

Premature aging caused by some HIV drugs, study shows

June 26 2011

A class of anti-retroviral drugs commonly used to treat HIV, particularly in Africa and low income countries, can cause premature ageing, according to research published today in the journal *Nature Genetics*. The study shows that the drugs damage DNA in the patient's mitochondria – the 'batteries' which power their cells.

The findings may explain why HIV-infected people treated with antiretroviral drugs sometimes show advanced signs of frailty and age-associated diseases such as cardiovascular disease and dementia at an early age.

Nucleoside analogue reverse-transcriptase inhibitors (NRTIs) – of which the most well known is Zidovudine, also known as AZT – were the first class of [drug](#) developed to treat [HIV](#). They were a major breakthrough in the treatment of the disease, greatly extending lifespan and leading the condition to be seen as a chronic, rather than terminal, condition.

In high income countries, such as Europe and North America, the older NRTIs are used less commonly now due to concerns over toxicity and side-effects when taken over a long period of time. However, as they are now off-licence and hence relatively cheap, the drugs have proved to be an important lifeline for people infected with HIV in [Africa](#) and low income countries.

Professor Patrick Chinnery, a Wellcome Senior Fellow in Clinical Science from the Institute of Genetic Medicine at Newcastle University,

says: "HIV clinics were seeing patients who had otherwise been successfully treated but who showed signs of being much older than their years. This was a real mystery. But colleagues recognised many similarities with patients affected by mitochondrial diseases – conditions that affect energy production in our cells – and referred them to our clinic."

Mitochondria are the 'batteries' in our cells which provide them with the energy to carry out their functions. During natural human ageing, these mitochondria acquire mutations, though it is unclear whether these mutations are a cause of ageing or a consequence.

In an attempt to understand what was happening at a cellular level, Professor Chinnery and colleagues studied muscle cells from HIV-infected adults, some of whom had previously been given NRTIs.

The researchers found that patients who had been treated with NRTIs – even as long ago as a decade previously – had damaged mitochondria which resembled that of a healthy aged person.

"The DNA in our [mitochondria](#) gets copied throughout our lifetimes and, as we age, naturally accumulates errors," explains Professor Chinnery. "We believe that these HIV drugs accelerate the rate at which these errors build up. So over the space of, say, ten years, a person's mitochondrial DNA may have accumulated the same amount of errors as a person who has naturally aged twenty or thirty years. What is surprising, though, is that patients who came off the medication many years ago may still be vulnerable to these changes."

Co-author and HIV specialist, Dr Brendan Payne, a Medical Research Council fellow from the Department of Infection and Tropical Medicine at the Royal Victoria Infirmary, Newcastle, believes that despite the side effects caused by NRTIs, they are still important drugs and the risks are

relative.

"These drugs may not be perfect, but we must remember that when they were introduced they gave people an extra ten or twenty years when they would otherwise have died," he says. "In Africa, where the HIV epidemic has hit hardest and where more expensive medications are not an option, they are an absolute necessity."

Provided by Wellcome Trust

Citation: Premature aging caused by some HIV drugs, study shows (2011, June 26) retrieved 4 May 2024 from <https://medicalxpress.com/news/2011-06-premature-aging-hiv-drugs.html>

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