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# hiv treatment update



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# hiv and aging

is growing older with HIV all bad news? *by Edwin J Bernard*

One of the tangible benefits of successfully treated HIV infection is the expectation of a longer - and healthier - life. A recent article in the *New York Times*, entitled 'AIDS patients face downside of living longer'<sup>1</sup> suggested otherwise.

It said that the cumulative effects of long-term HIV infection, anti-HIV drug side-effects and the diseases associated with aging (including heart disease, cancer, memory loss, and bone problems) made the cost of aging with HIV too great for some people to bear. The question it then posed was whether anti-HIV treatment leading to a longer life was, in fact, worth it.

"That is the question," it said, "heretical to some, that is now being voiced by scientists, doctors and patients encountering a constellation of ailments showing up prematurely or in disproportionate numbers among the first wave of AIDS survivors to reach late middle age."

The article paints a bleak picture of prematurely aging long-term survivors, and suggests that this may be the future for all HIV-positive individuals.

But how real are the risks of premature aging for someone on effective treatment today? Is it correct to call an increased risk of

heart disease, cancer, bone disease and other illnesses traditionally associated with aging 'premature aging'? And is it true that these health conditions are an inevitable result of living with HIV, and that we are powerless to do anything about it?

And what about the benefits of aging? If you are aging with HIV, doesn't that mean that you are still alive? And doesn't the wisdom that comes with aging with HIV mean anything?

Over the next eight pages, we will examine what we currently know about the links between HIV, getting older and the diseases associated with aging. The aim is to provide you with the latest information, and to help you understand the risks and how they can be modified. After all, to be forewarned is to be forearmed.

## How many of us are 'older'?

What exactly constitutes 'old' or 'older' is difficult to assess, with different government agencies, epidemiologists and other medical experts using different criteria for 'old' and 'older' to meet their own specific agendas. We should bear that in mind when we read studies about aging and 'older' people.

However, according to our last readers' survey (in 2006), half our readers are already aged 45 or over, which suggests that this newsletter is read by a disproportionately older readership. According to the Health Protection Agency (HPA), just 26% of people being treated for HIV in the United Kingdom in 2006 were aged 45 or over.

The HPA itself defines 'older' as 55 or over. In their latest report on the epidemiology of HIV in the UK<sup>2</sup> they note that, "increasing numbers of older, HIV-infected adults (55 years or over) accessed care between 1997 and 2006 (from 658 to 3,965). These older persons now account for 7.6% of all HIV-infected persons accessing care in 2006, an increase from 4.1% (653/16,075) in 1997."

This rise is attributable partly to advances in HIV treatments, which are keeping people who were infected ten or even twenty years ago alive long enough to become 'older', and partly to more recently diagnosed (and infected) individuals who were already 'older'. Although HIV is often characterised as a disease of young, sexually active people, the HPA tells us that the median age at diagnosis is now 34 (32 for women and 36 for men), and that some people are being infected with HIV much later in life. In 2005, 644 (9%) of new HIV diagnoses were in individuals aged over 50, of whom 175 were aged over 60.

## Does having HIV age us?

Just as our HIV infection affects each of us differently, so each of us ages differently, too. Although aging has become characterised as a disease

process by the health, beauty and pharmaceutical industries, it is important to remember that aging is a natural process. The rate at which we age depends on a variety of factors (including genetics, environment and behaviour), only some of which are under our control (such as stopping smoking, not being obese and getting regular sleep).

Nevertheless, it is well established that the immune system is affected by aging. Therefore, HIV infection - coupled with aging - may create additional challenges for us.

At last summer's Fourth IAS Conference on HIV Pathogenesis, Treatment and Prevention in Sydney, Australia, Professor Brian Gazzard, of London's Chelsea & Westminster Hospital, gave a plenary talk on HIV and aging (he is also one of three experts in this area to talk to us for this issue of *HTU*).

He explained that our immune system's ability to perform declines with age, and that these changes happen at all levels, from chemical changes in how our cells communicate with one another to changes in bodily organs, such as the thymus (where the immune system's T-cells are matured).

He said that untreated HIV could also affect some of the mechanisms that are linked to the aging process, such as apoptosis and senescence. Apoptosis is a type of programmed cell death, orchestrated to remove cell 'corpses' from the body.

Senescence is the capacity of cells to become redundant or 'die' after many divisions. With every cellular division, the terminal DNA repeats of their chromosomes become shorter, a phenomenon known as telomere shortening. Eventually, this telomere length is reduced to a point where division is no longer possible.

Professor Gazzard explained that untreated HIV can induce both of these processes in the immune system, due to high level activation and turnover of cells. It is the activation and turnover of CD4 cells that leads to CD4 cell loss in untreated HIV infection.

Another process of aging, oxidative stress, may exacerbate problems further. Oxidative stress is increased in people with untreated HIV, resulting in a compromise of the normal antioxidant defence system. Excess free radicals create a 'breeding ground' for HIV since it uses free radicals to help it replicate.

These various mechanisms produce considerable strain on the immune system, and Professor Gazzard highlighted the extent to which the immune disorder induced by untreated HIV resembles the immunological decline seen in the elderly.

## HIV, aging and disease progression

Since there appears to be a parallel between the natural immune down-regulation that occurs with aging, and HIV-related immune dysfunction, it might be assumed that older HIV-positive individuals would decline more rapidly than their younger counterparts.

Studies conducted before the advent of potent anti-HIV therapies found that when an older person was infected with HIV, CD4 cell loss was more pronounced compared to younger individuals. It was thought this was linked to a shrinking thymus, and that this would lead to a delayed immune response once anti-HIV treatment was begun.

However, more recent studies<sup>3,4</sup> have found similar increases in CD4 cell counts, and a higher proportion with 'undetectable' viral loads once anti-HIV treatment is initiated, in older people. This is thought to be due to older people being more likely to have better adherence to anti-HIV therapy than younger individuals.

### **HIV, aging and survival**

When it comes to survival, many cohort studies have suggested that older people with HIV do not survive as long as younger people with HIV. However, it is important to remember that this is true of the general population as well: the older you are the more likely you are to die!

Although a 2003 study that compared mortality before 1997 (the era before potent anti-HIV therapy) with the era after 1997 found that untreated, HIV-positive individuals over 45 were twice as likely to die than their younger, untreated counterparts<sup>5</sup>, a study done more recently found no significant differences in survival between younger and older individuals three months after starting anti-HIV treatment<sup>6</sup>.

The significant impact of effective anti-HIV treatments on the survival of 'older' people with HIV is illustrated by data from the HPA. Although the advent of potent anti-HIV therapy in the mid-1990s was associated with a dramatic decrease in mortality for all people who could access this therapy, the most dramatic decrease was seen in the oldest age groups. The mortality rate in people aged over 54 fell from 9.9% (65/658) in 1997 to 2.6% (103/3,965) in 2006, and the mortality rate in people aged 45-54 decreased from 7.2% (142/1,961) to 1.3% (125/9,833). The HPA says that the average mortality rate for HIV-positive people (of all ages) was 0.95% in 2006.

### **Aging and illness**

As people age, various illnesses become more common. Heart disease, cancer, diabetes, memory loss, depression, bone disease, kidney disease, arthritis, and vision and/or hearing loss become increasingly common with increasing age. Since many of these health problems can be related to HIV disease - and sometimes the treatments used to control HIV - understanding the underlying causes is difficult, and the subject of much current research.

We've covered many of these health concerns in great detail in previous issues of our newsletter, and there is not nearly enough space to cover them all in depth here. (see sidebar: **further information** for details)

In his talk last summer, Professor Gazzard named three illnesses as the 'geriatric giants' - cardiovascular (heart) disease (and stroke), cancer and dementia. These are the illnesses that the majority of the (western) population will die of in due course. Researchers are currently attempting to determine whether these giants of geriatric medicine will occur earlier or

more frequently in HIV-positive people as they age.

### **Cardiovascular disease**

Age is not only a well-established predictor of increased risk of cardiovascular disease in the general population, major studies such as the D:A:D study<sup>7</sup> and the SMART study<sup>8</sup> have also found that older age is independently associated with increased risk of heart attacks in HIV-positive people.

However, Professor Gazzard notes that the most important thing that will determine whether we get cardiovascular disease is our genetic makeup, and the second most important thing is smoking. "HIV itself is associated with a very big increase in cardiovascular risk and that is reduced enormously by antiretroviral drugs, but not necessarily back to completely normal," he said.

### **Cancer**

In the general population the risk of cancer increases with age. We are now realising that, as HIV-positive people age, cancers not traditionally associated with HIV are becoming more common. Indeed, recent data from the D:A:D study suggest that non-AIDS-defining cancers (notably of the lung and bowel) are now seen more frequently in HIV-positive people than the traditional AIDS-defining cancers<sup>9</sup>. The study also found that the risk of these cancers increases with lower CD4 cell count and with age.

According to Professor Gazzard, there are two possible reasons for this: it may be because those of us who are at risk of HIV infection are also at risk of acquiring cancer-causing viruses, such as HPV, and that HIV-infected immune systems don't work as well in controlling these viruses; or it may be that HIV itself is capable of promoting cancerous growth.

A recent meta-analysis of studies of people with cancer examined the increased risk of cancer in HIV-positive people as well as in people with suppressed immune systems following an organ transplant. It found that immunosuppression was associated with

an increased risk of certain types of cancers, particularly those caused by bacteria or viruses. These findings suggest that even a modest deficiency in immune performance is enough to increase the risk of a wide range of cancers<sup>10</sup>.

## Dementia

Today, AIDS-related dementia is seen very rarely, and usually only in people who have very low CD4 counts because they are not on anti-HIV treatment. However, a recent study<sup>11</sup> found that people over 50 on anti-HIV treatment do appear to have a three-fold higher chance of slowed-down movement or thought processes, or 'forgetfulness', than younger people on anti-HIV treatment. Nevertheless, these 'impaired cognitive functions' may be very mild, and often do not affect everyday life.

Professor Gazzard notes that much of the dementia in older people with HIV should perhaps be called dementia in the context of HIV rather than HIV dementia.

In addition, neurologists should not assume that all signs of dementia in people with HIV are related to HIV, according to recent research.<sup>12</sup> It suggests that as people with HIV age, neurologists should watch out for the early onset of degenerative disorders like Alzheimer's or Parkinson's disease.

## Drug interactions

Since many of these illnesses and health conditions require medications over and above anti-HIV drugs, there is potentially a high risk of drug-drug interactions, as well as the potential for anti-HIV drugs to exacerbate an underlying health problem, such as diabetes or high blood fats. One study

of HIV-positive individuals over 55 found that 89% had another health problem, and that 81% were taking non-HIV medications. However, the study did not find a greater incidence of anti-HIV-drug-related side-effects.<sup>5</sup>

## Benefits of aging with HIV

Any article about aging with HIV would not be balanced if it did not include some information about the benefits of aging with HIV. To begin with, if you are aging it means you are still alive: something that we often take for granted in the era of potent anti-HIV drugs. Of course, quality of life matters, too.

Studies have found that older adults living with HIV often feel that their total life experiences have provided them with skills to cope better with their health issues than younger adults.

In particular, researchers from Columbia University School of Public Health found that older HIV-positive adults (aged 50 or over) did not feel as cheated by the loss of their health as younger HIV-positive people; that they had greater respect for health and life; that they were more patient and content than their younger counterparts, and lived life in moderation; and that they could focus more on their own needs, rather than those of others, particularly their children.

## Improving the odds

It is clear that we are now much more likely to live well into our senior years, and that we may experience - or already be experiencing - age-related conditions we never expected to face.

Research is ongoing to discover exactly how HIV disease impacts (and is impacted by) the health problems associated with aging. There's no doubt that this is - and will be - a challenge not just for us, but also for the professionals who care for us.

Nevertheless, as you will read next, there are many ways to improve the odds that you will live a long and healthy life with HIV. A recent study of 25,000 Norfolk men and women aged between 45 to 79 found that simply by avoiding smoking; exercising regularly; eating lots of fruits and vegetables; and drinking only moderate amounts of alcohol; people lived on average 14 years longer than people who didn't do these four simple things<sup>13</sup>.



### further information

Previous issues of *AIDS Treatment Update* have covered the following age-related health concerns in depth. They can all be found online at: [www.aidsmap.com/cms1061207.asp](http://www.aidsmap.com/cms1061207.asp)

- Cardiovascular disease, metabolic syndrome, diabetes: ATU 130, Oct 2003.
- Bone problems, including osteoporosis: ATU 149, Sept 2005.
- Fatigue: ATU 155, April 2006.
- Drug interactions: ATU 165, April 2007.
- Neurological problems: ATU 171, Nov 2007.
- Dementia: ATU 136, May 2004.
- Cervical and anal cancer: ATU 151, Nov 2005.
- Kidney disease: ATU 157, June 2006.
- Depression: ATU 168, July 2007.
- Cancer: ATU 172, Dec 2007.