



FACTS ABOUT MULTI-DRUG RESISTANT AND DUAL-TROPIC HIV IN ASSOCIATION WITH RAPID PROGRESSION TO AIDS

Background:

On February 11, 2005, the New York City Department of Health and Mental Hygiene issued a public health alert based on an unusual case that represents the convergence of multi-drug resistant HIV and rapid disease progression to full-blown AIDS in a single patient. Speculation about an emerging “super-virus” was fueled by the media, but to date there is no evidence to suggest this is more than an isolated case.

Frequently Asked Questions:

What is multi-drug resistance?

HIV has the ability to rapidly reproduce and change. These changes, or mutations, which can cause resistance, occur naturally all the time in everyone with HIV. Some mutations may cause resistance or cross-resistance to medications.

Poor adherence or poor drug levels can lead to mutated, drug-resistant virus. Resistant virus can also be passed from one person to another sexually, more commonly at the time of initial HIV infection. HIV has the ability to become drug resistant, directly proportional to how **non-adherent** someone is to his/her medications.

Multi-drug resistance has been around for some time. Some studies show 15 to 21 percent of all new HIV infections are resistant to one or more class of antiretrovirals, and a much smaller percentage (less than three percent) resistant to all three classes. Likewise, rapid progressions have been observed before (most notably in the NIAID Multicenter AIDS Cohort Study), but it is not known if these have correlated well with drug resistance.

In the New York City case, testing showed resistance to some or all medications in three of the four classes of drugs currently available in the treatment of HIV.

What is viral fitness?

HIV **viral fitness** is a complex topic that is often meant to include the ability of the virus to reproduce efficiently (replicative capacity), to compete with other HIV strains and to kill CD4 cells. Some studies show that drug resistant viruses are less fit, with fitness being associated with viral mutation that created resistance in the first place.

Improved resistance testing and promising, newer protease inhibitors and some non-nucleosides that will work against strains resistant to known drugs will be part

of the next arsenal to fight resistant virus. Added to these drugs is a new class of antiretrovirals called attachment inhibitors that intervene with HIV during “attachment” to the CD4 receptors.

How common is transmission of multi-drug resistant virus?

Transmission of single and multi-drug resistant virus, seen worldwide, increased steadily between 1996 and 2000 and has since leveled off. It happens every year, with regularity. Data shows that drug resistant virus is more difficult to transmit than normal “wild type” virus. Multi-drug resistant virus is less likely to be transmitted because mutations make the virus less fit and therefore less aggressive than the original strain.

What is Dual Tropism (CCR5 & CXCR4)?

The way some viruses cause disease is by attacking specific (target) cells. The mechanism by which viruses do so is by identifying and attaching to specific protein receptors on the surface of the target cells; this mechanism is called **tropism** and, much like a special key and lock, allows entry to the cell. HIV has the ability of **dual tropism**, meaning that the virus can identify and attach to two different receptors on the host CD4 cell: CCR5 and CXCR4 (R5 and X4). The most common receptor that the virus uses is the R5, but when HIV uses the X4 receptor, the virus causes more damage to the cell. X4 viruses are associated with advanced stages of HIV disease and rapid progression to AIDS.

What is rapid progression to AIDS?

Based on national statistics, the mean average time to progress to AIDS is 8.2 years. Due to highly active antiretroviral treatment (HAART), many people living with HIV do not see disease progression to an AIDS diagnosis. About 1 to 2 percent of all people infected with HIV are “**slow progressors**” who may take decades to develop symptoms and get sick. The reasons vary, from genetic mutations that disable the receptors on the outside of the host CD4 cell, to other “host” or viral factors. At the other end of the spectrum, 1 to 2 percent are “**fast progressors**” who develop AIDS within months. A person receives an AIDS diagnosis when he/she has less than 200 CD4 cells and/or an opportunistic infection such as pneumocystis carinii pneumonia.

Rapid progression is rare, but can occur for different reasons: a person (the host) already has a weakened immune system (due to co-infections, such as cancer or Hepatitis B or C or persistent use of substance such as crystal); the virus is very aggressive (virulent); or there is multi-drug resistance to the HIV medications. It is believed that a fair amount of rapid progression cases are related to X4 viruses. “**Virulent,**” used to describe the New York City case, refers to the apparent rapid progression from time of infection to onset of AIDS and does not mean that it is transmitted more readily to others.

What is acute infection?

Acute infection refers to recent infection with HIV. Classic symptoms of acute (new, primary) HIV infection include: fevers; night sweats; weight loss; and swollen lymph glands. These symptoms can be confused with symptoms that are commonly associated with the flu. People exhibiting these symptoms who are at high risk for HIV infection (i.e., men who have sex with men) should get tested for HIV.

What can I do to avoid becoming infected with or transmitting HIV?

Consistent employment of effective safer sex and risk reduction strategies that include proper use of condoms or other latex barriers and not sharing syringes when injecting drugs, steroids or hormones continue to be the best ways to prevent HIV transmission.

Routine HIV and STI screening should become a part of everyone's routine health care regimen. Access and adherence to treatment is vital for people infected with HIV.

Sex while under the influence of any substance greatly increases the chance of HIV transmission, because a person's ability to negotiate safer sex may be impaired. Minimizing or eliminating the use of alcohol and/or drugs, especially before and during sex, is highly recommended. Treatment of addictions should be viewed as integral to our HIV prevention efforts.

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Reference: Markowitz M. A case of apparent recent infection with a multi-drug resistant and dual-tropic HIV-1 in association with rapid progression to AIDS. Program and abstracts of the 12th Conference on Retroviruses and Opportunistic Infections; February 22-25, 2005; Boston, Massachusetts. Abstract 973B.