

# aids treatment update



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I recently attended an excellent one-day seminar on improving the quality of life of people living with HIV held by Brent & Harrow Community Health Projects.

One young African woman told us that her HIV doctor just didn't understand why she would rather stop taking her anti-HIV drugs than see her once beautiful legs become disfigured due to lipodystrophy and incredibly dry skin.

When she looked in the mirror, she told us, she hated what she saw. "I could never again undress in front of a man," she admitted. "I'd rather have lived one day looking like 'me' than the rest of my life like this."

Fortunately, many people who work in HIV clinics understand that just living longer isn't enough; that our lives need to have meaning, and that we cannot just be grateful for life at any cost. We need to explain to those that don't understand that it's important that we are supported by them to make our own treatment choices.

The young woman is now on a different anti-HIV combination and doing very well.

Hippocrates' golden rule for doctors is to 'first, do no harm'. Let's try and make sure that, at the very least, anti-HIV drugs don't ruin our quality of life.

After all, isn't the main point of staying alive being able to aim for a full and happy life?

**page 3** This month in *Upfront*, Edwin J Bernard reports on new data that explains why HIV superinfection might not be as common as once thought.

**page 4** In *HIV and quality of life*, Edwin J Bernard examines how HIV impacts upon our quality of life and asks whether we should expect anti-HIV therapy to do more than improve the quantity of our lives.

**page 7** Are you *Sick of being tired*? Many people living with HIV experience long-lasting fatigue that impacts greatly upon their quality of life. Liz Highleyman explores the causes of fatigue in HIV-positive people, and provides options for reducing and resolving this troublesome and all-pervasive symptom.

**page 10** *ATU's* editor, Edwin J Bernard, shares his own experiences of *Living with fatigue*.

**page 12** Amongst the items in *News in Brief*, we learn about a new study from the United States which suggests that staying on highly active antiretroviral therapy (HAART) may reduce the incidence of AIDS-related disease events even when viral load is no longer under control and CD4 cell counts are low. Also, is boosted atazanavir better than *Kaletra*?

**page 14** Learn how signing up for a course in self-management could be the start of *Helping yourself* to a better quality of life.



## aids treatment update

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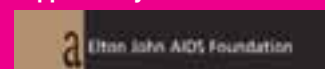
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# superinfection revisited

why superinfection might not be as common as once feared, by Edwin J Bernard

Since 2002, a handful of case reports have suggested that superinfection – especially if it is with a strain of HIV that is cross-resistant to one or more of the drugs that make up your current drug regimen – could lead to faster disease progression.

Four years later, however, science has so far been unable to show that HIV superinfection – the reinfection of an HIV-positive person with a genetically different strain of HIV to that seen during initial infection – is anything but a relatively rare occurrence.

It seems that those most at risk of superinfection are recently-infected individuals (superinfection is usually seen within twelve months – and no later than four years – after initial HIV infection) who either never started, or who took a break from, anti-HIV therapy.

Now, new data presented at the Thirteenth Retroviruses Conference (CROI) in Denver earlier this year may explain why this is so.

## Are neutralising antibodies the key?

After HIV infection, neutralising antibodies are produced by the immune system's B-cells which are able to stop other strains of HIV from attaching to CD4 T-cells, and the theory is that this ought to prevent superinfection.

Researchers from southern California, who had previously reported on sexually-acquired superinfection in three recently-infected men, wondered whether these men had fewer, or less powerful, neutralising antibodies than

other recently-infected people. So, they compared their neutralising antibody responses, before and after superinfection, with eleven recently-infected men with no evidence of superinfection despite having regular 'high risk' sex with their HIV-positive partners. They found that the men with superinfection did indeed have less powerful neutralising antibody responses than the non-superinfected men, before and even after superinfection.

The researchers think that this means some people are protected against superinfection more than others. "There might be a window of opportunity for superinfection to occur, and maybe that is timed by neutralising antibody response," said lead researcher, Davey Smith. "Some people might have neutralising antibody response that is slower [to develop] and therefore the window is larger." Researchers from San Francisco also compared neutralising antibody responses in four recently-infected men with suspected superinfection with the neutralising antibody responses of eight recently-infected HIV-positive couples who weren't superinfected despite constantly exposing each other to HIV. Again, they found significantly higher levels of neutralising antibody responses in the non-superinfected couples.

## Keeping superinfection 'local'

The San Francisco researchers also think that neutralising antibody responses might be preventing *clinically relevant* superinfection in chronically infected HIV-positive people. In theory, this would occur

whether or not someone is on anti-HIV therapy.

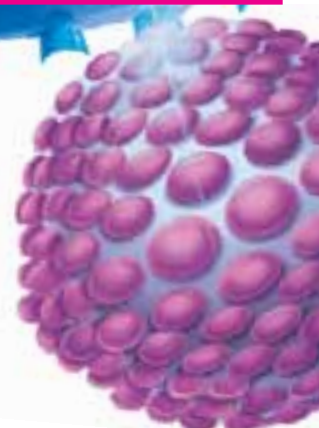
Early research suggests that new HIV strains – even drug-resistant HIV – are constantly being passed between HIV-positive people who aren't practising 'safer sex'. However, the new infection is being kept prisoner ('localised') within the immune cells of the genitals or rectum.

This means that 'localised' superinfection may be happening more often than previously thought, but that most people are able to keep this HIV under control before it can cause harm. But if a new HIV strain breaks out of these localised compartments and becomes the dominant strain of HIV in the body, 'systemic' superinfection will have occurred. As a handful of reports have already suggested, this can have devastating consequences.

## Making informed choices

The risk of *clinically relevant* superinfection appears greatest for recently-infected HIV-positive people; this includes people at 'high risk' but untested.

Remember, though, that unprotected sex between two HIV-positive people can transmit other infections with serious health consequences – especially syphilis and hepatitis C – and this risk increases as your number of partners increase. Using condoms, and having regular sexual health check-ups, can help reduce those risks. ■



# hiv and quality of life

how much does HIV and its treatment affect our quality of life? by Edwin J Bernard

Everyone talks about quality of life, but what does it really mean? On the surface, it seems very straightforward: 'a good life'. But what is 'a good life'? How do you measure it? Where does HIV fit in? And what is the impact of anti-HIV therapy on quality of life? Does it only improve the quantity, as opposed to the quality, of our lives?

## What is quality of life?

The Centre for Health Promotion at the University of Toronto, Canada, defines quality of life as: "The degree to which a person enjoys the important possibilities of his or her life." These 'important possibilities' are made up of various factors that can be different for different people, in different contexts. These factors can also change over time as our living situations change, and as we re-prioritise what is important to us.

## who am I?

Who we are covers not simply our physical selves - our health, our appearance, how we eat, whether we exercise - but also our psychological and spiritual selves. Are we positive or negative thinkers? How much control do we feel we have in our lives? What are our personal values and beliefs?

## do I belong?

Who we are in context with the world around us can also affect our quality of life. What are our relationships with others and our connections with the world around us? On a physical level this means our home, our neighbourhood, our community and our workplace or school. On a social level this means our intimate partners, our families, friends, co-workers, and neighbours. But how we fit in with this community also matters. Do we have enough money, work and education? How good are our health and social services? Are there places where we feel happy and comfortable socialising?

## what will I become?

A third component of quality of life looks to the future. What are our personal goals, hopes and aspirations? What do we want to achieve in life? Is surviving enough? How do we adapt to change?



## The influence of HIV on factors other than health

Living with HIV can impact upon many of the factors that affect our quality of life; not only our physical health, but also our mental and social well-being. After all, HIV is not simply a virus that causes disease, but also a social and historical event that impacts how others react towards us. Issues including personal safety and human rights as well as other aspects of the political and social infrastructure can radically affect our quality of life.

For example, in the UK, there is currently much confusion over whether the law acts as a shield or a sword for people living with HIV. Although the inclusion of HIV from December 2005 in the Disability Discrimination Act of 1995 now protects people living with HIV from discrimination in the areas of employment, access to goods and

services, education and housing, the recent apparent criminalisation of HIV transmission in the UK has led to much uncertainty over whether people with HIV are now all potential criminals or victims; neither is a life-enhancing prospect.

Our living conditions can also affect quality of life as much, if not more than HIV, its symptoms and treatment. Project Nasah<sup>[1]</sup>, a research project collaboration between NAM, the National AIDS Trust, and the African HIV Policy Network, conducted by Sigma Research in 2003, found that African people living with HIV in the UK had a significantly reduced quality of life than reported by mainly white British HIV-positive gay men a year earlier<sup>[2]</sup>. Having enough money to live on was the most common concern for HIV-positive Africans in the UK; and housing conditions and immigration

status were all cited as problems by at least half of African respondents.

However, mental health and relationship issues were found to have an equally serious impact on quality of life for both HIV-positive Africans in the UK and white British HIV-positive gay men: HIV-related stigma, bound up with homophobia and/or racism, also affects our quality of life.

Many people who work on the frontlines of the HIV sector - including social workers and community-based support organisations - argue that providing practical and emotional support for all of these non-health-related quality of life issues needs to be as much of a priority for the needs for HIV-positive people as treatment itself.

However, to many people living with HIV, it can appear as if their doctor



values quantity of life over quality. For example, the most recent British HIV Association HIV Treatment Guidelines say that "the main aim of treatment is...to prolong life and improve quality of life by maintaining suppression of virus replication for as long as possible."

#### further information

NAM's book, *Living with HIV*, includes a wealth of information about improving your quality of life, including firsthand inspirational testimonies from people living with HIV. A new edition will be published this summer. Visit NAM's publications centre at [www.aidsmap.com](http://www.aidsmap.com) or call 0207 840 0050 to order a copy.

### HIV and health-related quality of life

Does an 'undetectable' viral load bring about improved quality of life?

In the decade since potent anti-HIV therapies have radically improved the life expectancy of people living with HIV, many people living with HIV have been faced with a good news/bad news proposition: 'You're going to live, but you may not enjoy the rest of your life'.

An uncertain future is still a major part of an HIV diagnosis, but instead of asking, 'When and how am I going to die?' we now often wonder, 'How am I going to live?'

Concern about anti-HIV drugs' side-effects has now replaced worrying about an early death as the major issue affecting our health-related quality of life. Last year, a pan-European quality of life survey of over 500 HIV-positive people found that almost half of respondents reported dissatisfaction with their quality of life: visible and silent side-effects and difficulty in taking medicines were the most important treatment-related issues. Whilst future body shape changes, increased symptom visibility and physical disability ranked among the top three causes of concern, pain, fatigue and disrupted sleep were the most reported day-to-day consequences of HIV and its treatments.

For some, an HIV diagnosis can bring a greater appreciation of life, particularly when HIV is seen as more of a threat to health than concerns over treatment side-effects: a recent French study<sup>[4]</sup> found that people who started treatment with more severe symptoms of HIV disease were more likely to report an improved quality of life after a year of anti-HIV treatment. And an American study published earlier this year<sup>[5]</sup> found that although about half of the respondents believed that an HIV diagnosis reduced their health-related quality of life several years after testing HIV-positive, about one-third of respondents reported improved health-related quality of life several years after diagnosis. The researchers noted that for some people an HIV diagnosis is a wake-up call to improve all aspects of health, whereas

for others, including those who start anti-HIV therapy when they had previously felt well, managing life with HIV can be a difficult prospect.

### Blaming it all on HIV?

HIV and its treatments can affect many areas of health-related quality of life, including: symptoms and side-effects, especially pain, fatigue, body image and appearance; mood and mental health; and personal and sexual relationships. Assessing the impact of HIV and its treatments on quality of life is complex. It takes a lot of effort to untangle the physical effects of the virus, and the drugs we take to make the virus less lethal, from the wider emotional and social impact that HIV can have on our lives.

Nevertheless, it's important to remember that sometimes HIV has little or nothing to do with how (un)happy and (un)fulfilled we are. However, just like the chicken and the egg, it isn't easy to say which comes first? Is an improved quality of life only possible because better anti-HIV therapies mean we have a life to improve? Or should we (and our healthcare team) focus more on how to improve the quality of our lives? Does longevity lead to a better life in and of itself?

Perhaps making the most of ever-improving, but imperfect, anti-HIV therapies, when their benefit outweighs their risks, allows for the opportunity to take the next steps towards that often elusive 'good life'.



# sick of being tired

what causes fatigue, and what can you do about it?  
by Liz Highleyman

Fatigue - persistent tiredness or lack of energy - is one of the most common symptoms of living with HIV. It is also potentially one of the most debilitating, since, by interfering with your ability to work, rest and play, it can seriously affect your quality of life.

## Summary

- Fatigue is a common symptom of HIV disease, affecting quality of life.
- Fatigue can be caused a variety of factors, including anaemia, low testosterone, hepatitis coinfections and HIV itself.
- Fatigue can also be a side-effect of drugs used to treat HIV, hepatitis or other health problems.
- Depression can also cause fatigue, and vice versa.
- Persistent fatigue should be thoroughly investigated and its causes treated by your doctor.
- Eating well, exercising regularly and taking naps may help with mild fatigue.
- Fatigue is not inevitable, and can often be treated.

Though less common now in the developed world than it was earlier in the epidemic, when more people were living with advanced immune deficiency, recent studies have found that between 37% [1] and 65% [2] of people living with HIV experienced persistent fatigue, suggesting that fatigue affects one out of every two HIV-positive people at some point in their lives. It is difficult to say how this compares to the frequency of fatigue in the HIV-negative population because definitions vary and studies are few, but a recent United States survey [3] found that 12% of HIV-negative adults experienced fatigue lasting at least six months, whilst about 1% met the clinical definition of chronic fatigue syndrome.

Experts classify fatigue into three components: physical, mental/psychological, and emotional/motivational. People with physical fatigue may experience muscle weakness (myopathy) and a reduced ability to carry out activities that require even minimal exertion. People experiencing psychological fatigue may find it difficult to concentrate or think clearly, whilst those with emotional fatigue may lack motivation and lose interest in life.

Fatigue may be caused by a variety of factors, and so dealing with it requires a variety of different approaches.

Fatigue may be directly related to HIV infection, especially if it's untreated. The most common treatment-related cause is anaemia, often related to use of AZT (zidovudine, *Retrovir*). Other causes include coinfection with hepatitis viruses; nutritional or hormonal imbalances; depression; lack of physical activity; and use of alcohol or recreational drugs.

Dr Lisa Capaldini of the University of California at San Francisco, who has extensive experience with fatigued HIV-positive patients, says that often the physical causes of fatigue can be identified and successfully treated. In common with people with cancer and other serious chronic illnesses, people with more advanced HIV disease often have alterations in metabolism, hormones (like testosterone or adrenaline) and cytokines (the body's chemical messengers) that may contribute to fatigue. She estimates that roughly one-third of fatigue in people with HIV has a physical cause like anaemia or low testosterone, and fatigue in another third is likely to be related to depression or other mental health issues.

However, "idiopathic" HIV-related fatigue, for which no specific physical cause can be identified, is more challenging, and affects about one-third of her patients with HIV-related

fatigue. Nevertheless, there are many different ways to tackle fatigue, and in some cases multiple interventions may be the best approach.

### Anaemia

Anaemia occurs when red blood cells are in short supply or do not carry adequate oxygen. AZT (also present in the combination pills *Combivir* and *Trizivir*) can cause anaemia in people with HIV, since it damages the bone marrow, where new red blood cells are produced. Anaemia is the most common treatment-related cause of fatigue in people with HIV, and Dr Capaldini estimates that about 15% of her patients develop AZT-related anaemia.

However, anaemia may also be due to nutritional deficiencies, especially lack of iron, vitamin B12, or folic acid. There are also other types of anaemia, some of which are caused by: blood loss; haemolytic anaemia, an auto immune condition in which antibodies destroy red blood cells; concurrent infections, such as malaria; and chronic disease itself.

Along with fatigue, other symptoms of anaemia include shortness of breath, heart palpitations, pale skin, weakness, headache, and dizziness. Fatigue that worsens with physical activity - which increases the body's need for oxygen - is often due to anaemia. If you suffer



### HIV infection and anti-HIV treatments

When someone is first infected, fatigue may be a symptom of acute retroviral syndrome, a flu-like illness that affects some individuals during the first few weeks after exposure to the virus.

Studies have shown that fatigue is associated with high HIV viral load, and it often improves with effective anti-HIV therapy.

Likewise, the incidence of fatigue rises as CD4 counts fall below 500 cells/mm<sup>3</sup>, although even asymptomatic individuals with relatively intact immunity may still experience fatigue. In addition, some AIDS-related opportunistic illnesses, such as pneumonia and tuberculosis, can cause severe fatigue - in fact, fatigue may be the first sign of an underlying infection.

Even though anti-HIV therapy may ultimately improve energy levels, many anti-HIV medications may cause fatigue, along with a general feeling of being unwell and gastrointestinal side-effects, during the first few weeks or months of treatment, but these symptoms often improve over time.

from these symptoms, it's very important that you tell your doctor, since studies have shown that anaemia can have very serious consequences for people with HIV.

For anaemia due to AZT, the simplest solution may be to switch to a different nucleoside/nucleotide reverse transcriptase inhibitor. Recommended alternatives are tenofovir (*Viread*, also in the combination pill *Truvada*), and abacavir (*Ziagen*, also in the combination pill, *Kivexa*).

Another option is recombinant erythropoietin (EPO, *Eprex*, *NeoRecormon*). This is a genetically engineered version of a natural hormone produced by the kidneys that stimulates the bone marrow to make more red blood cells. The drug is administered by subcutaneous (under-the-skin) injection, usually two or three times weekly. Studies have shown that EPO alleviates anaemia and associated fatigue in people with HIV and it is often used to manage anaemia associated with AZT or the anti-hepatitis C drug, ribavirin.

### Hormone imbalances

Abnormal levels of certain hormones can also cause fatigue. Low testosterone is seen in both men and women with HIV, and can lead to weight loss, muscle weakness,

depression, and decreased libido, as well as fatigue. Some studies suggest that about one-quarter of HIV-positive men have low testosterone, rising toward 50% among those with advanced disease. Women also make and require small amounts of testosterone, and HIV can affect its production. One study [4] found that 26% of HIV-positive women with significant weight loss had total testosterone levels below the normal range.

Testosterone (administered as an injection, gel, or patch) has been shown to alleviate fatigue and depression in HIV-positive men, and although there has been less research in women, low-dose testosterone replacement appears to have similar beneficial effects. Testosterone replacement is only available in the UK for individuals with low levels of natural testosterone; there is no evidence that supraphysiologic doses (higher than the natural range) are beneficial, and they may be harmful.

Low levels of hormones produced by the adrenal glands and thyroid can also contribute to fatigue, although both are relatively uncommon in people with HIV. If necessary, adrenal insufficiency may be treated with synthetic glucocorticoids such as hydrocortisone or dexamethasone,

whilst low thyroid levels can be corrected by synthetic thyroxine.

### Viral hepatitis

Persistent fatigue is one of the most common symptoms of hepatitis A, B and C, the latter two affecting an estimated 8% of HIV-positive people in the UK. Unfortunately, treatments for hepatitis can also cause fatigue; ribavirin to treat hepatitis C may cause anaemia which often leads to fatigue; and treatment of hepatitis B or C with interferon can cause fatigue, either alone or as part of a depressive illness.

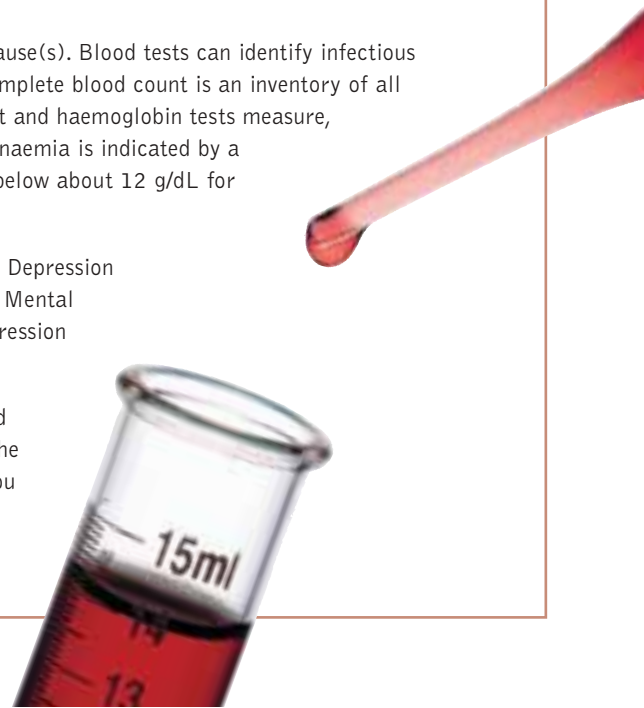
At the Second International Workshop on HIV and Hepatitis Coinfection held in Amsterdam earlier this year, Dr Kristina Jones from Weill Cornell Medical College presented data showing that fatigue is twice as common as depression - and may in fact be diagnosed as depression - in coinfecting individuals receiving pegylated interferon plus ribavirin [5]. In her study of 93 coinfecting patients, 70% experienced fatigue and 33% were diagnosed with clinical depression during treatment. In addition, most (77%) of the patients who developed anaemia reported fatigue, compared with just 20% of non-anaemic patients. Fatigue usually developed within the first week after starting anti-hepatitis C treatment, whilst depression was slower to develop.

### How do you find out and measure the causes of fatigue?

The mainstay of fatigue management is diagnosing and correcting the underlying cause(s). Blood tests can identify infectious organisms, anaemia, hormone deficiencies, and certain nutritional imbalances. A complete blood count is an inventory of all types of cells in the blood; a low red blood cell count indicates anaemia. Hematocrit and haemoglobin tests measure, respectively, the percentage of red blood cells and their oxygen-carrying capacity. Anaemia is indicated by a hematocrit below about 36% for women or 40% for men, or a haemoglobin level below about 12 g/dL for women or 14 g/dL for men.

Depression can be assessed using a variety of standardised tools including the Beck Depression Inventory and the diagnostic questions in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) Appropriate diagnostic tests can help distinguish between depression and fatigue.

Because fatigue may develop slowly, it may be beneficial to keep a journal to record changes over time, noting information such as diet, sleep patterns, endurance (e.g. the distance you can walk without exertion), and strength (e.g. the amount of weight you can lift at the gym, or your ability to carry a shopping bag). Dr Capaldini recommends that people with HIV assess fatigue status every six months and report any changes to their HIV clinic.



## Depression

Fatigue and depression also often occur together in people with HIV alone, and here it also often difficult to sort out which is present and whether one is causing the other. Fatigue is a common symptom of depression, and being socially isolated and/or unable to carry out normal activities due to fatigue can also lead to depressed mood.

Depression is most likely to occur in individuals with a personal or family history of psychiatric problems and in those with a history of substance abuse, but it can affect anyone living with HIV.

If fatigue is present when waking in the morning and does not improve with rest (and physical exertion doesn't make it any worse) then depression is likely a contributing factor.

For fatigue linked to depression, identifying the cause and combining some kind of talking therapy with one of a variety of antidepressant medications is the ideal treatment. The most common medicines used to treat depression are the selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine (*Prozac*), paroxetine

(*Paxil*), and sertraline (*Zoloft*), although the antidepressant citalopram (*Cipramil*) is often used because it has few interactions with anti-HIV drugs. It usually takes at least a few weeks before the beneficial effects of antidepressants are fully realised, and it often requires some trial-and-error to determine which drug works best for a particular individual.

## Diet, exercise, and sleep

Along with anaemia due to specific nutritional deficiencies, overall poor nutrition can also lead to fatigue. This happens in part because the body is not receiving adequate nutritional fuel and it signals the brain to conserve energy by reducing activity.

Unfortunately, some HIV-positive people find it hard to maintain an adequate diet due to loss of appetite or symptoms such as nausea, mouth sores, or taste changes that make eating difficult or painful.

It may seem paradoxical, but lack of physical activity can be a major contributor to fatigue. Daytime fatigue may also be related to inadequate sleep at night or inability to reach the deepest stages of sleep (known as non-restorative sleep). Not feeling

refreshed when waking in the morning is a sign of inadequate or non-restorative sleep.

Several factors may contribute to insomnia or poor sleep, including sleep apnoea (repeated interruptions of breathing); symptoms such as diarrhoea or pain; use of caffeine, alcohol, or recreational drugs; and medication side-effects such as the unusual dreams associated with efavirenz (*Sustiva*).

Maintaining a healthy lifestyle is the first step in managing fatigue. Trying to eat a well-balanced diet containing adequate amounts of essential nutrients can help, and while nutritionists agree that the best way to obtain nutrients is through food, certain supplements may help correct specific deficiencies. Some people find that eating several small meals throughout the day helps them maintain a higher level of energy.

According to Dr Mike Youle of London's Royal Free Hospital, exercise is often the best treatment for fatigue. Studies have shown that moderate exercise can enhance energy levels, reduce depression, promote healthy sleep, and improve overall quality of

# living with fatigue

by Edwin J Bernard

A decade ago I was living in Vancouver, the Canadian city that held the 1996 International AIDS Conference which ushered in the era of highly active antiretroviral therapy (HAART). Ironically, I didn't benefit: I was already cross-resistant to all of the available protease inhibitors and non-nucleosides, having taken them sequentially in early clinical trials, and was just about holding my own on a dual combination of d4T (stavudine, *Videx*) and 3TC (lamivudine, *Epivir*).

My energy levels had been slowly diminishing since my CD4 count fell below 200 back in 1993, and without realising it, I had been adapting my lifestyle accordingly. With a very caring partner, the fatigue hadn't seemed so problematic at first. Instead of shopping, cooking and cleaning for myself, I concentrated on saving my energy for work, the gym, and occasional socialising.

By 1999, with a rising viral load, plummeting CD4s, and an angry, fatty liver, there seemed to be no point in carrying on with anti-HIV therapy, and my HIV doc suggested a treatment break: he also told me to make the most of (what was left of my) life.

I continued with my acupuncture, Chinese herbs, meditation and massages, and at first, I didn't feel so different. But soon I was having to decide where to expend my limited energy. Even after sleeping for ten hours, I would wake up feeling as if I had been running an overnight marathon, and no amount of needling, caffeine or herbal remedy would provide more than a very temporary boost.

I became increasingly more withdrawn from the world. Each day, I would have to decide whether or not to leave the apartment, and if so, choose just one task before exhaustion hit me with a knockout force. After a few hours

life. If you are just starting to exercise, it is probably best to begin slowly with light to moderate activity; even 15 minutes daily can be beneficial.

Getting enough sleep at night and taking rests if needed during the day can also help. For some people, it can be beneficial to cut back on - or stop using - alcohol, tobacco, and/or recreational drugs. Even substances like caffeine and pseudoephedrine that increase energy in the short term can interfere with sleep and worsen fatigue over the long run.

Alternative and complementary therapies are also popular for alleviating fatigue. Although there is little controlled research on most complementary approaches, many people find that acupuncture, yoga, t'ai chi, and massage therapy offer relaxation, enhance energy levels, and improve overall quality of life.

### Treating fatigue with no apparent cause

More controversial – and experimental – is the use of psychostimulants such as methylphenidate (*Ritalin*) and modafinil (*Provigil*) to treat fatigue in people with HIV. A 2001 study [6] found that

methylphenidate improved symptoms of severe persistent fatigue, as well as depression and overall quality of life, but that it often led to hyperactivity or "jitteriness."

More recently, a pilot four-week open-label trial [7] of modafinil in 30 HIV-positive patients on anti-HIV therapy with "clinically significant" fatigue, found that 80% showed significant improvement in fatigue and depression; the most common side-effects were headache, irritability, and feeling "hyper."

The United States National Institutes of Health is currently sponsoring a larger study examining the use of modafinil in people with HIV-related "idiopathic" fatigue. However, the use of psychostimulants to treat fatigue in people with HIV remains experimental, and unless there is more evidence that leads to approval in Europe, it is unlikely that these drugs will be prescribed in the UK.

### Fatigue is not inevitable

The incidence of severe fatigue has decreased in the past decade since the use of combination anti-HIV therapy became widespread in the developed

world, but it remains a frustrating and often significant problem for some people living with HIV. Mild fatigue may even be on the increase since HIV became a chronic illness, since managing a chronic illness and living a fuller life (gained, or regained, through better long-term health) can take its toll, according to Lisa Capaldini. However, Mike Youle says fatigue has become a less frequently reported symptom in recent years amongst his patients.

Fortunately, several approaches are useful for managing fatigue and associated depression, ranging from lifestyle changes to pharmacological interventions. For those with mild fatigue, practical measures, such as taking short daily naps, reorganising the home and workplace to maximise efficiency and minimise effort, alternating restful and physically strenuous activities, and scheduling the most demanding tasks for times of the day when energy levels are highest, may be sufficient.

Fatigue need not be an inevitable result of living with HIV. Talk to your doctor about which fatigue-management strategies are most appropriate for you.

on the computer - for work, or health research - I'd slump uneasily into my easy chair, tilting it back, closing my eyes and only returning to fuzzy consciousness in time for dinner and another night of TV.

For a whole year, my world was as limited as my energy. The fatigue had ravaged my life, destroyed my self-confidence, and rendered this once energetic thirtysomething into an old man way before my time.

Of course, during that year off therapy, my body had become an HIV factory; although I was extremely lucky I didn't experience any AIDS-defining illnesses, the virus had managed to wipe out my middling energy levels and my quality of life. Although I fought back in 2000 with mega-HAART (eight drugs, including the then brand new *Kaletra*) my energy was still under-par: the HIV had also affected my ability to produce testosterone, a potentially

symbolic castration I countered with testosterone replacement therapy. By 2001 the dark cloud of disabling fatigue finally vanished and I was able to start living 'normally' again.

Now, I get tired and when I rest, I recover. Amazing! I can burn the candle at both ends: manage a chronic illness, keep a demanding job, a long-distance relationship, go to the gym three times a week, and sometimes even have late nights and early mornings.

So, if fatigue is affecting your life, don't take it lying (or sitting) down: investigate the causes and treat it. And if there's no apparent cause, see if you can persuade your doctor to prescribe you something to boost your energy. As Sally Bowles sings in *Cabaret*: "What use is sitting alone in your room?"

## latest research

## Don't give up on HAART even after it's 'failed'

A small but significant number of people living with HIV in the UK are close to running out, or have already run out, of treatment options, but a new study from the United States suggests that staying on highly active antiretroviral therapy (HAART) may reduce the incidence of AIDS-related disease events even when viral load is no longer under control and CD4 cell counts are low.

The investigators, from the University of Michigan, analysed the rates of AIDS-related events in the medical records of 302 HIV-positive patients at the university's HIV clinic. These people had very advanced HIV disease with CD4 cell counts below 200 cells/mm<sup>3</sup> before starting anti-HIV treatment.

They discovered that the patients with a poor response to HAART were less likely to experience AIDS events like *Pneumocystis pneumonia* (PCP) and oesophageal candidiasis or 'thrush' than patients who had similar CD4 cell counts before powerful HIV drug combinations were available. The effect of HAART was even true when the investigators limited their analysis to patients who had high viral loads despite being on antiretroviral therapy. This suggests that HAART is still useful in preventing disease when the virological and immunological responses to treatment appear to be inadequate.

The investigators offer two possible explanations. It could be that being on HAART with persistent detectable HIV may lead to more drug-resistant viruses that have a lower disease-causing potential than 'wild type' HIV.

Alternatively, they suggest that HAART-treated patients have more memory CD4 T-cells than people with similar CD4 counts who never took HAART. These may recognise disease-causing organisms to which the patient has been exposed in the past, resulting in a lower incidence of AIDS events despite overall CD4 cell counts remaining low.

The bottom line, however, is the need for new classes of drugs that work with multidrug-resistant HIV. "Although our study suggests that there may be some value in maintaining HAART even for patients who have immunologic and virologic failure," the investigators conclude, "it also stresses the need for development of new antiretroviral agents that have activity against drug-resistant HIV strains, in hope of sustaining the overall decrease in AIDS-associated illnesses that has been witnessed since the introduction of HAART."

## medical monitoring

## Resistance testing possible with low viral load

Currently, an HIV viral load below 50 copies/ml means that anti-HIV therapy is successful, and resistance is unlikely to emerge. But what happens when your viral load is above 50?

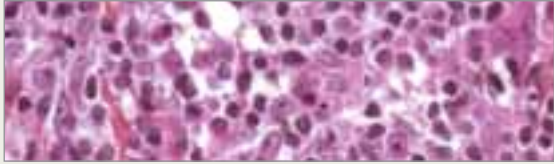
Evidence suggests that continuing on a regimen that is failing to suppress viral load leads to the accumulation of HIV mutations that are not only resistant to the anti-HIV drugs you are currently taking but also possibly cross-resistant to future therapies.

But putting together the most powerful new drug regimen requires knowing which drug-resistant mutations are currently circulating in your body. However, most clinics will only do resistance testing when viral load is above 1000 copies/ml because it is thought that the tests aren't accurate enough with less circulating virus. But waiting until your viral load reaches 1000 means an increased chance of more resistance.

The ideal solution would be to use standard genotypic resistance testing earlier to help provide an accurate assessment of drug resistance even when viral load levels are low, and this is what has been happening at London's Chelsea and Westminster HIV clinic for several years.

Doctors there report that standard genotypic resistance testing is more than 90% successful in individuals with a viral load between 200-1000 copies/ml and say that it should be offered earlier than is currently practised to everyone 'failing' antiretroviral therapy in order to inform a treatment switch sooner and to prevent the possible development of further resistance.

#### latest research



## Use anti-HIV therapy and chemotherapy together for lymphoma

Since the introduction of effective anti-HIV therapy, the prognosis of people diagnosed with lymphoma has improved. However, because HIV-positive individuals are less likely to die of other AIDS-related illness, the proportion of illness and death attributable to non-Hodgkin's lymphoma has actually increased in recent years.

Even though it is known that the use of anti-HIV therapy can lead to a significant improvement in the health and life expectancy of HIV-positive individuals, concerns that it might interact with anti-cancer drugs mean that doctors usually delay initiating antiretroviral treatment until anti-cancer therapy has been completed, or interrupt HIV treatment for the duration of chemotherapy.

But according to a new German study using anti-HIV therapy and chemotherapy together is safe and effective, leading to an HIV-positive non-Hodgkin's lymphoma survival rate that was comparable to that of HIV-negative individuals treated with chemotherapy alone.

The study found that HIV-positive individuals who had not experienced severe immune damage experienced the most benefit from simultaneous antiretroviral therapy and chemotherapy, and that the toxicity of chemotherapy was assessed as "moderate" by the investigators.

#### latest research

## Is boosted atazanavir better than *Kaletra*?

According to results from a study conducted by atazanavir's manufacturer Bristol Myers Squibb atazanavir (*Reyataz*) boosted with low dose ritonavir is as effective as *Kaletra* (lopinavir/ritonavir) at suppressing viral load over two years in treatment-experienced individuals, when combined with tenofovir (*Viread*) and a third drug. The study also suggests that people taking atazanavir are less likely to experience diarrhoea than those taking *Kaletra* and that atazanavir-treated individuals may have an improvement in their blood fats, whereas those on *Kaletra* may experience a worsening of their lipid profile. Nevertheless, rates of "severe" side-effects were similar on both drugs. As expected, jaundice and increases in bilirubin were associated with atazanavir treatment, although nobody stopped treatment because of this side-effect.

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#### Is boosted atazanavir better than Kaletra?

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# helping yourself

*now there's a practical way to improve your quality of life, by Edwin J Bernard*

If you read *AIDS Treatment Update* regularly, hopefully you'll have acquired a lot of information about how to live well with HIV. In fact, all of NAM's resources aim to help anyone living with HIV to take more control over the various factors that affect HIV-positive health. This is known as self-management, and includes everything from exercising regularly and eating well, to choosing and adhering to anti-HIV medicines and coping with their side-effects.

Everybody has self-management skills, but our abilities can change at different times in our lives. Living with HIV is a roller coaster: there are times of calm and times of crisis, and there will be times when you're feeling overwhelmed, or under-confident, about dealing with all the fears and frustrations that are part of with living with HIV. To improve your overall quality of life you might need to learn (or be reminded of) some skills about how to best help yourself.

Chronic illness self-management was pioneered in the 1970s by Kate Lorig, now a Professor of Medicine at California's Stanford University, who devised the model widely used today. Although her original programme focused on living with arthritis it was later developed to include people living with all kinds of chronic health conditions and championed by the Long Term Medical Conditions Alliance (LMCA) in the UK. In 2001, self-management was taken up by the government as the centrepiece of the NHS's 'patient power' approach to chronic illness management. Renamed the Expert Patients Programme (EPP), the NHS now funds and runs a six week training programme specifically designed to help people living with chronic conditions to become equal partners with their health professionals, and develop skills which would enable them to take greater control over their own illness.

Although people living with HIV can participate in the EPP, which is available throughout England and Wales, the six week EPP course is not specific to HIV. There are strong arguments for an HIV-specific course, however, since HIV is different from most other chronic conditions because it is transmissible and because it often affects marginalised members of society. Given the stigma that surrounds HIV, meeting in a safe space to learn about HIV-specific issues, like anti-HIV medicines, sex and disclosure, may be what's needed to included everyone with HIV who would like to learn about improving their quality of life.

Now there is such a course: the Positive Self-Management Programme (PSMP), an American programme devised at Stanford University, has been adapted for the UK and promoted by a small group of passionate individuals and organisations independent of the EPP. Spread over seven weekly sessions of two-and-half hours, the PSMP covers a wealth of empowering subjects, including practical advice on diet, exercise, and coping with depression, difficult emotions, fatigue and side-effects. The course helps participants find their own ways of dealing with these and other issues – such as collaborating with their healthcare team – by focusing on problem-solving, goal-setting and making future plans.

*ATU* spoke with Ian Hayes, who has been involved with self-management for the last eight years, and has been working with others to promote the PSMP in the UK.

## **Ian, how did you get to be involved with the Positive Self-Management Programme?**

I was born with haemophilia, contracted HIV and hepatitis C roughly 25 years ago, and was diagnosed with HIV 21 years ago. I was a finance director for the NHS until I was medically retired in the mid-1990s. Before I got sick I had tried my very best to ignore my conditions, drinking heavily and abusing drugs, and whenever I could I avoided using all



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the services available to help me. Then, when the new combination therapies saved my life in 1998, although I felt physically better, my quality of life was very poor. I felt I'd lost most of 'me' and my ability and confidence to make decisions about anything. I wasn't well enough to go back into the very pressured work environment I'd been in, so I started to do some volunteering for the Living with Long-term Illness Project (LILL) which was the UK's first attempt to look at chronic illness self-management. The medication, my subsequent joint replacement and the self-management came together and recatalyzed my life. It was a brilliant start to a process of change for me. And as self-management really took off in this country, I was involved the early stages of the development of the EPP, and worked with a really inspiring group of enthusiasts to bring the PSMP to the UK. This has been deeply rewarding for me and has been invaluable in helping me come to terms with my own life with HIV.

### Who is the PSMP for?

The programme works equally well for people relatively newly diagnosed with HIV as well as long-term survivors. It gives newly diagnosed people the confidence and skills to cope, and those who are already living well with HIV a chance to reassess the way they are living. It can work if you can't read; it can work if your grasp of the language is poor; it can work if you come from different cultures. It works for gay men and heterosexuals, for people of all ethnicities and belief systems, because

it's rooted in what we have in common, rather than on our differences.

### What can people learn?

The most important things that happen in the course are about teaching skills and attitudes, getting people to think about solving problems for themselves, rather than being spoon-fed by professionals. The whole thing is designed towards building confidence, rebuilding the belief that you can affect change in respect of your own health, but also affect change in respect to aspects of your own life.

### What's the difference between the EPP and the PSMP?

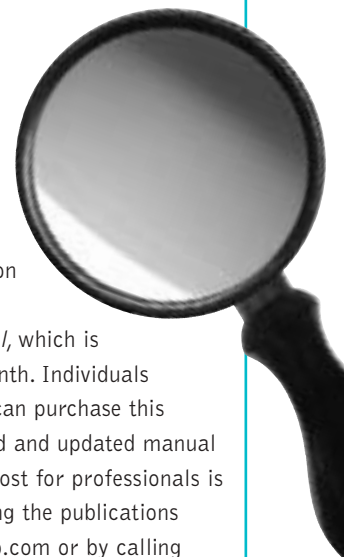
The PSMP is held in an environment that is safe and confidential for people with HIV, and also tailored specifically for us. It lasts a week longer than the EPP, and that extra time allows for more information on HIV medication, sex, intimacy and disclosure. Unlike the EPP, the PSMP is run with course leaders who themselves are living with HIV. Until now, the PSMP has developed on a piecemeal basis, where it's only really been available in London and Manchester. But recently, people who've been involved with the PSMP came together to see if it's possible to set up a national network with help and support from the EPP. We want to ensure that the PSMP is made available to as many HIV-positive people as possible in this country. If you're interested in taking part, or developing programmes where you live, please let me know!

### further information

You can access the Positive Self-Management Programme by contacting these organisations:

- Living Well, London ([www.livingwelluk.com](http://www.livingwelluk.com)). For people who attend an HIV treatment centre or live/work in the following London boroughs: Hammersmith & Fulham; Ealing; Hounslow; Hillingdon; Brent & Harrow; Westminster; Redbridge; and Waltham Forest.
- Positive Place, London ([www.thepositiveplace.org.uk](http://www.thepositiveplace.org.uk)). For people who attend an HIV treatment centre or live/work in south London.
- Body Positive North West, Manchester ([www.bpnw.org.uk](http://www.bpnw.org.uk)). For people who live in the north west of England.
- Contact Ian Hayes directly ([mail@ianhayes.com](mailto:mail@ianhayes.com)) if you are interested in participating and don't live in the regions above.
- Alternatively, the Expert Patients Programme runs non-HIV-specific courses throughout England and Wales, and also on-line. For more information visit: [www.expertpatients.nhs.uk](http://www.expertpatients.nhs.uk)

Ian Hayes has written a chapter on self-management in the latest edition of NAM's *AIDS Reference Manual*, which is published this month. Individuals affected by HIV can purchase this completely revised and updated manual for £12.95 (the cost for professionals is £54.95) by visiting the publications centre at [aidsmap.com](http://aidsmap.com) or by calling NAM on 020 7840 0050.



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## Where to find out more about HIV

### ■ Find out more about HIV treatment:

NAM's factsheets, booklets, directories and website, keep you up to date about key topics, and are designed to help you make your healthcare and HIV treatment decisions. Contact NAM to find out more and order your copies.

### ■ Information events in London

On the last Monday of every month, an expert speaker discusses an HIV treatment related topic. Entry is free. The next topic is 'Side-effects', and will be held on 24th April 2006. For more details, go to [www.aidsmap.com/forums](http://www.aidsmap.com/forums).

### ■ [www.aidsmap.com](http://www.aidsmap.com)

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# there's a life outside your clinic

the hiv & aids reference manual contains everything you need to know about the social aspects of living with hiv

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- Disability and Discrimination Act
- The criminalisation of HIV transmission
- Immigration, asylum and HIV
- Vaccines
- The transmission of drug resistance virus



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