 1999, syphilis broke out among a group of gay and bisexual men who had met their partners over the Internet. Since then, rates of the disease have grown in the city, disproportionately among gay and bisexual men. An analysis of these cases by researchers at the University of California San Francisco found that more of the men had met partners online than through other venues.

The technology changes the dynamics of sexual encounters. Men who might have been leery of venturing into bathhouses or clubs can now arrange anonymous sex in privacy. A number of websites and chat rooms extol unprotected anal sex, or barebacking – though just as many sites, if not more, harshly criticize this behavior.

The relatively unregulated and diffuse nature of the Internet poses new challenges for prevention workers, since efforts like the Use Me program cannot reach these people by circulating in gay night spots. In fact, gay nightclub owners have complained that attendance has dropped over the past few years, in part because more people are meeting on the Internet.

“The normal way of accessing people has been cut out from us,” Jon Vincent said. Prevention groups have been exploring ways of targeting safety messages to web sites or to have educators join in on chats. But currently there are no proven models to follow.

As Dusty Latimer hands out condoms at the Machine, one man shakes his head at the packet offered to him and explains that he used to do similar things for AIDS Action nearly 20 years ago. “It’s great what you’re doing,” he said, adding that he lost many friends in the years when AIDS was at its height.

Many older gay men lament the rise in unsafe behavior among young people who did not suffer through the times when AIDS decimated an entire generation of gay men.

Fred Cowan has been a volunteer at AIDS Action, New England’s oldest and largest AIDS service organization, for more than 20 years, first handling the fledgling organization’s finances, and then working at its HIV hotline and participating in trainings and education. Cowan, a 55-year-old gay man, is not HIV-positive but he and his partner have lost most of their friends to the disease.

Before AIDS appeared, Cowan enjoyed a period of time in which life for well-to-do gay men in Boston flourished. “There was very much a feeling of ‘come out come out wherever you are,’” he said. Cowan, with his cultured speaking voice and face like Russell Crowe, was popular in this large social circle. He and his partner, a physician, frequented gay bars, attended parties every week, and held regular gatherings at their house. “We had hundreds of friends.” As part of their rejection of societal norms, the group often used sex to codify and reciprocate friendship.

But suddenly some of those friends began dying mysteriously. "It was silent, sudden, and unexpected," Cowan said. In all, the couple lost over 200 friends and acquaintances to AIDS.

In those days, AIDS Action operated under a "siege mentality," said Cowan. People were in constant crisis. There was very little help from government. The group struggled to do business because creditors were afraid that no one would survive to pay their debts. The hotline initially had very little information to offer. "I spent most of my time holding people's hands and being eloquent in saying 'I don't know,'" Cowan said.

Now, Cowan has lots of information to give to callers. He has stayed with the organization even as it has changed its staff and activities to reflect a changed epidemic. Women and younger people now have taken leading roles. Many of the new staff members cannot share his memories of the people who worked valiantly at the organization before dying.

The current success of treatments for HIV for Cowan is tempered by his memories of the past. "[Writer] Paul Monette said once: 'I want a cure *and* I want my friends back, and that was sort of my feeling when the triple therapies began to emerge,'" Cowan said. "It was a hollow feeling for me. Frankly, most of my friends were dead by that time." Now, he and his partner arrange trips and outings that they can do alone, and loneliness is something that Cowan has gotten used to.

The new generation of gay men is living in a different reality, and the siege mentality is gone. While information about HIV is abundant, people are no longer desperate to know it. Cowan used to see daily obituaries of people he knew who had died of AIDS. Diego Maldonado admits that he had worked in HIV prevention for two years before he ever met anyone he knew to have HIV. In some ways, he and Dusty Latimer face a greater challenge in convincing a new generation that HIV is still a problem.

"People like Dusty and Diego and the others, they listen. They have the physical presence to be useful in today's world, whereas I don't," Cowan said. "They have the energy and the creative spirit that is dulled in me. And they're under tremendous pressures to perform without the overt support system that I had."

The systems to help people infected with HIV in Massachusetts came about in the midst of a crisis, and those systems, for the most part, are still in place. AIDS Action still draws crowds for its annual AIDS Walk, and volunteers still staff the service organizations that help people infected with HIV. The state policies and programs designed to help HIV-infected individuals access medications and health care are still robust. Boston is flush with specialized clinics and health care workers trained in caring for people with HIV and AIDS.

But as funding for AIDS programs slowly decreases and public interest wanes, it is unclear what the future of the disease will be. The treatments, so far, have been highly effective, but they are problematic over the long term and still are no cure. Even if treatments continue to keep people with HIV infection living relatively healthy lives, what consequences will a growing population of HIV-infected people have on the continued spread of the disease?

When HIV infection was considered a death sentence, it provoked dramatic changes in sexual behavior, health care, and social policy. Now that AIDS is becoming a chronic disease in the U.S., it is forcing those behaviors and systems to adapt to a new reality. In some ways, the crisis may be over but the challenges are more complex. In the siege mentality, “we were asking for profound change, but there’s a timeline to that and then you’ll get your life back,” said Cowan. “Now we’re asking for lifestyle changes.”

These lifestyle changes require constant adherence, just like treatment regimens for HIV. As AIDS is redefined as a chronic disease, it will require chronic attention, funding, support, and dissemination of information to new generations. Just as physicians have had to adapt treatments to a constantly mutating virus, prevention workers will have to adapt their strategies to these new social realities, to keep AIDS from becoming a crisis again.

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Note on Sources

I very much wanted this thesis to be about people and their personal responses to HIV, so I relied heavily on interviews with HIV-infected people, health care workers, and others working in AIDS service organizations. For national statistics on the HIV/AIDS epidemic I relied on the Centers for Disease Control and Prevention website, and for Massachusetts statistics I relied on epidemiological profiles from the Massachusetts Department of Public Health website. Journal articles and books helped support the anecdotal information I heard in interviews and also gave me background on the historical, social, and political context of the HIV epidemic.

Interviews

Patricia Case, assistant professor of social medicine, Harvard Medical School, 4/8/2004

Dan Church, epidemiologist at Massachusetts Department of Public Health (MDPH), 3/1/2004

Fred Cowan, volunteer at AIDS Action, 4/20/2004

Natalie Cramer, Prevention and Education Unit, MDPH, 2/18/2004

Larry Day, Boston Living Center staff and HIV-positive, 2/27/2004 and 3/2/2004

"Bill Dudley," HIV-positive, 1/09/2004, and 5/4/2004

Sandra Escalera, HIV-positive, 2/24/2004

Maura Fagan, medical director of the Center for Infectious Diseases at BMC, 1/29/2004

Julie Freedman, nurse at Massachusetts General Hospital (MGH) STD unit, 12/4/2003

Edward Feinberg, chair of BMC Department of Ophthalmology, 1/8/2004

Howard Heller, physician at MIT Medical Center and MGH, 12/06/2003

Martin Hirsch, director of clinical AIDS research, MGH, 3/31/2004

Carole Hohl, director of Health Care for the Homeless Specialty Services Clinic, BMC, 2/17/2004

Charlotte Johnson, HIV-positive, 2/27/2004

Kevin Koerner, HIV-positive, 2/27/2004 and 4/13/2004

Dusty Latimer, outreach coordinator, AIDS Action, 3/31/2004 and 4/2/2004

Harvey Makadon, physician at Beth Israel Deaconess Medical Center 12/15/2003 and 4/8/2004

Health Care for the Homeless Special Services Clinic staff: Georgia Thomas, Michael O'Connor, and Peggi Marini, 1/20/2004, 2/24/2004

Diego Maldonado, outreach coordinator, AIDS Action, 3/31/2004 and 4/2/2004

Sandra McLaghlin, social worker, MGH, 1/16/2004

Cathy Morales, executive director, Boston Living Center, 1/29/2004

Michael Pinnolis, ophthalmologist, Harvard Vanguard Medical Associates, 1/29/2004

Charles Riley, HIV-positive, 1/20/2004

Eric Rubenstein, epidemiologist, MDPH, 2/27/2004

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About the Author

Having always had a penchant for writing, I graduated cum laude from the University of Washington with a major in English and a minor in technical communication. I then spent more than three years writing about biomedical research and health for Harvard Medical School, where I developed an interest in examining the social dimension of medicine and science. I was awarded an Ida M. Greene fellowship for my studies at MIT, where I have had the opportunity to broaden my knowledge of science and explore the social impact of medicine more fully.