Peripheral Nerve Damage Remains Common Despite HIV Therapy

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The prevalence of a sometimes-painful nerve condition called peripheral neuropathy (PN) remains high in people with HIV despite effective antiretroviral (ARV) therapy, according to a study published in the April 24 issue of *AIDS*. Older age, diabetes, a low CD4 count and the use of nerve-toxic ARV drugs were the strongest predictors of developing the condition.

Earlier in the epidemic, the three most common neurological conditions in people with HIV were the development of HIV-associated dementia (HAD), infection-related neurological diseases and PN. Since the introduction of effective combination ARVs in the late 1990s, however, the rates of HAD and infection-related diseases have fallen dramatically—leaving a continued high level of PN in people with the virus.

Peripheral neuropathy occurs when the long and short nerve fibers running from the brain to the hands and feet become damaged. Some people with PN don't have noticeable symptoms, and the only way to diagnose the disease is for a provider to test whether they have a loss of sensation in their big toes or reduced reflexes in the ankles. Others, however, can have persistent tingling sensations or sharp shooting or throbbing pain in their feet and legs.

In the early to middle years of the epidemic, the factors most commonly associated with PN were low CD4s, high viral loads, diabetes and the use of either protease inhibitors (which can reduce the body's ability to control blood sugar) or nucleoside reverse transcriptase inhibitors (NRTIs) that damage nerve cells—most notably Zerit (stavudine) and Retrovir (zidovudine).

To determine the prevalence of PN in the modern ARV era, and the factors associated with it, Scott Evans, PhD, from the Harvard School of Public Health in Boston, and his colleagues followed 2,141 HIV-positive people between 2000 and 2007 who started ARV therapy for the first time in six different studies sponsored by the AIDS Clinical Trials Group (ACTG).

People were tested for peripheral neuropathy every 48 weeks during the seven years of the study. Eighty-one percent of the participants were men, 32 percent were black, and the average age was 39. Before starting ARV therapy, 21 percent had PN, though most—80 percent—did not have symptoms.

Evans and his colleagues found that PN not only persisted but also continued to be diagnosed,

despite the fact that 82 percent of the participants got and kept their HIV levels under control after starting ARVs. Over the course of seven years, the majority who were initially diagnosed with PN had persistence of the disease, and an additional 20 percent developed neuropathy, though the vast majority continued to be without symptoms.

Evans's team found that the factors most strongly associated with developing PN were older age, diabetes, the use of nerve-toxic NRTIs and having a CD4 count less than 200. Other factors associated with developing PN included taller height, the use of protease inhibitors and the use of statin drugs, though these associations were much weaker.

For those who developed PN while on nerve-toxic NRTIs, just over half continued to have PN and 36 percent continued to have symptomatic PN after the drugs were withdrawn. The only factor associated with recovery from PN was younger age.

Overall, the authors conclude that providers should take particular care to prevent neuropathy or to intervene, when possible, quickly when symptoms develop. Most important, they say, is to develop alternatives to nerve-toxic NRTIs in the developing world, and to watch closely for neuropathy in older people with HIV, people who start ARV therapy late or who have persistently low CD4 counts and in people who have diabetes or nutritional deficiencies.

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