Investigation of a New Diagnosis of Multidrug-Resistant, Dual-Tropic HIV-1 Infection—New York City, 2005

In December 2004, infection with a strain of multidrug-resistant (MDR), dual-tropic* human immunodeficiency virus (HIV)-1 was newly diagnosed in a man aged 46 years in New York City (NYC). The man (i.e., the index patient) had no history of antiretroviral treatment and reported having sex with multiple named and anonymous male partners, using crystal methamphetamine, and engaging in unprotected insertive and receptive anal intercourse. He had rapid progression to acquired immunodeficiency syndrome (AIDS) after experiencing signs and symptoms of acute HIV infection. The case was reported to the New York City Department of Health and Mental Hygiene (NYCDOH) in late January 2005 and has been described previously.1 This report describes the public health investigation of the index patient’s reported contacts and a review of viral genetic sequencing (genotype) results from other HIV-infected patients in the NYC region to estimate the prevalence of this strain of HIV. The investigation, conducted by NYCDOH, Connecticut Department of Public Health, Aaron Diamond AIDS Research Center, New York State Department of Health, and CDC, identified three other patients with similar risk factors who engaged in high-risk sexual activity at the same time and in the same venues as the index patient and who were infected with a genotypically homologous strain of HIV. The findings demonstrate the usefulness of population-based reporting of HIV genotyping data to identify exact matches of new HIV mutations associated with drug resistance and to determine their characteristics and public health importance. The findings also demonstrate the continued risk for HIV transmission among men who have sex with men (MSM) through high-risk behaviors and the need to find effective methods to prevent HIV transmission in this population.

Case Report
The index patient had tested negative for HIV infection in May 2003 and reported no history of treatment with antiretroviral drugs (ARVs). In early November 2004, he experienced onset of persistent fever, fatigue, and pharyngitis. In mid-December 2004, he tested positive for HIV-1 by enzyme-linked immunosorbent assay (ELISA) and Western blot. The patient’s HIV infection progressed rapidly to AIDS during a period of 4-20 months; his exact date of infection was unknown. His CD4+ T lymphocyte count decreased from 80 cells/µL on December 29, 2004, to 28 cells/µL on January 19, 2005. His plasma HIV RNA levels ranged from 100,000 to 650,000 copies/mL during January 2005.

Genotypic analysis of the viral polymerase (pol) gene predicted that the patient’s virus was resistant to most agents in three classes of ARVs: nucleoside or nucleotide analogue reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and protease inhibitors. Phenotypic drug-resistance testing indicated that the strain was susceptible to enfuvirtide and efavirenz. The virus was subtype B; the viral population was relatively homogeneous, with an average intrasample diversity for the p17 and V3 regions ranging from 0.4% to 1.7%. The virus was dual tropic and had replication capacity 36% greater than wild-type HIV strains. The patient tested negative for all known genetic host-susceptibility factors associated with rapid AIDS progression (e.g., presence of D32 homo- or heterozygosity, HLA A-B-C homozygosity, or specific Class I and Class II alleles).2,3

Contact Investigation
After the case was reported to NYCDOH, the index patient provided the names and contact information for 14 sex partners during a standard, voluntary, confidential interview. The named partners were contacted by NYCDOH in February 2005 and were offered HIV testing. Ten of the 14 named partners had been reported previously to the NYCDOH HIV/AIDS registry as seropositive. Eight of these 10 partners either had a recent blood test for HIV genotype (i.e., within 1 year of the index diagnosis) or consented to a new blood draw for genotyping. Chart review indicated that all 10 named partners were clinically stable, and none had a genotype matching that of the index patient. Of the four partners who had not been previously reported to NYCDOH, one could not be reached despite multiple attempts; the three others all either reported a recent negative HIV test or refused testing.

Laboratory Reporting
In response to this case, on February 11, 2005, NYCDOH requested that all physicians and laboratories in NYC report patients with newly diagnosed MDR HIV-1 and rapidly progressive disease. Laboratories conducting genotypic drug-resistance testing were asked to report all genotypes identified during June 1, 2004—June 30, 2005, that exhibited resistance to four or more nucleoside/nucleotide analogue re-
verse transcriptase inhibitors, one or more non-nucleoside reverse transcriptase inhibitors, or four or more protease inhibitors. In response, laboratories reported 189 MDR genotypes, representing 134 persons, of whom 121 had medical records available for review in NYC. An attempt to match each person to those in the HIV/AIDS registry confirmed that 116 persons had diagnoses of HIV infection before January 1, 2000; five had infections diagnosed during 2000-2004. Two of these patients (with infections diagnosed in 2001 and 2003, respectively) had no record of ARV therapy in their charts; two others were on ARV therapy before the MDR HIV-1 genotype was identified in the index patient in December 2004.

During February 11–June 30, 2005, health-care providers were encouraged to perform genotyping on all patients who tested newly HIV positive and to report by telephone any patients with newly diagnosed MDR HIV-1 infection who had never been treated with ARVs.

In February–March 2005, the 28 laboratories conducting HIV genotyping on NYC residents were asked to match the pol genotype of the index patient against the nucleotide sequences in their sequence databases. The index patient’s pol genotype also was matched against sequence libraries at CDC, the New York State Department of Health Wadsworth Center, three large commercial laboratories in the United States, two laboratories in Canada, and one in Europe. Three male patients, one in Connecticut and two in NYC, had nucleotide sequences with >95% homology to the index patient’s pol sequence. The three patients with matching genotypes were interviewed either by their primary-care providers or by NYCDOH. Information from the interviews indicated a strong likelihood that the index patient and Connecticut patient had been sex partners. Although none of the three patients with matching genotypes identified each other or the index patient by name, all reported engaging in sexual activity at the same events or venues or at similar events attended by the index patient during the preceding 2 years. Both the Connecticut patient and the index patient described a sex partner attending at least one of these events who resembled the other in terms of general appearance, occupation, and serostatus (self-reported). All three men with genotypes that matched the index patient’s genotype were clinically stable on ARV regimens at the time of their interviews. Sufficient data were not available to determine the rate of disease progression before diagnosis of HIV infection or initiation of ARV therapy in any of the three patients with matching genotypes.

**Sequencing**

Confirmatory sequencing of pol and additional portions of the genome was conducted by three independent laboratories on new blood samples from the index patient and the three patients with matching genotypes. This testing confirmed the pol homology of the viruses and homology of other genomic regions. However, because of the incomplete epidemiologic information, a definite chain of transmission among these four genotypically related cases could not be established.

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**CDC Editorial Note:** This report describes the public health investigation surrounding a previously reported case of MDR HIV-1 infection. The investigation was conducted to identify contacts of the index patient, to offer HIV testing and partner notification, and to search for other persons with diagnosed HIV infection who shared the index patient’s HIV genotype. Data obtained from interviews, laboratory matching, and supplemental laboratory testing identified only three persons as infected with strains of HIV similar to that of the index patient. As of July 21, 2006, the index patient and two of the patients with matching genotypes were clinically stable and responding to ARVs. The third patient with a matching genotype was clinically stable and responding to ARVs through April 2005 but has since been lost to follow-up; he had not been matched to the New York City Death Registry as of June 30, 2006.

Investigators were not able to determine exactly when or how, during May 2003–December 2004, the index patient was infected, whether transmission of the HIV strain to the index patient was direct from one of the three patients with matching genotypes or indirect (i.e., passed through an unknown intermediate person), or whether the index patient’s viral genotype was from a single viral infection or from recombination or superinfection. The index patient had multiple partners, many anonymous, during the period in which he became infected. The cluster of three patients with matching genotypes represents only cases detected through laboratory matching and only through June 30, 2005. At least 6,400 HIV-infected MSM in NYC have never been tested for HIV, and many other persons with diagnosed HIV infection have never had genotyping. Therefore, the actual prevalence of this or a similar MDR HIV genotype in NYC is unknown.

The index patient’s HIV infection progressed to AIDS in <20 months; the median period for transition to AIDS without treatment is 8-10 years. Available laboratory and medical records data were not sufficient to establish whether this viral genotype was associated with rapid progression to AIDS. Accelerated progression to AIDS and transmission of MDR HIV-1 have been reported previously.
although not with this combination of high-level resistance and rapid progression. Newly diagnosed MDR HIV in a sexually active MSM who had never received ARV treatment raises several public health concerns. Approximately 70% of the named partners of the index patient had HIV infection, and the majority had other recent sexually transmitted disease infections, indicating substantial potential for transmission of HIV and possibly also MDR HIV. The findings in this report, along with increasing syphilis rates, continuing gonorrhea transmission, and the emergence of lymphogranuloma venereum in HIV-positive MSM, reflects a resurgence of unsafe sex among MSM. This behavior also has been associated with increasing use of methamphetamine.7

The genotype data collected by NYCDOH indicated a low prevalence of MDR genotypes among persons who had not been treated with ARVs and who had HIV infections diagnosed during June 1, 2004–June 30, 2005. Drug-resistant HIV compromises the effectiveness of standard ARV regimens and can limit the treatment options available to persons with newly diagnosed HIV infection.5 Therefore, CDC has provided funding to four city and 17 state health departments to conduct drug-resistance surveillance on remnant sera obtained from all patients with newly diagnosed HIV infection.6 Provisional data from these areas indicate that as many as 15% of these patients are infected with an HIV strain that has mutations associated with resistance to ARVs, and 3.2% have mutations associated with resistance to two or more classes of such medications.6

Case reports such as the one described here and results from surveillance of newly diagnosed, drug-resistant HIV infections contributed to recent changes in HIV-1 treatment guidelines issued by the U.S. Department of Health and Human Services.9 These guidelines now recommend performing drug-resistance testing before initiation of therapy in patients who have never received ARV treatment. To reduce HIV-associated morbidity and mortality in the United States, public health officials should intensify measures to improve early diagnosis, partner notification, and prevention counseling for persons (particularly MSM) who are HIV positive and should conduct population-based genotype surveillance to monitor the emergence of unusual strains of HIV, particularly those with mutations associated with ARV resistance.8,10

REFERENCES

*Virus has capacity to use both CCR5 and CXCR4 coreceptors for attachment and entry into CD4 lymphocytes.

Notice to Readers: Clinical Vaccinology Course—November 3-5, 2006

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CDC AND FOUR OTHER NATIONAL ORGANIZATIONS are collaborating with the National Foundation for Infectious Diseases (NFID), Emory University School of Medicine, and Emory Vaccine Center to sponsor a Clinical Vaccinology Course to be held November 3-5, 2006, at the Crowne Plaza Atlanta-Buckhead in Atlanta, Georgia. The course will focus on new developments and concerns related to use of vaccines in pediatric, adolescent, and adult populations. Approximately 20 experts will present symposia on adult immunization, pediatric immunization, ensuring use of vaccines, vaccine safety and supply, the evolving adolescent immunization platform, and travel and international vaccines.

This course is specifically designed for primary-care physicians, family physicians, internal medicine specialists, pediatricians, public health specialists, nurse practitioners, physician assistants, clinical practice nurses, infectious disease specialists, and other health-care professionals involved with clinical aspects of vaccinology. The course also will be of interest to health-care professionals involved in prevention and control of infectious diseases, including federal, state, and local public health officials. Continuing education credits will be offered for physicians, nurses, and pharmacists, and prescribed credits for family physicians.

Information regarding the preliminary program, registration, and hotel accommodations is available at http://www.nfid.org/conferences/id-course06, or by e-mail (idcourse@nfid.org), fax (301-907-0878), telephone (301-656-0003, ext. 19), and mail (NFID, Suite 750, 4733 Bethesda Avenue, Bethesda, MD 20814).