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hiv treatment update



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in this issue

This month we examine the issue of HIV and aging. Growing older with HIV is something many of us never expected to face, and some people are wondering whether the added burden of age-related illnesses (some of which may arrive earlier in HIV-positive people) and age-related isolation will be more than they can bear.

David Evans, writing eloquently on the subject in the American publication *Poz*, suggests that, "in order to soften the combined blows of old age and HIV...the best hope for a brighter future will probably lay in the bonds that HIV-positive people form with each other - bonds that, over the years, have brought thousands through sickness and uncertainty and changed policies and society in ways many thought impossible."

Perhaps that kind of safety in numbers will also be of comfort to the numerous long-term survivors likely to be affected by the current review of 'special rules' awards of Disability Living Allowance (and Attendance Allowance). It will be hard for some to adjust to life without benefits, and rather than just take away the money, it would be wise - and ethical - for the Disability and Carers Service to provide real and practical help as some people are forced to move from state dependency to self-sufficiency.

page 3 In this month's *Upfront* we look at the *New drugs bonanza* heading our way, including the UK approval of the first-ever integrase inhibitor, raltegravir (*Isentress*), the US approval of a second-generation NNRTI and new formulations of existing drugs.

page 4 In *HIV and aging* we 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.

page 8 Growing older is bringing a new set of challenges to people living with HIV. For insights into managing health and well-being while growing older, *HTU* spoke with three leading clinicians and researchers in the field of HIV and aging: Professor Brian Gazzard, Stephen Karpiak, PhD and Charles Emlet, PhD.

page 12 Amongst the items in *News in Brief* are a study from the UK that adds to the growing body of evidence that we have a much better life expectancy now than ever before, and a European study that found that our risk of developing pancreatitis on treatment is much lower than expected.

page 14 In *Not so 'special'?*, we examine how the review of 'special rules' for certain benefits may affect you.



hiv treatment update

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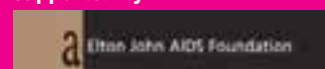
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new drugs bonanza continues by Edwin J Bernard

In last month's *HTU*, we focused on the new drugs available, or about to become available, in the UK. Since then, the first-ever integrase inhibitor, raltegravir (*Isentress*), has become available sooner than we expected, and other new drugs, and new formulations, are also headed our way.

Atripla

Atripla, which contains the drugs efavirenz, tenofovir and FTC in one pill, and which can be taken once daily, was made available in the UK on December 20th, 2007. *Atripla* should be taken on an empty stomach at bedtime.

However, rather than being approved as a first-line therapy (as it is in the United States), in the UK (and the rest of Europe) *Atripla* is only approved for people whose anti-HIV treatment has already successfully lowered viral load to undetectable levels for at least three months.

In addition, *Atripla* is only recommended for people who haven't developed resistance to anti-HIV drugs. So it's likely that people starting treatment for the first time (and who haven't been infected with drug-resistant HIV) will be offered *Atripla*'s components (as *Sustiva* and *Truvada*), and then move to *Atripla* once - and if - their viral load has become undetectable.

This is because the European drug approval body, the European Medicines Agency (EMA), said that the demonstration of the benefit of *Atripla* is primarily based on 24-week data from a clinical trial in which people who already had an undetectable viral load switched to *Atripla*, and that no

data are currently available from clinical trials on *Atripla* in people taking it as first-line therapy.

Raltegravir

Raltegravir received formal EU marketing approval in late December and became available in the UK on January 23rd. It should be used in combination with other anti-HIV drugs, and is only approved for use by treatment-experienced adults with evidence of HIV replication despite ongoing antiretroviral therapy.

The drug belongs to a brand new class of antiretrovirals called integrase inhibitors. It works against HIV's integrase protein, inhibiting the virus's integration into human cells. It has no known cross-resistance with any other currently available antiretroviral, making it an attractive option for heavily treatment-experienced individuals.

The approved dose of raltegravir is 400mg twice daily. Possible known side-effects include diarrhoea, nausea and headache.

Although raltegravir can initially only be used as a therapy for treatment-experienced individuals, encouraging data regarding its safety and efficacy in treatment-naïve patients were presented to last year's International AIDS Society Conference in Sydney. The manufacturer of raltegravir, Merck Sharp & Dohme Ltd (MSD), has said that it intends to submit an application in 2009 for the use of the drug in treatment-naïve individuals.

Kaletra for kids

In January, a new lower-dose tablet formulation of the protease inhibitor

Kaletra

(lopinavir/ritonavir) for paediatric use was given a positive opinion by the EMA's scientific committee. This is key step towards formal marketing approval by the European Union, which is expected by April. It was approved in the US last November.

Containing 100mg of lopinavir and 25mg of ritonavir, the lower-dose paediatric formulation of *Kaletra* contains half the standard adult dose and, as with standard *Kaletra*, can be taken with or without food and does not require refrigeration.

European approval also means that the lower-dose tablet can be made available in many resource-limited countries.

Etravirine

The second-generation NNRTI, etravirine, has now been approved in the US. Etravirine used to be known as TMC 125, and now has the trade name *Intelence*. Although etravirine is currently only available in the UK and Europe as part of an expanded access scheme, full approval is expected later in 2008.

Etravirine is reserved for people who have previously taken anti-HIV treatment and who have a detectable viral load with evidence of resistance to the existing NNRTIs, but it won't work if you have already accumulated a lot of NNRTI resistance mutations.





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'¹ 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 UK² 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^{3,4} 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 counterparts⁵, a study done more recently found no significant differences in survival between younger and older individuals three months after starting anti-HIV treatment⁶.

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 study⁷ and the SMART study⁸ 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 cancers⁹. 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 cancers¹⁰.

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 study¹¹ 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.¹² 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.⁵

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 things¹³.



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

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



Growing older is bringing a whole new set of challenges to people living with HIV. HIV infection, treatments, and the aging process itself all bring their own challenges; and it's becoming clear that these may interact in complex ways. For insights into managing health and well-being while living longer with HIV, *HTU* spoke with three leading clinicians and researchers in the field of HIV and aging.

Professor Brian G Gazzard

is Professor of Medicine at Imperial College School of Medicine; HIV Research Director at Chelsea and Westminster Hospital; and former chair of the British HIV Association.

Stephen E Karpiak PhD

is Associate Director of Research with the AIDS Community Research Initiative of America (ACRIA).

Charles A Emlet PhD, ACSW

is Associate Professor of the Social Work Program, University of Washington, Tacoma.

HTU: Let's start by asking what HIV infection looks like in older adults. How does an HIV-positive person's age affect his or her prognosis?

Stephen Karpiak (SK) First of all, "older adult" is a bit of a catchall phrase: being 50 is quite different from being 80. An HIV diagnosis when you're aged 50-65 is not all that different from a diagnosis when you're 30. There are some disagreements about this, but essentially you can start therapy with nearly the same hope of getting a good response whether you are 30, 50, or 60.

Brian Gazzard (BG) The long-term answer is that we don't entirely know, because we haven't been able to observe people for long enough. Short-term treatment responses are slightly less good in the elderly: for each additional

aging

question & answers

interviews by Derek Thaczuk

year of age, the likelihood of reaching undetectable viral load is slightly lessened, and the rise you can expect in CD4 counts is also slightly lessened. However, that doesn't necessarily translate to any real decrease in ability to fight off infections.

There's a fair amount of data showing that treatment adherence tends to be better in older people, so that is one advantage you are likely to have.

What about the so-called "co-morbidities" - the complicating health conditions that can affect people with HIV, such as cardiovascular disease?

Charles Emlet (CE) Earlier in the epidemic, people simply didn't live as long. That has changed dramatically: now longevity is possible, and you can

now grow old with HIV. So, many people have learned to manage and deal with their long-term HIV infection over time. But then, many of the aging-related diseases that many of us will face (diabetes, osteoporosis, hypertension) begin to come into play. And you find yourself having to deal with these things, which may not have been on your radar screen.

BG The immune abnormalities of HIV resemble exaggerated forms of the immune abnormalities you tend to get with aging, so there's a parallel there. Also, the major things that tend to kill us as we get older become more important if you are also HIV-positive - cardiovascular health, neoplasias [cancers].

SK There is certainly evidence of an increased risk of cardiovascular disease. Whether that's due to HIV or to antiretroviral medications or to

other factors entirely is still open to some debate. We did find that over half of the people in our study (ROAH - Research on Older Adults with HIV) smoked. That's at least twice the rate of the general population here, and it's a huge risk for heart disease. We could accomplish a lot by encouraging smoking cessation programmes.

BG I think we've put a lot of blame on antiretroviral treatments for causing cardiovascular risk, and I think we've got that wrong. A lot of data now shows a dramatic reduction in cardiovascular risk once you're on treatment. I think it's very clear that HIV *per se* increases that risk quite markedly. While there may be some increased risk attached to some antiretrovirals (but not others), the overall impact of treatment is to improve your prognosis from a cardiovascular perspective.

Also, while lipids (blood levels of fats such as cholesterol) certainly affect your cardiovascular risk, it's long been thought that atherosclerosis (hardening of the arteries) is partly caused by an infectious process. HIV may be an important stimulator of that process - which is another argument in favour of antiretroviral treatment.

What about some of the other major health risks? The likelihoods of kidney disease, osteoporosis, and various types of cancer all appear to be greater in people who have been living with HIV for a longer time.

BG There are a number of neoplasms [cancers] that are seen more commonly as HIV progresses. These include several that are well-known to be associated with HIV (cervical and anal cancer, Kaposi's sarcoma, non-Hodgkin's lymphoma) but there are others as well: lung cancer, cancer of the neck, and probably myeloma (a blood cell disorder) and others.

The question, then, is whether we can prevent any of these cancers by starting treatment earlier. Years ago, data from our own group here suggested that we could - that if your CD4 count had ever been below 350, you would have a greater risk of developing non-Hodgkin's lymphoma, even if you had subsequent CD4 increases. That is no longer clear from more recent studies. It's still a very current question as to whether earlier treatment can decrease cancer risk. We also don't know how big an issue this will become down the road. It may not be the case that these cancers will become very widespread problems; they may continue to affect relatively few people.

As far as what people can do to limit their risk, smoking certainly presents many health risks, including cardiovascular disease and cancer. I'm strongly in favour of wider screening for anal cancer - there's a role for the community in campaigning for that.

Diet also plays a role in cancer risk and a healthy diet could have a significant risk-reducing effect.

Renal (kidney) disease is very much related to genetics; in the UK it is much more common in those with black Caribbean or African backgrounds. But HIVAN (HIV-associated nephropathy, or renal disease) presents yet another argument for earlier treatment: if you get on treatment before you get significant kidney disease, you tend not to develop it.

CE A lot of aging-related diseases also impact on your activities of daily living - simply getting your housework done and being able to get out of the house and do everyday things. People often say, "I thought I was going to die, then I found out I was going to live - and now I have to deal with all these other problems." It's another level of complication to deal with.

SK We can't see aging as simply a medical issue. We have to do more to mainstream this group of people, to create ways for them to be accepted and not be treated differently, or feel ostracized.

It seems as though early treatment is one of the single best things people can do to limit the risk of a great many HIV-related problems.

BG There has always been a difficult balance between the side-effects and the benefits of treatments. I think one benefit that was largely ignored until the SMART study was that treatment effectively prevents many illnesses we didn't realize were HIV-related: the kidney disease and heart disease we've discussed, and possibly several forms of cancer as well.

Keep in mind here that when we discuss large groups of patients, such as "older adults," we talk in terms of "relative risk". Those are statistics that apply to populations as a whole. But the question for any one individual is, what

is his or her own absolute risk? If somebody comes to see me now with a CD4 count of more than 300, I would say their absolute risk of having something serious in the next year is about 1%. Is that risk large enough to warrant treatment? That's for that person to say.

What about a particularly frightening prospect - "AIDS-related dementia"? Are we necessarily seeing a progressive, Alzheimer's-like loss of mental faculties?

BG Personally, I don't believe there are any hard data whatsoever that premature dementia occurs in people with HIV on proper treatment. In untreated HIV disease, you would often see forgetfulness, often quite prominent stumbling about as HIV affected the cerebellum - which controls balance - and distressing changes in personality: sometimes very aggressive, sometimes very passive. But that is a completely reversible process on treatment.

There may be subtle remaining deficits - if you want to play computer games at breakneck speed, there may be a difference there even if you're treated. But you wouldn't notice that unless you were studying it very carefully. I really don't think it's something people need worry about too much.

SK The idea that there is still a lot of dementia among people - especially older people - with HIV, is very persistent. But when you look at people who are HIV-positive today and you compare them to people without HIV who are similar in terms of education, of economic level, of social circumstances, the reality is that their mental functioning is not very different. We have reported on this data at a symposium at the Gerontological Society of America. The actual word "dementia" should be used a lot more carefully: the last thing this group of people needs is another stigma.

First of all, cognitive function does not really become a serious issue until it is quite significantly compromised. Many of the studies that are done on dementia today are done in people with HIV who are literally quite close to death, and nobody's mental functioning is going to be exceptional at that point! Secondly, you have to look at someone's whole social and educational background. Someone may be perceived as having some level of dementia if they are different from us. But we too often forget the bell curve and that half the population is below the mean when it comes to cognitive function, but are quite capable.

Just keeping active mentally - and you don't need any special tools to do that - can maintain and improve your cognitive function. We should not forget the importance of health literacy. HIV is a fairly complex topic to discuss with our clients. If you don't deliver that information in a comprehensible way, you can't blame people for having trouble comprehending it. That failure by the provider often causes them and others to see the client as being cognitively impaired.

How widespread is depression among older HIV-positive adults - and how is it linked to social isolation?

BG HIV is still an isolating phenomenon, especially as we get older. There's a cult of young-and-beautiful among gay men that contributes to that. For people over 50, the stigma associated with being gay and having HIV is much greater; those people were brought up in very different circumstances. So I think depression has a lot to do with these social and emotional reasons, not necessarily inherent organic processes. I think this is something the community has to grapple with.

It does seem that mania (extremely elevated mood, energy, and unusual thought patterns, often associated with bipolar disorder) is a much more

common symptom of depression in people with HIV. That difference might argue for a biological cause.

SK Many studies, including ours, have found high rates of depression symptoms in this HIV-infected population. Often depression is misdiagnosed or overlooked as a serious illness that is treatable. Many people don't realise they're depressed. They don't think of it as something they can address and manage. There is a stigma associated with depression that prevents people from coming forward and actively engaging their health care provider for help. Even the way depression manifests itself can vary greatly. We have almost an expectation of angry or curmudgeonly behaviour in the elderly, which can be a manifestation of depression that you wouldn't see in someone younger.

Depression can be compounded by social isolation and loneliness, both factors that we found to characterise the aging HIV population in our research study, ROAH. This can be a very difficult situation to break out of. Younger people have more social venues, more opportunities, to interact. Where do you go if you're older, you've lost friends, and you face the barriers and fears that occur because of HIV-based stigma. Dr Emlett has studied this issue and written eloquently on how it impacts upon the lives of these older adults.

CE Many long-term survivors see their social networks decline as they lose countless friends and family members. We've consistently found that older adults with HIV are more likely to live alone. The question becomes: how do you rebuild, or grow, a healthy social network? There's a systemic part to that: what can we do as service providers to support people in doing that?

But the quality of a person's social network does not necessarily depend on its size. If you are someone who has not been terribly social as a younger person, that is not going to change as

you grow older. You may be very comfortable with even just one relationship that is solid, that is meaningful to you.

Let's say you have a person who is very isolated, but not by choice, and that person could be very prone to depression, to substance use, loneliness, and a downward spiral. But take someone who has been fairly self-sufficient all their life, and that kind of isolation may actually be perfectly fine for them until, let's say, they need someone to help with the shopping. We often create social programmes based on group needs, but we do have to remember that we are serving individuals, not groups, and that what is a problem for one person may not be for the next.

The Research on Older Adults with HIV (ROAH) study actually found that older adults with HIV scored quite highly on many scales of mental well-being - including sense of independence, personal growth, and ability to adapt to life environments. Might older adults have strengths and skills they've developed over a lifetime of dealing with challenges?

SK These people are, truly, survivors. They haven't just lived this long, they've coped and survived and have developed mechanisms to do that. Many people have speculated that these survivors will be better able to cope with the issues of aging. But the challenges you encounter as you grow older are not the same ones you experienced when you were younger. We know that you have to re-invent coping mechanisms as you age. I know that many of those in our study are very empowered. They amaze me.

CE So many people have said, "I'm not going to die of AIDS." It doesn't make the living with it any easier, but there is this sense of defiance, that yes, you can continue to be a fighter. ■

news in brief



life expectancy

Study predicts better prognosis for most

The risk of death for someone who has been diagnosed soon after becoming infected with HIV in the UK has fallen by 97% since the introduction of potent antiretroviral therapy, according to a study which followed more than 2200 people between 1994 and 2006.

The study predicts that, thanks to better care and treatment, 99% of people can expect to be alive five years after being infected with HIV, that 94% will be alive after ten years and that 89% will be alive after 15 years. This is a huge improvement on the days before potent HIV treatment became available, when fewer than 28% of people lived for 15 years after infection with HIV.

However, the study found that HIV-positive injecting drug users had a worse prognosis than other people with HIV, even though they had a good response to treatment when they accessed it. The investigators mostly attribute this increased risk of death to co-infections with hepatitis B virus and hepatitis C virus.

tests

Drug level monitoring doubles treatment success

A new study suggests that using therapeutic drug monitoring (TDM) as part of a well-tailored HIV care plan can approximately double the chances reaching target blood levels of medication.

It is well established that there can be considerable variations between individuals - factors like gender, weight, diet, and other medications can all affect the level of a drug in a patient's blood.

It has been possible to test levels of drugs in the blood for at least eight years, although TDM is only recommended in certain circumstances. Part of the reason for this is a lack of solid data pinpointing who might best benefit from this expensive and time-consuming procedure.

This Californian study involved 200 people, most of whom had previously taken anti-HIV drugs, and lasted one year. During this time, almost two-thirds of study participants were found to have drug levels that were so low that they were at risk of increases in viral load, drug resistance and treatment failure.

Using drug level results, doctors were able to make specific recommendations to patients about ways in which they could make sure their drug levels were correct. Such recommendations included: increasing the dose of anti-HIV medicines; improving adherence; changing diet; and checking for drug interactions with any other drugs taken alongside anti-HIV therapy.

The study also found that heavier patients and those taking efavirenz (*Sustiva*) or lopinavir/ritonavir (*Kaletra*) were most likely to have low drug levels and therefore most likely to benefit from drug level monitoring.

side-effects

Pancreatitis risk found to be lower than expected

A large European study has found that about 1% of people on anti-HIV treatment developed pancreatitis (inflammation of the pancreas), a side-effect associated primarily with d4T (stavudine, *Zerit*) and ddI (didanosine, *Videx*). Previous research had suggested that about 5% of people on anti-HIV treatment developed this potentially very serious condition.

Surprisingly, the study found no correlation between pancreatitis and treatment with any particular anti-HIV drugs. In fact, the only risk factor they identified was a low CD4 cell count when anti-HIV treatment was started.

It's unclear why this study had different findings from earlier research. But it could be because the use of both d4T and ddI fell in Europe during the study period, between 2001 and 2006.

news in brief

drug resistance

Extensive drug resistance emerges slowly

A study of almost 8,000 patients from ten HIV treatment centres in the UK has found that ten years after starting potent anti-HIV treatment, only about 10% of patients have resistance to drugs from all of the three main classes of antiretrovirals (NRTIs, NNRTIs and protease inhibitors).

The study also found that 60% of patients with extensive triple-class failure had at least one viral load measurement below 50 copies/ml *after* failure had

occurred, suggesting that failed treatment continued to have some antiretroviral effect. Furthermore, there was good survival five years after the emergence of extensive virological failure, the cumulative risk of death being 10.6%.

In addition, results from a separate French study suggest that HIV-positive individuals who have a low CD4 cell count and no new treatment options and are taking antiretroviral therapy which is not controlling their viral load should

remain on their therapy rather than interrupt treatment.

The study found that individuals who interrupted treatment were much more likely to experience disease progression and develop new HIV-related illnesses than those who stayed on their virologically 'failing' regimen.

Several new classes of drugs have become available in recent months, and very few people should now be faced with this problem of a lack of treatment options.

lifestyle



Recreational drug use and the immune system

The use of some recreational drugs doesn't appear to have an effect on numbers of CD4 and CD8 immune cells, American researchers have concluded after conducting a large study involving gay men who were both HIV-positive and HIV-negative. Many of these men used recreational drugs including amphetamines, cannabis, cocaine, and poppers. Blood tests were carried out to see what effects drug use had on the number of their CD4 and CD8 immune system cells.

Surprisingly, and contrary to previous findings based on animal and test-tube research,

there was no real evidence that the use of any of these drugs lowered the number of CD4 or CD8 cells. Men who used poppers once a week or more had slightly lower CD4 cell counts than men who didn't use this drug, but the difference, at only 4%, was not considered to be statistically or clinically significant.

However, the investigators point out that their research looked only at the effect of drug use on the *number* of key cells. They hadn't examined the effect of drug use on how well the immune system was able to function.

illness

HIV treatment significantly lowers lymphoma risk

Swiss researchers have found that effective anti-HIV treatment lowers the risk of non-Hodgkin's lymphoma in the long term. Non-Hodgkin's lymphoma is an AIDS-defining cancer and was a frequent cause of illness and death in people with HIV before effective anti-HIV treatment became available.

The latest research found that the risk of developing non-Hodgkin's lymphoma starts to fall as soon as a person starts anti-HIV treatment, with the risk continuing to decline thereafter.

A particularly important finding was that anti-HIV treatment lowered the risk of non-Hodgkin's lymphoma regardless of the individual's CD4 count when they began treatment.

Correction

In the January/February issue of *HTU* a table on page 11 included a list of drugs in the pipeline. Two of the entries for the integrase inhibitor, elvitegravir, were incorrect: it currently does not have a trade name (*Isentress* is the trade name for raltegravir) and it is dosed once daily, boosted with ritonavir.

not so special

Last November, the Disability and Carers Service (DCS) - the section of the government's Department of Work and Pensions (DWP) that oversees Disability Living Allowance (DLA) and Attendance Allowance (AA) - announced that it was going to review most cases of DLA and AA awarded under the 'special rules'. This is likely to affect many HIV-positive people who were diagnosed in the 1980s and early 1990s and who have survived longer than expected due to potent antiretroviral therapy.

What are DLA and AA?

DLA is a tax-free state benefit that is paid to people aged under 65 who have a disability, in order to help with the increased cost of daily living due to their disability. AA is a similar benefit for people aged 65 and older.

What are the 'special rules'?

The 'special rules' apply to someone who is awarded DLA or AA because, in the opinion of their doctor, they have a progressive disease and their death is reasonably to be expected within six months. The 'special rules' mean that the person qualifies for help with personal care at the highest rate automatically - and, until 2006, indefinitely - even if no help is needed.

Where does HIV fit in?

Because of the extremely unpredictable nature of HIV illness in the 1980s and 1990s, doctors often erred on the side of generosity and recommended that patients with a CD4 count below 200 cells/mm³ were awarded 'special rules' DLA even though some of them could have been reasonably expected to live longer than six months. Of course, before potent antiretroviral therapy became available in 1995/6, many people with low CD4 counts went on to die of an HIV-related illness. Although

this still happens, it is now rare in the UK, and is linked to either late diagnosis of HIV infection, or, to lesser extent, running out of treatment options. Obtaining DLA under the 'special rules' has become increasingly difficult for someone who is HIV-positive in the era of potent antiretroviral therapy.

What else changed?

The regulations changed for new 'special rules' awards of AA and DLA in September 2006. Rather than being awarded indefinitely, the benefit was now to be given for a fixed period of three years. Around this time, a review undertaken by the DCS found that many people had been receiving DLA (and AA) under the 'special rules' provisions for much longer than three years. A legal review (which found that the DCS could reassess 'special rules' awards), a consultation with relevant care groups (in the case of HIV, this was with THT) and a pilot survey of a small number of awards made more than seven years ago led to the November 2007 announcement.

Who is affected?

The DCS will review the cases of most people who have received DLA or AA under the 'special rules' provision for more than three years. They will start with people receiving DLA who are 55 or younger, and then move on to people aged between 55 and 64. They will also look at a "sample" of people receiving AA who are aged between 65 and 84 years. The review process began in November 2007 and is expected to last 12 months.

What should I do?

If you have been receiving DLA or AA under the 'special rules' for more than three years, you will initially receive an enquiry form by post, which asks for up-to-date information about your medical

condition and current medical practitioner. THT recommends the following:

- Do not ignore the letter because a decision may be made about your benefit in the absence of the most up-to-date medical information.
- If you want to talk to someone before you complete the form, call THT Direct on 0845 12 21 200.
- Let your hospital consultant, GP or specialist know that they will be getting a letter asking for information about your DLA claim.
- Take that opportunity to discuss your medical condition with your doctor or consultant so that they can provide the most up-to-date and accurate information about your condition.
- If you do not want your GP (or any other persons or organisations) to be contacted, please tick the relevant box on page 8 of the form.
- If, as a result of this review, your benefit changes and you are unhappy about it, get in touch with THT Direct so that they can help you decide what to do next and, where appropriate, help you find an advice agency in your area.

What happens at a review?

If the review shows that someone claiming DLA under the 'special rules' still satisfies the requirements of the award, the DCS will not change their benefits. However, if this is not the case, the DCS will make further enquiries to find out what, if any, entitlement that person has under normal rules. Rest assured, though - the DCS will not seek to reclaim any money already paid to people who are no longer found to be eligible under the 'special rules'. They may, however, change the benefits payable from the date of their individual review.

how the review of 'special rules' DLA may affect you

by Edwin J Bernard

Will I lose other benefits?

Not everyone receiving DLA or AA receives other benefits (if they are well and working, for example), but some people do receive other benefits, including Incapacity Benefit (which is paid to people because they are unfit to work because of ill health or disability), Income Support (which provides financial help for people between 16 and 60 who are on a low income who are not in full-time paid work), Pension Credit (similar to Income Support for the over-60s) and Housing Benefit.

Even if the review finds that you are no longer entitled to get as much (or any) DLA, this does not necessarily mean you will not be entitled to Incapacity Benefit. This is because the criteria for these benefits are entirely different.

However, the amount of Income Support, Pension Credit and Housing Benefit you receive may change if your entitlement to DLA changes.

It is thought, however, that the DCS will not automatically review decisions about other benefits except in exceptional situations (for example, if fraud is uncovered). (And being paid DLA in error because the risk of death within six months hasn't applied for some years doesn't count as fraud, as long as the claim wasn't fraudulent at the start.)

Planning for the future

If you are concerned about a change in your entitlement to benefits, now is the time to get advice on:

- how the DLA review might affect you and your income;
- other benefits or sources of income; and
- when this might happen.

You also may need to plan for managing any change, including adapting to and budgeting on a lower income, planning for the longer term, education, training and work options, and dealing with any mental health issues.

Thanks to Chris Morley, Policy and Publications Co-ordinator at Manchester's George House Trust, who assisted greatly with this article.

further information

THT has produced general advice on the DLA review:
<http://tinyurl.com/2m46rm>

For specific advice, call THT Direct on 0845 12 21 200 or, if you live in the North West of England, contact George House Trust on 0161 274 4499 or via <http://www.ght.org.uk/>

For more on the background to the review, see:
www.disabilityalliance.org/special.htm

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