

Can the HIV/AIDS Epidemic in New York City Be Stopped?

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AS OF DECEMBER 31, 2003, A TOTAL OF 88,479 NEW YORKERS HAVE BEEN diagnosed, reported, and are known to be living with HIV or AIDS. Dr. Frieden explained that 57,316 (64.7%) have already received an AIDS diagnosis and that 31,163 (35.3%) are infected with HIV but have not met the immunologic or clinical case definition for AIDS. "Of central concern to us," Dr. Frieden said, "is that we probably have another 20,000 New York City residents who are HIV-positive but aren't aware of their status."

Based on these data, New York City remains the epicenter of the HIV/AIDS epidemic in the United States (Figure 1). New York City has the highest AIDS case rate in the United States; while it is home to less than 3% of the U.S. population, the city accounts for 17% of national AIDS deaths. "We have more cases than Los Angeles, San Francisco, Miami, and Washington, D.C., combined," Dr. Frieden noted. "Our case rate is 60 times the national target for 2010, four times the U.S. average, and higher than any other city in the U.S."

Dr. Frieden also noted a number of epidemiologic disparities. More than 80% of new AIDS diagnoses and deaths in New York City are among African Americans and Latinos. And as has been documented nationally, an increasing proportion of new AIDS cases are among women, most notably women of color. Rates of AIDS cases and HIV infections vary widely among New York City's neighborhoods. As many as one in four men who have sex with men (MSM) residing in the Chelsea-

Clinton section of Manhattan are infected with HIV. In Greenwich Village and Soho, as many as one in six MSM are infected. And in Central Harlem, approximately one in ten MSM are HIV-positive.

Black male residents of New York City, who are nearly three times more likely to be living with HIV/AIDS than other New Yorkers, have been especially hard hit by the epidemic. Dr. Frieden explained that one in 14 black men between the ages of 40 and 54 is living with HIV/AIDS—seven times the rate of other New Yorkers. The only groups with higher infection rates are men who self-identify as gay or bisexual (one in ten are estimated to be living with HIV/AIDS) and injection drug users (one in seven are believed to be living with HIV/AIDS).

Women bear an increasing burden of the epidemic in New York City. Approximately a third of new AIDS diagnoses and deaths from AIDS in the City are among women. This rate is up from 1 in 4 in 1992 and 1 in 10 in 1985. More than 90% of AIDS cases in women are among Black and Hispanic women. Comparatively speaking, HIV/AIDS incidence is five times higher among African-American women and three times higher among Latina women than among Caucasian women. "The majority of these women whose risk is reported became infected from heterosexual sex with an infected partner," Dr. Frieden commented. "Heterosexual sex has surpassed intravenous drug use as the primary mode of transmission of HIV to women."

The cumulative number of deaths in New Yorkers living with HIV or AIDS is 84,808. Until recently, greater than 90% of deaths were due to HIV-related causes. While AIDS deaths are down 75% since the peak in 1994, nearly 1,700 HIV-positive New Yorkers died of AIDS-related complications last year, and another 600 died of other causes (most notably substance abuse, cardiovascular disease, or malignant neoplasms). "HIV is still a leading cause of death among New Yorkers," Dr. Frieden said, "and is the leading cause of death among New Yorkers between the ages of 35 and 44." Almost 180,000 New Yorkers have been diagnosed and reported with HIV or AIDS since the start of the epidemic.

As has been seen on the national level, NYC DOHMH epidemiologic data indicate that New Yorkers infected with HIV are living longer. "This translates into increased need for treatment, increased need for social services, and increased need for housing," Dr. Frieden pointed out. "The number of people living with AIDS in New York City has doubled in the past decade. This means double the need for all the services that are so important to helping them live longer and healthier lives."

Fortunately, there are encouraging data to draw upon as well. For example, perinatal HIV transmission has decreased by more than 95% since the peak in 1990. "Due to efforts to increase the proportion of women who know their HIV status, along with the proportion of HIV-infected women who receive prenatal care and antiretroviral therapy, we've seen a dramatic decrease in the number of infants being born with HIV infection in New York City." According to NYC

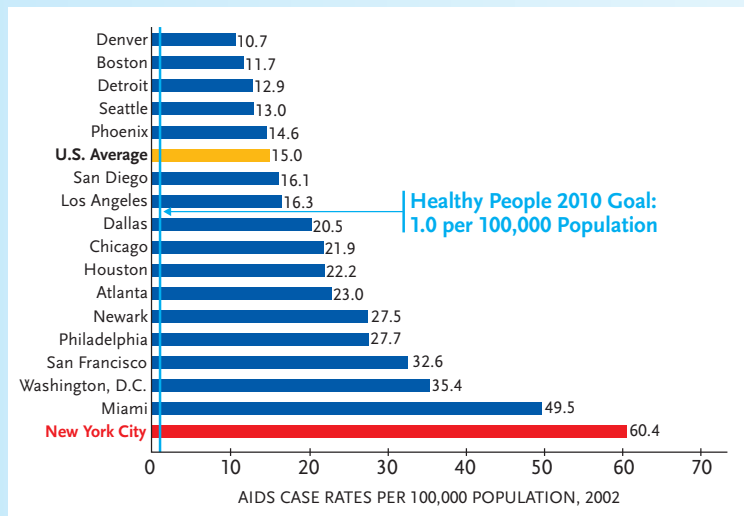


FIGURE 1. New York City AIDS Case Rate Highest in U.S.

New York City remains the epicenter of the HIV/AIDS epidemic in the United States. New York City has the highest AIDS case rate in the United States; while it is home to less than 3% of the U.S. population, the city accounts for 17% of national AIDS deaths. As this figure illustrates, New York City has more cases than Los Angeles, San Francisco, Miami, and Washington, D.C., combined. New York City's case rate is 60 times the national target for 2010 (blue line), four times the U.S. average.

Source: New York City Department of Health and Mental Hygiene

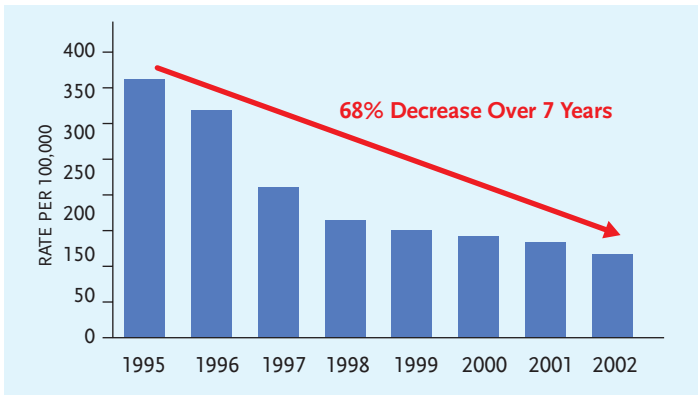


FIGURE 2. HIV-Related Hospitalizations in New York City

While much HIV/AIDS epidemiological data for New York City are disturbing, encouraging data are available as well. For example, perinatal HIV transmission has decreased by more than 95% since the peak in 1990. What's more, HIV seroprevalence among intravenous drug users entering care has also decreased by 75% from the early 1980s. As is shown in this bar graph, there has also been a significant decline in AIDS-related hospitalizations—a 68% decrease since 1995, according to the New York Statewide Planning and Research Cooperative System (SPRCS).

Source: Statewide Planning and Research Cooperative System

DOHMH reports, only five perinatally infected babies were born in New York City last year.

HIV seroprevalence among intravenous drug users entering care has also decreased by 75% from the early 1980s. “Between the early 1980s to the early 1990s, HIV seroprevalence among IDUs was approximately 50%; today, seroprevalence is estimated at around 14%,” Dr. Frieden explained. “That’s still 14% too high, but it’s a striking decrease in the proportion of people who use drugs intravenously who have HIV infection.”

There has also been a drastic decline in AIDS-related hospitalizations (see Figure 2). However, Dr. Frieden noted that “resources saved from this decline have not really been invested in expansion of effective outpatient care.”

HIV/AIDS in NYC: Can it be Stopped and Reversed?

WHILE DATA HAVE DEMONSTRATED THAT THE HIV/AIDS EPIDEMIC IN New York City has slowed, HIV is still endemic in the city: last year, 4,200 people were newly diagnosed with HIV. In turn, a central question remains: can this epidemic be stopped and reversed? Dr. Frieden explained that the most critical step in controlling an epidemic is stopping its transmission. The key is provided by a fundamental epidemiologic parameter called the basic reproductive number, or R_0 , which measures the potential for the spread of an infectious disease. Formally, R_0 is defined as the expected number of secondary infectious cases generated by an average infectious case in a susceptible population. R_0 not only tells epidemiologists the potential for an epidemic to continue spreading in the absence of interventions, it also allows them to predict the ability of control measures to reduce transmission.

If R_0 equals 1—that is, each infected person infects exactly one other person—the epidemic will remain steady over time. If R_0 is greater than 1—each infected person infects more than one other person—the epidemic will worsen, with the number of cases increasing over time. However, if interventions can reduce R_0 to less than 1—meaning that each HIV-infected person infects fewer than one other person—the epidemic will

be reduced and eventually dissipate. “Stopping the HIV/AIDS epidemic will require breaking the chain of HIV transmission,” Dr. Frieden added. “Every new HIV infection starts with someone who is already infected.” The good news is that longevity and quality of life are increasing for New Yorkers with HIV/AIDS. But the growth of the prevalence pool poses new challenges in controlling transmission.

Why has the HIV epidemic been sustained in New York City and the rest of the United States? For starters, there are issues related to early diagnosis. “If everyone infected with HIV learned of their diagnosis soon after infection, we could get these individuals into treatment and get them to take steps to protect themselves and their partners,” Dr. Frieden said. “This alone would cause a sharp decline in the number of new HIV infections in New York.”

There are also problems linking HIV-positive patients to treatment and care. Dr. Frieden explained that approximately 20% of HIV-positive individuals are not in care within one year of receiving their diagnosis. “Plus,” he said, “a large number in care are not in consistent care. Although we don’t have firm data, it appears that, at most, half of those patients in consistent care have adequate viral load suppression.” As for ensuring that HIV-infected individuals aren’t spreading HIV to those who are HIV-negative, Dr. Frieden noted that there’s more work to be done in the area. “Because every new infection is transmitted by someone who is already HIV-positive, we need to redouble our efforts to: 1) raise awareness that HIV can infect anyone, 2) offer testing to every New Yorker, and 3) ensure that HIV-positive people take steps so that they don’t infect others.”

There is also the issue of ensuring that HIV-negative individuals aren’t exposing themselves to HIV through risky behaviors. “We really haven’t done a very good job in any of these areas,” Dr. Frieden said. “However, in each of these areas, there are improvements that we can make to break the chains of transmission.”

Prompt Diagnosis

FOUR-THOUSAND TWO-HUNDRED NEW YORK CITY RESIDENTS WERE DIAGNOSED with HIV infection in 2003. However, more than 1,000 of them learned they were HIV-positive at the time of the AIDS diagnosis, meaning that they had been infected with the virus for an average of 10–12 years. “Most of these individuals had contact with the health care system,” Dr. Frieden said. “Had testing been offered as a routine part of their medical care, they would have been diagnosed early and fewer of their partners would have become infected.”

Ensuring prompt diagnosis of HIV infection will require expanded testing. Dr. Frieden explained that HIV testing needs to become a normal part of medical care. What’s more, rapid testing initiatives need to be expanded. “HIV testing needs to be implemented much more widely at correctional facilities, such as Riker’s Island, STD clinics, community sites where large numbers of at-risk people congregate, community organizations, hospital emergency departments, inpatient units, homeless populations, chemical dependency programs, and other areas. Testing should also be coordinated with housing and other social services.”

The end result of early HIV diagnosis is clear. “It enables effective medical treatment and access to a variety of social services,” Dr. Frieden said. “This, in turn, can enable us to initiate prophylaxis for opportunistic infections if indicated, suppress viral load, prevent hospitalizations, prevent drug resistance, prolong life, improve the quality of HIV-infected individuals’ lives and, with all these, reduce the risk of HIV transmission.”

HIV testing has come a long way since the beginning of the epidemic. Twenty years ago, people with AIDS could not expect to live more than a year after receiving their diagnosis. The epidemic was

generally limited to highly stigmatized groups and testing generally meant a one- to two-week wait for results. Today, HIV-positive people are living longer and healthier lives. The epidemic is more widely spread in the general population and HIV testing has become highly sensitive, with results available using rapid assays in less than an hour (see: “Understanding and Utilizing New Techniques for HIV Testing” in the December 2003 *Notebook*.) “Back in the mid-1980s,” Dr. Frieden pointed out, “the benefits of testing were more or less uncertain; the benefits of testing only slightly outweighed the risks. Today, there is a clear benefit associated with early diagnosis for the patient, for his or her family, other contacts, and the community. In other words, the benefits of testing today clearly outweigh the risks.”

Implementing expanded HIV testing requires an understanding of current barriers to testing. For the most part, testing is still based on a clinician’s assessment of individual risk. “Doctors and patients are often uncomfortable discussing sexual history and drug use, which can prevent clinicians from accurately assessing an individual’s risk factors,” Dr. Frieden said. Because HIV testing has not yet been incorporated as a normal part of health care in all primary care practices, HIV testing is often sidestepped and viewed, by some, as an addition to standard medical practice, not a routine component of it. Legal requirements for intensive counseling and written consent, while appropriate at the time, also decrease the number of people tested.

“While continuing to ensure informed consent, confidentiality, and the voluntary nature of testing, we need to change to the current model of HIV testing,” Dr. Frieden proclaimed. Routine, voluntary HIV screening will reduce testing-related stigma, he argued. “More patients will accept an HIV test if it is offered routinely than if it is offered based on a risk assessment.” The U.S. Centers for Disease Control recommends universal testing in settings with greater than 1% prevalence; in New York City, the overall prevalence of HIV is approximately 1.5%. “And when we consider that some populations in New York City have an overall prevalence of up to 25%, universal testing should certainly be a priority.”

Dr. Frieden, the NYC DOHMH, and other experts cite well-documented evidence that, once an HIV-positive person knows his or her status, he or she will reduce risky behavior. Early diagnosis means that people can start to reduce risky behavior early in the course of infection, not years into their infection. “Many people at high risk of HIV infection don’t perceive themselves to be at risk,” he said. “More than half of new HIV infections are transmitted by people who do not know their status. People who know their HIV status are, on average, more likely to reduce risky behaviors to avoid infecting others.”

Effective Treatment and Counseling

AS HAS BEEN DISCUSSED IN NUMEROUS PAST ISSUES OF *THE PRN Notebook*, an HIV-infected patient’s viral load—especially when the patient is unaware of his HIV serostatus—is a significant determinant of infectiousness. Antiretroviral therapy has been documented to reduce viral load, which includes among its many benefits decreased transmission risk. “The problem is that individuals who don’t know their HIV status are not aware that they are infectious and are not receiving treatment to reduce their viral loads,” Dr. Frieden said. “We also need to continually reiterate key HIV prevention messages to our HIV-positive patients: that abstinence is 100% effective, and that limiting the number of sex partners, always using condoms, and never using dirty needles prevent HIV transmission.”

While educating HIV-infected individuals about transmission risks and their responsibilities to reduce those risks is not new, it has become

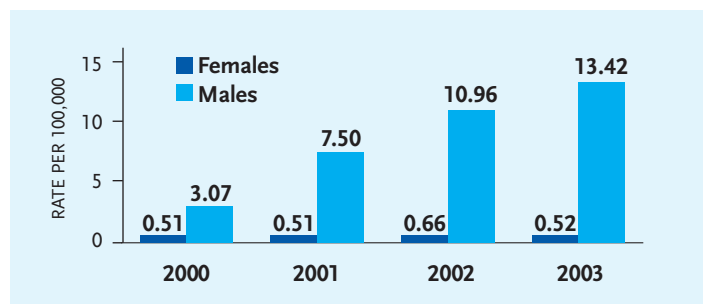


FIGURE 3. Reported Primary and Secondary Syphilis Case Rates in New York City, 2000–2003

A fundamental goal of New York City Department of Health and Mental Hygiene HIV/AIDS programming is to curb the epidemic. However, there are significant challenges ahead, including the well-documented resurgence of risky sexual behavior. As is shown here, syphilis cases in New York City have increased more than four-fold over the past three years. The number of syphilis cases doubled between 2000 and 2001, increased another 46% in 2002, and another 22% in 2003. The increase is almost entirely among men, especially MSM.

Source: New York City Department of Health and Mental Hygiene

a central component of prevention programs being developed and funded by the CDC and State/City departments of health across the nation. “Prevention with Positives” is the term for this stepped-up approach, which is intended to integrate prevention counseling and other initiatives into the treatment and care of HIV-positive individuals. “Prevention activities have traditionally targeted HIV-negative populations,” Dr. Frieden explained. “Now we’re working towards integrating prevention into HIV/AIDS care and treatment. Longer life expectancies of people with HIV/AIDS require new lifelong prevention strategies.”

Components of Prevention with Positives include safer sex messages, condom use, condom distribution, disclosure of serostatus (“do ask, do tell”), syringe exchange and other harm-reduction programs, and bridging the gap between prevention and treatment. All of these require clinicians to play a much more active role in communicating with their patients about risk factors. “Every HIV-positive individual needs to assume ownership of the HIV/AIDS epidemic, just as each community must, to encourage open discussions about HIV status, risk factors, and taking responsibility to protect themselves and others,” Dr. Frieden suggested. “Prevention with Positives can work. It is potentially more effective to target the 100,000 HIV-positive New Yorkers than to target the 7.9 million who are uninfected. All new infections start with a person who is HIV-positive. If all HIV-positive individuals knew their status and participated in Prevention with Positives, further spread of the virus could be stopped.”

There are significant challenges ahead. There has been a well-documented resurgence in risky sexual behavior. Syphilis cases have increased more than four-fold over the past three years (Figure 3). The number of syphilis cases doubled between 2000 and 2001, increased another 46% in 2002, and another 22% in 2003. The increase is almost entirely among men, especially MSM. Might this foreshadow a future increase in HIV infection rates? Yes. “Sixty-seven percent of MSM diagnosed with syphilis in 2002 reported HIV coinfection and 100% of people diagnosed with syphilis engaged in unsafe sexual practices,” Dr. Frieden cited. “Our data show that 70% of HIV/syphilis-coinfected MSM knowingly engaged in behaviors that put others at risk for both HIV and syphilis. The Health Department can’t reverse this upswing in risky be-

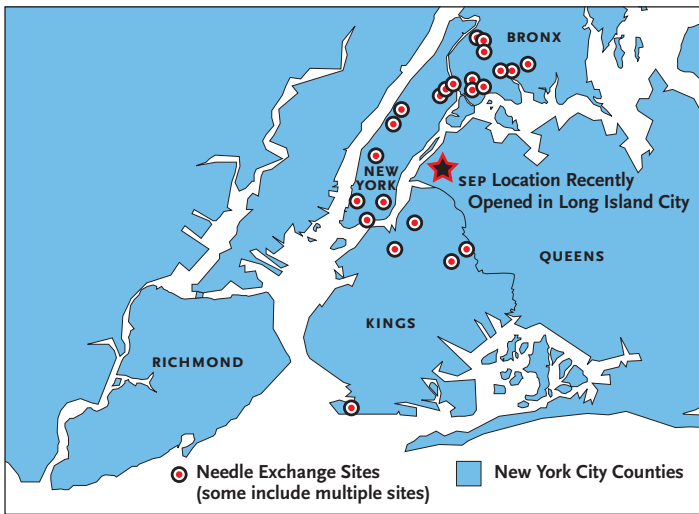


FIGURE 4. SEP Locations in New York City

Syringe exchange programs (SEPs) have been operating in the City for more than a decade, and the New York City Department of Health and Mental Hygiene is currently working to expand these programs into neighborhoods with demonstrated need for them, which includes the most recent SEP in Long Island City. Studies have demonstrated that SEPs do not increase illicit drug use, increase discarded needles around the city, or increase violence or crime in neighborhoods hosting these programs. Because of their counseling components, SEPs have also been documented to reduce drug use and provide a gateway to drug treatment and other services.

Source: New York City Department of Health and Mental Hygiene

havior alone. This has to spring from community-based initiatives that say we're going to take responsibility for protecting our community. The phenomena we're seeing with syphilis in New York City is not encouraging. We need to figure out ways that we can do better."

Protecting the Uninfected

STOPPING THE HIV/AIDS EPIDEMIC IN NEW YORK CITY WILL ALSO REQUIRE continued attention by individuals who are not infected with the virus. In a large-scale telephone survey conducted in the city, it was determined that 350,000 (7%) adult New Yorkers are at a high risk of HIV infection. The term high-risk was applied to any individual who: 1) reported three or more sex partners during the previous year and not using condoms during the last sexual encounter, 2) reported using intravenous drugs, 3) had an STD in the 12 months prior to the survey, 4) has a history of exchanging sex for money or drugs, or 5) ever had unprotected anal intercourse. "Only one in three of these high-risk individuals had been tested for HIV within 18 months prior to the survey," Dr. Frieden said. "We're seeing low testing rates in many of the neighborhoods with the largest percentages of people at high risk for HIV infection."

There are believed to be more than 150,000 active intravenous drug users in New York City, with 30% to 40% of them most likely still sharing needles. In terms of stemming addiction, treatment—including both methadone and buprenorphine programs—is not always readily available. The prevalence of HIV among IDUs is estimated to be 14%.

Syringe exchange programs (SEPs) have been operating in the City for more than a decade, and the NYC DOHMH is working to expand these programs into neighborhoods with demonstrated need for them (Figure 4). "SEPs are successful," Dr. Frieden said. "SEPs do not increase illicit drug


use, increase discarded needles around the city, or increase violence or crime in neighborhoods hosting these programs. SEPs do save lives and prevent HIV transmission. And because of their counseling components, they do reduce drug use and provide a gateway to drug treatment and other services. They're probably the single most effective HIV prevention program in this city."

Dr. Frieden also addressed the issue of crystal methamphetamine use in New York City, a subject that PRN will be taking on in much more detail during a planned future meeting. "It's a big problem that we're facing," he admitted. "We don't have as serious a problem as is being seen in other parts of the county, but it's still a major issue in New York City. Use appears to be increasing and there's anecdotal evidence that it may play a role in half or more of new HIV infections among MSM. We need to expand programs to treat those who are addicted and to prevent and protect those who are not addicted from becoming hooked on the drug."

The Need for Coordinated Care

FOR NEW YORK CITY TO RESPOND FULLY AND EFFECTIVELY TO THE HIV/AIDS epidemic—ensuring the health of those infected and putting various prevention strategies into practice—coordinated care is going to be essential. "We provide a lot of housing for people living with HIV," he explained. "We also provide a lot of medical care. We also provide a lot of social services. The problem is, these aren't being coordinated. We need to do a much better job. We need to make sure that all other services are tied to either housing or medical care. That housing is tied to medical care and that medical care is accountable for suppressing viral load, reducing hospitalizations, increasing life expectancy, using a harm reduction approach to get people into drug and alcohol treatment, and providing prevention messages aimed at reducing risky behavior. The connection between housing and medical care is important. We can't get people into treatment and provide necessary support services or counseling, if they're not stably housed."

The needs of New York City, in terms of effectively coping with the HIV/AIDS epidemic, are extensive. "We're talking about the care of 100,000 HIV-positive individuals and the prevention needs of the 7.9 million not infected," Dr. Frieden said. "New York City offers as extensive HIV/AIDS services as any other city in the world. We also have a vibrant advocacy community that will always push for more services, which we consider to be good." While current funding levels are insufficient in terms of keeping up with care and prevention needs, Dr. Frieden argues that many of the services and programs currently available in New York City can be made more efficient.

No coordinated plan currently exists for HIV/AIDS prevention, treatment, and care in New York City. Services are provided by many agencies and organizations, including the NYC DOHMH, the Human Resources Administration, the New York State AIDS Institute, and community-based organizations. "There's quite a bit of overlap between city, state, and private agencies, in terms of services offered," Dr. Frieden said. "As a result, effective case management suffers. We're seeing a lot of services being provided in a piecemeal fashion in a polarized political environment, which is problematic. What we need to do is bring the various parties together to make sure that services are being provided to all those who need them, and that these services are working effectively." 

References

The New York City Department of Health and Mental Hygiene. *HIV Epidemiology Program 4th Quarter Report*. October 2004. Accessed at: <http://www.nyc.gov/html/doh/pdf/dires/dires-2004-report-qtr4.pdf>

Multiple-drug-resistant, Dual-tropic HIV in Recently Infected NYC Man Experiencing Rapid Disease Progression

ON FRIDAY, FEBRUARY 11TH, THE NEW YORK City Department of Health and Mental Hygiene (NYC DOHMH) held a press conference to present a sobering case report: a man recently infected with a multiple-drug-resistant (MDR), dual-tropic HIV variant who was experiencing rapid disease progression. Within hours, the case was being reported by media organizations all over the world. Soon thereafter, experts and community activists started questioning the scientific validity and the public health relevance of a single case report, particularly as it was being portrayed by the media.

In an effort to settle the brewing controversy, Drs. Marty Markowitz and David Ho of the Aaron Diamond Research AIDS Center (ADARC) have each publicly presented specific details of this case, first at the PRN meeting on February 15th and then at the 12th Conference on Retroviruses and Opportunistic Infections in late February in Boston. ADARC received the patient after he was referred to Dr. Markowitz by a clinician in New York City and has been working closely with the NYC DOHMH.

Case History

THE PATIENT IS A MAN IN HIS LATE FORTIES. He had repeatedly tested negative for HIV antibodies between September 2000 and May 2003. In early November 2004, he experienced fever, pharyngitis, weakness, and fatigue. The symptoms abated after approximately a week, but intractable sore throat, fatigue, and malaise recurred, prompting a visit to his private physician in mid-December 2004, when he was found to be HIV-antibody positive.

In late December 2004, his CD4+ count was 80 cells/mm³, his CD8+ count was 1012 cells/mm³, and his viral load was 280,000 copies/mL. He was then referred to ADARC for evaluation as a possible case of recent HIV infection.

When he was seen at ADARC in mid-January 2005, the positive HIV serology using a standard EIA was confirmed. A detuned EIA was performed and was also found to be positive, indicating that his infection was likely beyond the acute or primary phase.

However, given his established EIA testing history, it has been concluded that this patient was infected within the last four to 20 months.

A number of viral load, CD4+, and CD8+ cell measurements were taken serially. On January 13, 2005, his CD4+ count was 65 and his CD8+ count was 839. On January 20, 2005, his CD4+ count was 28 cells/mm³ and his CD8+ count was 434 cells/mm³. And on February 3, 2005, his CD4+ count was 39 cells/mm³ and his CD8+ count was 57 cells/mm³. Collectively, the results suggest that he had rapidly progressed to AIDS.

The patient reported that he had been sexually active with countless male partners over the years, often in conjunction with methamphetamine use. In particular, he believed he was infected while having risky sex with multiple partners, including both insertive and receptive anal intercourse without condoms, in the third week of October 2004. The patient reported stopping methamphetamine in November 2004, but continued to have sex with approximately 10 partners until the end of December 2004, when sexual activities ceased due to his deteriorating health.

Drug Resistance

THE PATIENT'S HIV WAS EXAMINED FOR SUSCEPTIBILITY TO antiretroviral drugs. Genotyping results revealed broad resistance to NRTI, NNRTI, and PI. A review of the documented mutations suggests resistance to thymidine analogues, lamivudine (Epivir) and emtricitabine (Emtriva), reduced susceptibility to abacavir (Ziagen) and tenofovir (Viread), high-level resistance to nevirapine (Viramune), possibly an attenuated response to efavirenz (Sustiva), and broad resistance to protease inhibitors.

Phenotyping was also performed and has yielded conflicting results as to whether the patient is truly dealing with an "untreatable" variant of HIV, as was stated by the media. Susceptibility of the patient's virus was comparable to a drug-susceptible reference virus for a number of NRTIs, including abacavir, didanosine (Videx), stavudine (Zerit), zidovudine (Retrovir), and tenofovir.

Low levels of reduced susceptibility to lamivudine and emtricitabine were observed.

While these phenotypic data suggest little evidence of drug resistance to these agents, Drs. Markowitz and Ho argue that the presence of the cross-resistance mutations at positions 184, 210, and 215 in reverse transcriptase may be a more noteworthy and ominous sign of what will happen once NRTI therapy is commenced.

The phenotyping assay also showed that the virus was highly resistant to nevirapine and all commercially available protease inhibitors. However, the virus tested sensitive to two NNRTIs, efavirenz and delavirdine (Rescriptor), and to enfuvirtide (Fuzeon).

Only time will tell how well this patient responds to his current regimen consisting of enfuvirtide, efavirenz, tenofovir and didanosine.

Of note, the replication capacity of this patient's HIV was measured at 136%, compared to a median value of 100% derived from a large number of wild-type viruses. In other words, this MDR virus replicates as well as most wild-type drug-susceptible viruses.

Coreceptor Usage

IT WAS FOUND THAT THE PATIENT'S VIRUS readily forms syncytia in both MT-2 cells and normal-donor PBMC. This finding strongly indicates the presence of X4-tropic viruses. The use of a tropism assay also demonstrated that the viral quasiespecies in this patient are able to infect cells using both CCR5 and CXCR4. However, it is not yet known whether he has a mixture of R5 and X4 viruses or dual-tropic population that uses both CCR5 and CXCR4.

Dr. Markowitz and Ho have also noted that declining and low CD8+ cell counts, as was seen with this patient, are indicative of X4-tropic virus progression. Whereas CD8+ cells typically expand in primary HIV infection, they diminished significantly in this patient. This has been documented in previously published reports involving patients infected with dual-tropic and X4-tropic virus.

(continued on page 19)