One in Six New HIV Cases Involves Drug-Resistant Virus

March 1, 2010 By Tim Horn

About one of every six new HIV cases diagnosed in 2007 involved virus with antiretroviral (ARV) drug-resistance mutations, according to data reported by the U.S. Centers for Disease Control and Prevention (CDC) on Wednesday, February 17, at the 17th Conference on Retroviruses and Opportunistic Infections (CROI) in San Francisco.

The latest data, shared at CROI by David Kim, MD, of the CDC, hint that rates of drug-resistant HIV transmission are possibly increasing in the United States. Whereas slightly more than 10 percent of new HIV cases documented between January 2003 and October 2006 involved virus at least partially resistant to at least one drug, the report from this year's CROI suggests a rate closer to 16 percent.

The U.S. Variant, Atypical and Resistant HIV Surveillance (VARHS) system, in which HIV specimens from newly diagnosed individuals are tested for drug-resistance mutations, was established by the CDC to provide the clearest picture to date of the scope and type of resistance in the United States.

The analysis reported at CROI included 2,480 individuals in 11 states—about 24 percent of 10,496 new HIV diagnoses in VARHS sampling areas in 2007. The system uses standard genotypic resistance testing, which identifies specific viral mutations associated with drug resistance. Because these individuals had not yet started treatment, the presence of any HIV drug resistance mutations in their blood would indicate that the resistant virus was transmitted to them at the time of their infection.

HIV drug resistance mutations were documented in 15.6 percent of the patients included in the 2007 analysis. About 13 percent involved mutations pertaining to one class of ARV drugs, 1.7 percent of cases had mutations conferring some degree of resistance to ARVs in two classes of drugs, and 0.5 percent had mutations conferring resistance to ARVs in three drug classes.

Mutations conferring resistance to the non-nucleoside reverse transcriptase inhibitors (NNRTs) were the most common, documented in about 8 percent of new HIV cases in 2007. The most common mutations were K103N and Y181C in HIV's reverse transcriptase gene, both conferring high-level resistance to popular first-line NNRTIs nevirapine (Viramune) and efavirenz (found in Sustiva and Atripla).

Mutations conferring resistance to some members of the nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) class were documented in about 6 percent of newly diagnosed individuals. The M41L mutation in HIV's reverse transcriptase gene was the most common (32 percent) and is known to cause low-level resistance to zidovudine (found in Retrovir and Combivir), stavudine (Zerit) and possibly abacavir (found in Ziagen and Epzicom) and tenofovir (found in Viread, Truvada and Atripla). The T69N mutation, associated with multi-NRTI resistance, was documented in roughly 17 percent of new cases in 2007.

As for transmitted HIV with resistance to the protease inhibitors, this accounted for about 4 percent of cases. The L90M mutation in HIV's protease gene was found in 35 percent of cases. It contributes significantly to resistance to nelfinavir (Viracept) and ritonavir (Norvir)–boosted saquinavir (Invirase) and partially to resistance to several other protease inhibitors when other mutations are present.

According to Kim, the highest rates of transmitted drug resistance were among women infected via heterosexual contact and individuals younger than 20 at the time of their diagnosis.

As with their original 2007 report, the CDC researchers reiterated that HIV drug resistance has been a growing concern for many years, as greater numbers of HIV-positive individuals are taking antiretroviral drugs for an increased amount of time. The possibility of infection with strains of HIV that are more difficult to treat underscores the importance of HIV prevention efforts and the continued need to identify more effective treatment strategies. The CDC will continue using the VARHS system to monitor trends in resistance over time.

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http://beta.docker.poz.com/article/hiv-drug-resistance-transmission-18071-9005