Small Study Implicates HIV in Fat Cell Defects

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HIV might damage cellular mitochondria, the suspected cause of face and body fat loss attributed to older antiretroviral (ARV) medications. These data, from a small exploratory study, were published online December 14 in AIDS.

Lipoatrophy (abnormal fat loss) and lipohypertrophy (abnormal fat gain) continue to plague people living with HIV, though their prevalence has diminished since newer less-toxic ARVs were introduced during the past five years. While scientists are still trying to understand what causes both conditions, there has been fairly substantial evidence that lipoatrophy is caused primarily by defects in mitochondria.

Mitochondria are tiny molecular machines inside cells that process proteins and sugars and provide energy for the cells to function. When the mitochondria are damaged, cells cease to function properly and eventually die. Two older nucleoside reverse transcriptase inhibitors (NRTIs) have been found to cause significant mitochondrial damage: Zerit (stavudine) to the greatest degree and Retrovir (zidovudine) to a moderate degree.

Researchers have observed two phenomena that suggest that HIV itself might also contribute to mitochondrial damage. The first example involves relatively rare cases of severe lipoatrophy in people who have never taken ARVs. The second relates to the fact that lipoatrophy almost never completely reverses after a person stops taking Zerit or Retrovir.

To test the theory that HIV might contribute to mitochondrial damage, Glória Garrabou, PhD, from the University of Barcelona, and her colleagues, compared mitochondrial integrity and function in fat cells from 24 HIV-negative and 18 HIV-positive individuals. Eleven of the 18 HIV-positive participants had never taken ARVs, and the remaining seven were on ARV therapy—all of whom had a history of taking either Zerit or Retrovir. Fat samples were taken from either the abdomen or the upper arm under anesthesia.

Garrabou's team found that mitochondrial DNA integrity and mitochondrial function were more defective in both groups of HIV-positive participants than in HIV negative participants. In the HIV-positive group with no ARV experience, about 38 percent of fat cells had defective mitochondrial DNA and 25 percent had reduced mitochondrial function. In those on ARVs, 31 percent of fat cells had damaged DNA and 30 percent had reduced function. The lower a person's CD4 cell count and

the higher the viral load, the more likely he or she was to have damaged mitochondrial DNA and reduced mitochondrial function.

Garrabou and her colleagues acknowledge the small size of their study but suggest that their findings lend weight to the trend to start ARV therapy much earlier. Not only does this potentially reduce the risk of cellular inflammation and activation—two other factors believed to contribute to abnormal fat loss and gain—but it also reduces the risk of mitochondrial damage.
