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www.aidsmap.com
issue 168 july 2007

aids treatment update



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Even before the nelfinavir recall, it was clear that life with HIV brings with it all kinds of anxieties - from concerns about side-effects, illness and life-expectancy to worries about the effects of stigma, discrimination, and the criminalisation of transmission.

The discovery that a potentially cancer-causing substance has contaminated some batches of an - admittedly infrequently prescribed - anti-HIV drug may have somewhat dented our confidence in the safety of anti-HIV drugs. Certainly, there are some people who believe all anti-HIV drugs are toxic, and who refuse to take them despite substantial, well-documented evidence that they are far less harmful than untreated HIV.

However, learning to adjust to life with HIV means learning to understand the risk/benefit trade-off. Sometimes that's harder than we expect. I hope that for the 550 people (and tens of thousands worldwide) affected by the nelfinavir recall, Roche can determine exactly which batches have and have not been contaminated and set at least some minds at rest.

This month, we take a long hard look at another anti-HIV drug creating anxiety - efavirenz - as well as mental health in general. Both articles highlight the need for a proactive approach by doctors and patients to reduce anxiety and/or treat depression, no matter what the cause.

page 3 In this month's *Upfront*, we examine last month's unprecedented recall by drug giant Roche of their protease inhibitor nelfinavir (*Viracept*) due to the discovery that some batches of the drug had been contaminated with a potentially gene-changing, cancer-causing chemical.

page 4 The powerful anti-HIV drug efavirenz has a unique set of psycho-neurological side-effects that impacts upon how we perceive and tolerate it. In *The psychology of Sustiva*, Gus Cairns reviews what we know, and what we don't, about efavirenz and its psychological side-effects.

page 8 Those of us living with HIV are likely to have difficulties with mental health problems like depression and anxiety at some point in our lives. In *Understanding depression*, psychiatry and psychotherapy expert, Dr Pepe Catalan, explains how to recognise when it's time to ask for help.

page 12 In *News in Brief* we discover that two more studies conclude that starting anti-HIV therapy before CD4 counts drop below 350 cells/mm³ provides the best possible outcome; that an alternative to *New-Fill* is safe and effective; and that some HIV-positive non-smokers may have an increased risk of lung cancer.

page 14 With this month's *ATU* you'll find the *What do you need?* survey. Peter Keogh of Sigma Research explains why filling it in is an especially important opportunity to help others understand the needs of people living with HIV.



aids treatment update

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sub-editing & proofreading Anu Liisanantti
production Anu Liisanantti
printing Cambrian Printers
ISSN 0969-4706
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charity number 1011220

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nelfinavir recall latest

by Edwin J Bernard

Last month's recall by drug giant Roche of their protease inhibitor nelfinavir (*Viracept*) due to the discovery that some batches of the drug had been contaminated with a potentially gene-changing, cancer-causing chemical is unprecedented in the history of HIV treatments. Hopefully by now, everyone in the UK and the rest of Europe who had been taking nelfinavir has now safely switched to another regimen.

Unprecedented situation

The unprecedented recall affects about 45,000 people worldwide other than the United States, Canada and Japan (where Pfizer manufactures its own, slightly different, version). Although the need for a sudden switch is stressful and worrying for everyone, the situation is much more desperate for people in less developed nations where alternative regimens are not easily obtainable. Although a Roche spokesperson told ATU that they were "working closely with the [organisations] that supply medications to these countries" in an attempt to deal with what was described as "a very difficult situation", this has been complicated by the temporary suspension of nelfinavir's licence by the European Medicines Agency (EMA) two weeks after the recall. Obtaining stocks from Pfizer is not simple either, due to EMA regulations. "The Pfizer formulations of *Viracept* are not registered [in the EU and] we cannot simply buy the stock for other countries and distribute it," says the spokesperson.

Human error

The recall was prompted after Roche received reports that the drug had an unusual smell; six patients from at least two different countries (France and Spain) made the complaint within a week of each other, with two experiencing nausea. Roche tested these samples and some were found to contain abnormally high levels of ethyl mesylate, a substance that may cause cancer, or if taken during pregnancy, lead to genetic changes in an unborn child. The contamination was tracked down to the Roche manufacturing plant in Switzerland, where says another Roche spokesperson "human error during standard maintenance of the production line at the end of 2006" produced a reaction between the drug and ethanol-based cleaning products, resulting in higher than normal levels of ethyl mesylate.

Assessing the risk

According to Dr Dilruwan Chaminda Herath, Roche UK's Associate Head of Medical Affairs, ethyl mesylate is a normal by-product of nelfinavir's manufacturing process that is allowed to be present in extremely low quantities (less than three parts per million). The investigation of the initial samples found levels which, according to Dr Herath, in the "worse case reached 2,300 parts per million." Roche initially calculated that these "would be 100 fold less than was found to cause tumours in rats." However, studies on the long-term risk of ethyl mesylate and in rats.

Roche has now been asked by the EMA to conduct new studies in animals in order to calculate toxic levels of ethyl mesylate more precisely. Preliminary results from these studies should be available by the end of the year. Roche has also since discovered that although the highest level of contamination was seen in the batches of nelfinavir released after March 2007, some lower level contamination had also taken place before that date. Roche is now attempting to identify exactly which batches were affected, so that individuals who have taken potentially contaminated nelfinavir can be traced, identified and followed-up. The EMA has requested that Roche arrange for the close monitoring of everyone who may have been exposed to the medicine made from highly contaminated batches, as well as women who took the medicine during pregnancy and children who have taken nelfinavir at any time or were exposed to it in the womb.

The end of nelfinavir?

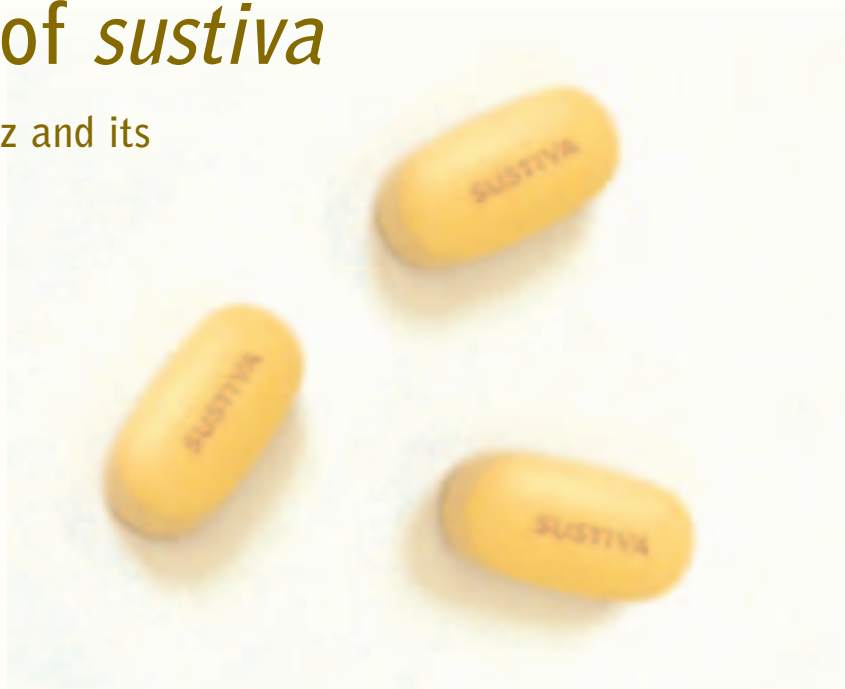
Doctors and patient advocates alike contacted by ATU believe that nelfinavir is unlikely to be used again in the UK, since few patients were taking it and all will now have switched to other drugs, most usually *Kaletra*. It is also currently unclear if, or when, the EMA will lift the suspension of nelfinavir's licence.

For the latest updates on the nelfinavir recall, visit www.aidsmap.com



the psychology of *sustiva*

what we know about efavirenz and its psychological side-effects,
by Gus Cairns



Even before the non-nucleoside (NNRTI) anti-HIV drug, efavirenz (*Sustiva*), was licensed in the EU, in June 1999, it was hailed by HIV treatment experts as "a major advance in the treatment of HIV infection."¹ UK, US and international treatment guidelines have recommended it as a first-line treatment option ever since, and it is now the most frequently prescribed first-line anti-HIV drug (of all the NNRTIs or PIs) in the UK. Efavirenz will soon be available combined with tenofovir/FTC (*Truvada*) as a component of *Atripla*, the first one pill, once daily anti-HIV combination.

There's no denying that efavirenz is a very powerful anti-HIV drug. In its registration trial, DMP006², 60% of participants on efavirenz (plus two nucleoside 'backbone' drugs) achieved viral loads below 50 copies/ml compared with 40% on the (unboosted) PI, indinavir (*Crixivan*) plus two nucleosides after 48 weeks. Since then, regimens containing the drug have consistently outperformed other drugs in head-to-head comparison trials. Most recently - and surprisingly - the ACTG 5142 study³ found that after almost two years, 89% of participants on an efavirenz-based regimen maintained viral loads under 50 copies/ml compared with 77% on a regimen based on lopinavir/r (*Kaletra*).

But, like all anti-HIV drugs, efavirenz is not perfect. Like the only other EU-licensed NNRTI, nevirapine (*Viramune*), HIV can become resistant to it relatively easily if more than a few doses a month are missed. And, like

nevirapine, efavirenz can cause a rash during the first few weeks of therapy - although it rarely causes the severe skin reactions sometimes seen with nevirapine, and it is not associated with the severe liver toxicity seen in some people starting nevirapine (notably those with higher CD4 counts). This is the main reason why efavirenz is the NNRTI recommended by the British HIV Association's treatment guidelines for first-line use. In short, doctors feel more comfortable with it.

Trippy and groggy

But some people on efavirenz don't feel quite so comfortable. Efavirenz has a unique set of psycho-neurological side-effects that are very rarely fatal or physically dangerous but which may impact so significantly on a person's quality of life that they can't be tolerated. These can include dizziness; headache; confusion; lack of concentration; depersonalisation (a sense of unreality); insomnia; abnormal or vivid dreams; and what one

questionnaire called 'hangover-type drowsiness' and 'cognitive dissonance' (a sense that one's thoughts are not one's own).

"When I started efavirenz," says Jimmy, an HIV-positive man, "I had the usual array of psychedelia associated with it - a 'stoned' feeling, incredibly vivid dreams - but it didn't particularly bother me for the first 18 months. If anything, it was quite fun! I took it late at night, so it was just a matter of being slightly 'stoned' before bed, and a little groggy in the morning. However, the effects began to accumulate, and I found that it made me increasingly more groggy. Eventually I was unable to think clearly or even communicate properly before noon. I was looking to go back to work at that point, so after about two years on efavirenz, I switched to nevirapine and have had no problems for the last four years."

Efavirenz's psychoactive effects were no big surprise. In the first year of the three-year DMP006 study, 53% of participants taking efavirenz experienced some kind of psycho-neurological side-effects compared with 23% not taking the drug. However, although 40% experienced these effects in the first month and 22% in the second, by the end of the first year only 7% still reported them at any one visit, and by the end of the second year this fell to only 2%. Since only six of 851 participants discontinued efavirenz directly due to these central nervous system (CNS) side-effects, the study's authors concluded that most of efavirenz's CNS side-effects were transient and tolerable.

'Real world' experience, however, has often differed from these early conclusions. "I think the clinical trials have underestimated the CNS disturbance most of us see in practice," says Dr Martin Fisher, HIV/GUM consultant at Brighton and Sussex University Hospital.

In fact, a closer look at the evidence reveals that, even in the registration

study, efavirenz's CNS side-effects didn't go away entirely with time. During year two of the DMP006 study, the frequency of *new onset* psychological problems was 13% for patients on efavirenz compared with 11% on indinavir, and in year three, 10% for patients on efavirenz compared with 4% on indinavir.

"There are two questions, really," notes Dr Fisher. "Do initial side-effects persist? Or do they develop over time? A minority of patients report persisting side-effects, while in another minority they apparently develop after some time - although in the latter case patients may have been soldiering on thinking they had depression when efavirenz was the cause of their symptoms all along. I've had a number of patients who've switched from efavirenz after several years on the drug and have come back saying 'Blimey, what a difference!'"

Brad, another HIV-positive man, didn't have such an understanding doctor, however. "For me the side-effects remained as long as I stayed on efavirenz," he says. "The main issue was the vivid dreams, which were so strong as to wake me up frequently during what should have been a good night's sleep. This was manageable as long as I worked part-time. As soon as I started full-time work, it became far more difficult to deal with. I could not cope with both the disturbed sleep and the busy workload. My doctor seemed to think that because I told him that I couldn't cope with it any more that my symptoms were getting worse - and his opinion was that this couldn't happen with this drug. However, I wasn't saying that things were getting any worse, rather my life was changing and that the pre-existing side-effects of efavirenz were no longer compatible with my new life. I eventually changed over to nevirapine."

Is it me, HIV or the drug?

As Dr Fisher notes, some people are unable to tell the difference between depression and efavirenz's side-effects. Rates of psychological distress are very high in people with HIV. One large US

study⁴ found that more than one in three HIV-positive people experienced depression and about one in six experienced generalised anxiety disorder. Another study found that three out of every four HIV-positive people had experienced sleep problems at some time.⁵

HIV itself may play a role, too: one recent study⁶ found that a small minority of HIV-positive people may have the mild brain impairment known as Mild Cognitive and Motor Disorder (MCDC); symptoms include impaired concentration and 'psychomotor slowing' - a kind of mild unsteadiness and clumsiness, which appear very much like some of efavirenz's side-effects.

Efavirenz, then, can mimic the effects of both living with HIV and of HIV itself, and both doctors and their patients may assume that there's something wrong with them when, in fact their problems may be due to, or being made worse by, their medication.

How common are the side-effects?

Prospective cohort studies, where groups of patients are followed in the real world (where it is more difficult to infer causality) have either concluded that CNS toxicity rates for efavirenz are higher than initially reported in

“ I would say that between five and ten percent of my patients on efavirenz get significant problems, depending on whether you wait for them to self-report or proactively ask about side-effects. ”

Dr Martin Fisher

clinical trials or have reported that CNS toxicity declines only slowly over time, if at all. In one study of patients at London's Royal Free Hospital⁷ 37% stopped efavirenz within two years of starting it, and of those, 13% did so explicitly because of CNS symptoms - almost one in twenty of the whole patient group.

This fits in with the real world experience of Dr Fisher. "I would say that between five and ten percent of my patients on efavirenz get significant problems, depending on whether you wait for them to self-report or proactively ask about side-effects," he notes.

Rates differ in different studies, however, because 'CNS side-effects' can have very different definitions. One Spanish study⁸ of HIV-positive patients without previously diagnosed psychiatric illness found just over half of the people on efavirenz for at least a year had some symptoms of neuro-psychiatric disorder compared with one in four taking a PI. However, symptoms could include any one of "dizziness, sadness, mood changes, irritability, lightheadedness, nervousness, poor concentration, disturbed dreams and sleepiness". Nevertheless, in line with other studies, efavirenz appeared to roughly double the frequency of any of the symptoms compared to a PI.

When it comes to more serious problems, a US study⁹ looked specifically at neuropsychiatric problems associated with efavirenz in people with pre-existing psychiatric illness. Of 1600 participants randomly selected from those attending the clinic at New York's Presbyterian Hospital, 400 had already been prescribed efavirenz by January 1999, testifying to its popularity (the drug was licensed in 1998 in the USA).

Of those taking efavirenz, 58% had a pre-existing psychiatric disorder; 56% had substance abuse or dependence, and 38% had both. Almost half developed a new psychiatric side-effect on efavirenz: most commonly, depression (48%), vivid dreams, (22%), anxiety (9%) and insomnia

(7%). Although 4% developed suicidal feelings and 2% developed auditory hallucinations fewer than one in 16 stopped efavirenz due to these side-effects. There were no suicides, attempted suicides, violence or psychiatric hospitalisations in patients on efavirenz, even in the people who stopped due to the side-effects.

Side-effects and drug levels

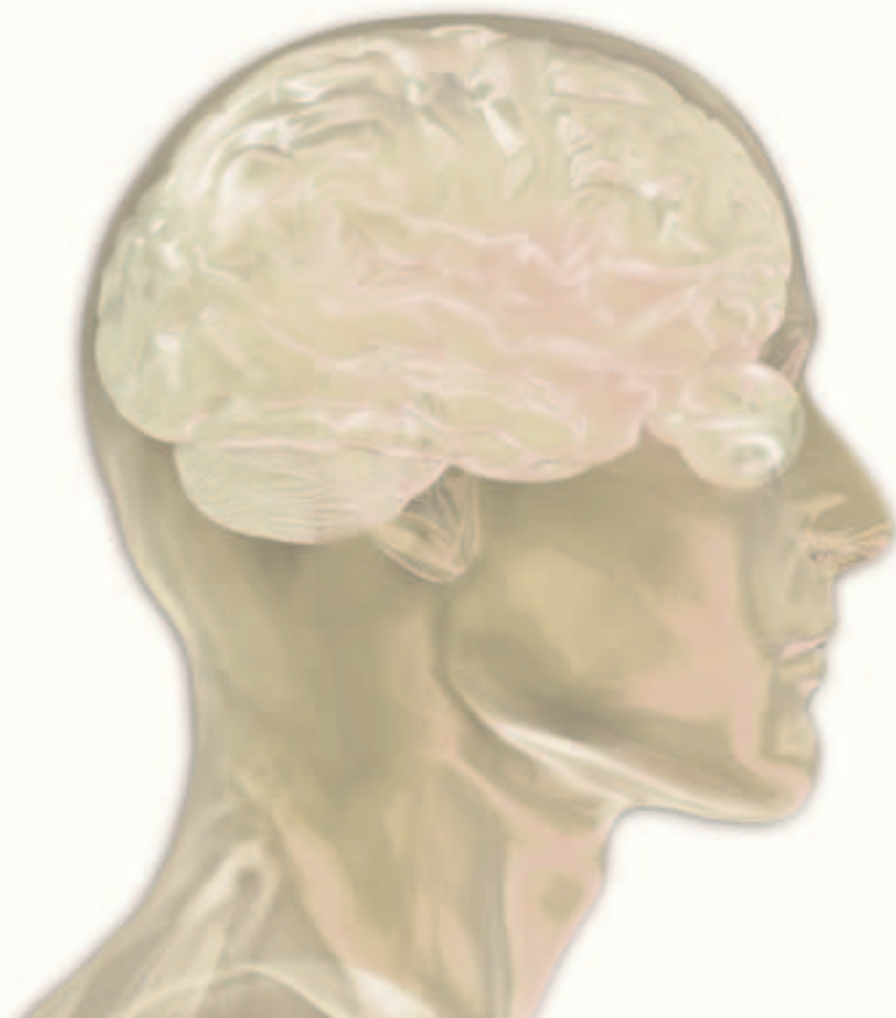
Whilst there have been case reports of extreme reactions to efavirenz, many of these have been linked to extremely high levels of the drug. Efavirenz has the longest half-life of any of the licensed HIV drugs, taking at least two days for its plasma level to halve after a single dose.

There is some evidence that liver disease¹⁰ or drug interactions¹¹ may cause a build-up of the drug in the bodies of individuals taking a normal daily dose. A small Spanish study¹² found that average blood concentrations of efavirenz in people who experienced CNS side-effects were up to three times higher than those who did not; indeed, blood efavirenz

levels were the only significant predictor of CNS side-effects.

Black Africans may be particularly prone to developing high levels of the drug. Efavirenz is eliminated by the liver enzyme, CYP2B6. A mutation at position 516 of the gene for this enzyme is known to produce much slower elimination of efavirenz from the body. A US study¹³ found that 20% of African Americans but only 3% of European Americans had this mutation and a small UK study¹⁴ found that efavirenz lingered in the blood of African women for much longer than in European men.

Dr Fisher isn't sure how relevant this is for what is seen in the clinic, however. "Yes, CNS side-effects may be related to drug levels, but I see side-effects in people without high levels, and high levels in people without side-effects. Cultural issues may be important. Africans may experience worse effects but may also be more stoic or more reticent to talk about them. And European gay men may be more predisposed to anxiety and depression,



or more likely to tell their doctor about their symptoms."

Switching and treating

If his patients need to switch from efavirenz to another anti-HIV drug, Dr Fisher prefers the boosted protease inhibitor *Kaletra* "since by the time most of my patients want to switch, their CD4 counts are above the threshold where it's safe to start nevirapine from new (400 cells/mm³ for men and 250 cell/mm³ for women), and we don't have enough data on whether it's safer at these levels if you've already taken efavirenz."

If you can't, or don't want to, switch from efavirenz, although there's little research specifically into medication for efavirenz's side-effects, there are good data on the treatment of depression in HIV-positive people which suggest a 65-90% response rate to antidepressants including fluoxetine, sertraline, and imipramine, compared with a 23-47% response to an inactive lookalike pill^{15,16}. However, many of these drugs can have side-effects of their own.

What causes it?

Very little is clear about what causes the CNS side-effects associated with efavirenz, but there are two theories. One is that efavirenz primarily disturbs the part of the brain that controls both dreaming (REM) and deep (slow-wave) sleep. The vivid dreams and insomnia are the primary side-effect; the depression, irritability and lack of concentration are thought to be caused by accumulated sleep deprivation. This echoes Brad's experience that "I regularly woke up feeling that I had had a 'hard' night's sleep".

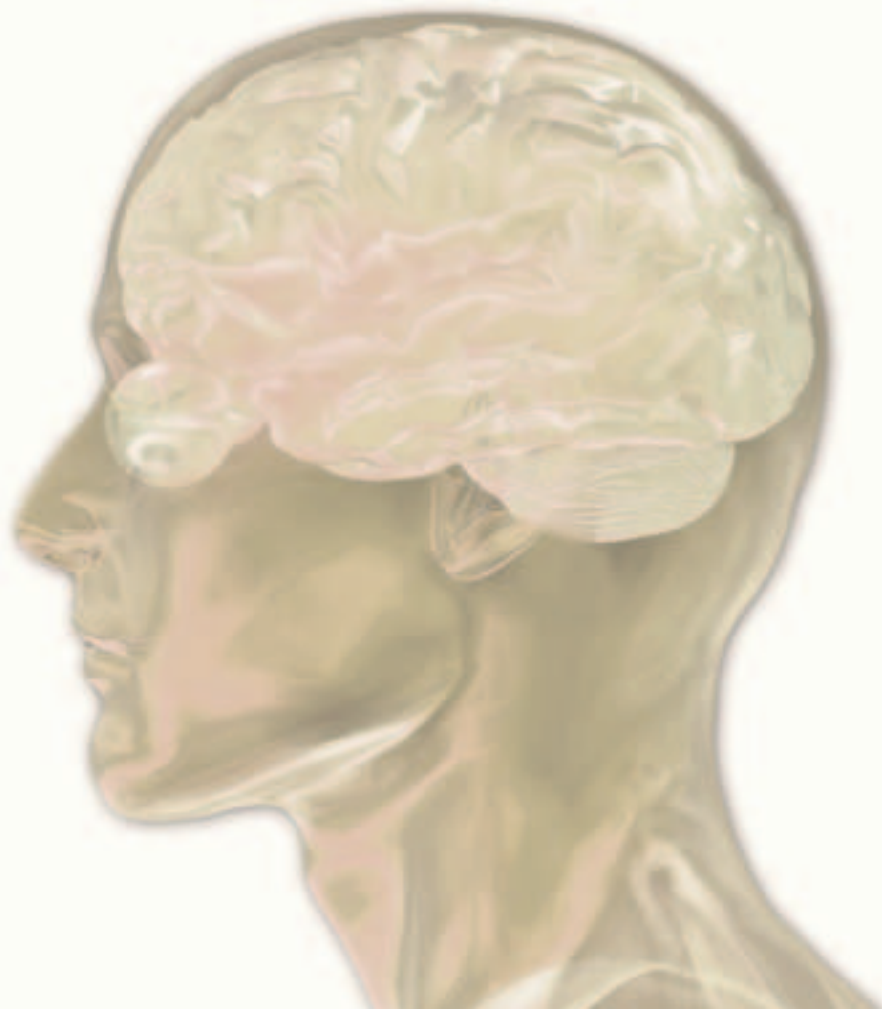
A small Spanish study¹⁷ supports this idea. It recruited 18 HIV-positive people taking efavirenz and compared them with their HIV-negative counterparts. It found that the people taking efavirenz only had 80% of the sleep of their counterparts; and spent less time in REM sleep and slow-wave sleep. In addition, poor sleepers had, on average, 75% more efavirenz in their blood compared with good sleepers - 4.3mcg/ml versus 2.5mcg/ml.

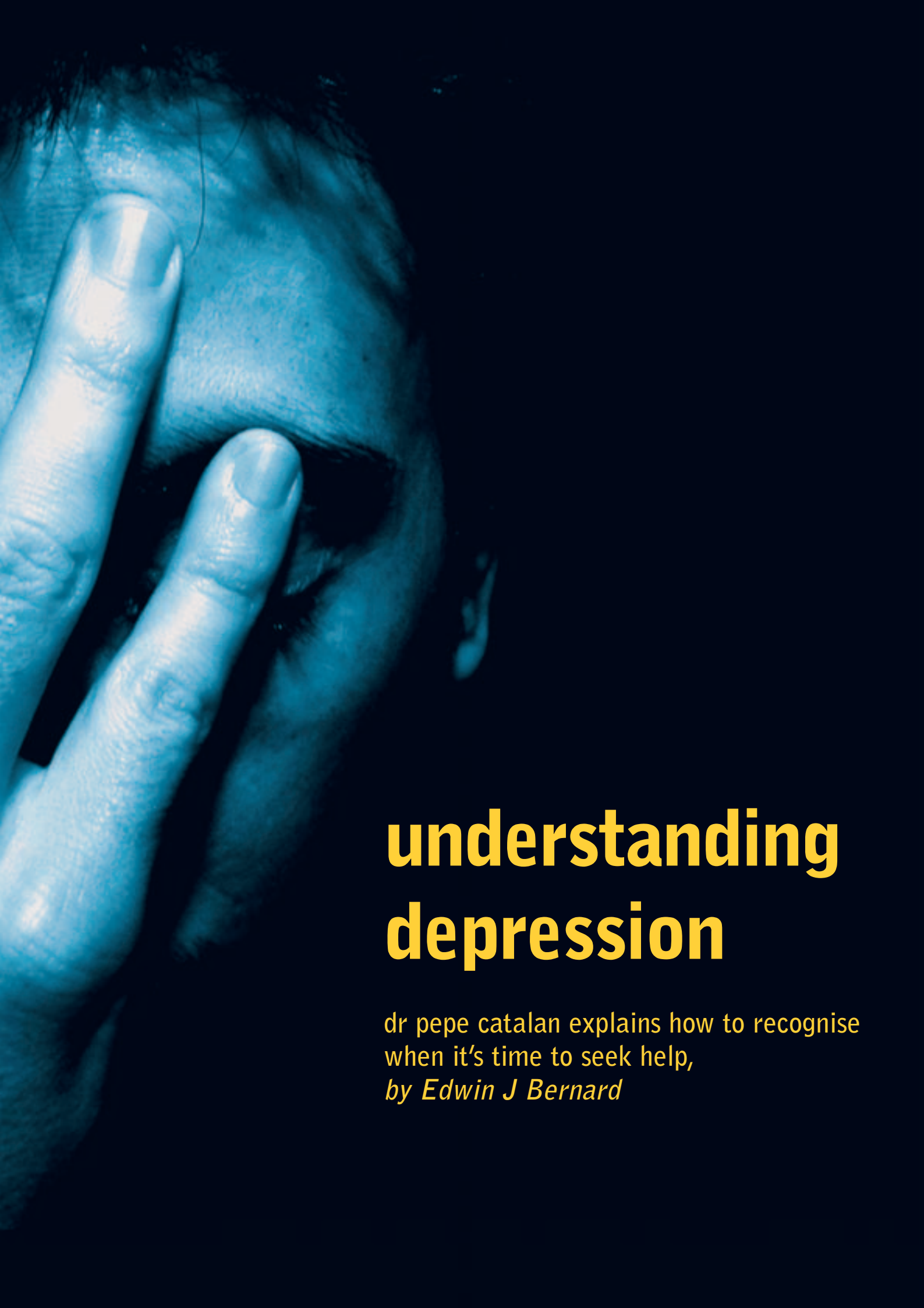
The second theory is that efavirenz is causing the immune system to produce too many pro-inflammatory chemicals, known as cytokines, which can cause depressive symptoms. Efavirenz may have direct cytokine-stimulating effects, or its potency may allow the body to mount a more sustained cytokine attack on HIV and especially on HIV-infected brain cells.

Although no studies have been undertaken in people, a study in rats supports this theory. It found that their cytokine levels increased, and they had 'depression-like behaviour' when they were given efavirenz. Cytokine levels dropped and their depression improved when they were given the antidepressant paroxetine.¹⁸ If depressive symptoms are somehow linked to the potency of anti-HIV drugs, it may also explain why sporadic reports continue to be received that treatment with other anti-HIV drugs are also - albeit less commonly - associated with psychological side-effects. There have been reports from the UK that patients treated with nevirapine developed vivid dreams and, in a few cases, mania.^{19, 20} And at the recent BHIVA Spring Conference there was a report on three individuals who developed psychotic symptoms after taking the PI, atazanavir, which resolved when the drug was stopped.²¹

Focus on quality of life

It's important to remember that many people have no problems with efavirenz and Martin Fisher notes that, like Jimmy, some of his patients "quite like the side-effects." Since all anti-HIV drugs have some side-effects, the issue is to find a combination that you can live with, one that fits in with your lifestyle. If you find that the CNS side-effects don't wear off after a few weeks, or if they impact on your quality of life at a later date, talk to your doctor. Some doctors might still need to be reminded that we have to live with - not just put up with - anti-HIV drugs for the rest of our lives.





understanding depression

dr pepe catalan explains how to recognise
when it's time to seek help,
by Edwin J Bernard

Those of us living with HIV are thought to be at a higher risk of mental health problems, such as depression or anxiety, than our HIV-negative counterparts. This depression or anxiety is frequently the result of, or the reaction to, illness or to problems we had before our HIV diagnosis; however, sometimes no specific cause or factors can be identified.

Someone who knows a lot about the mental health needs of HIV-positive people is Dr Pepe Catalan, consultant psychiatrist at London's Chelsea and Westminster Hospital. Since establishing specialist HIV mental health services at the Chelsea and Westminster in 1989, Dr Catalan has been at the forefront of HIV psychiatry and psychotherapy, achieving an international reputation.

We talked with Dr Catalan about the variety of psychological issues that most HIV-positive people have to deal with at some point in their lives, how to recognise them, and where to go for help.

AIDS Treatment Update (ATU): When, typically, is someone referred to your clinic? Is it during the 'crisis' moments, such as a new HIV diagnosis, or starting or changing anti-HIV treatments, or during other specific times in someone's life?

Dr Pepe Catalan (PC): What's interesting is that, while in the past we used to see people experiencing acute crisis moments, such as a new diagnosis, starting medication, or disease progression, nowadays the people that we mostly see are experiencing more chronic problems - issues from the past that have resurfaced in the present. Before people get to us they've often had to go through many hurdles, many other services in order to get a referral, so they may not be typical of those experiencing problems. But many of the people that get to us tend to be those experiencing persistent, long-term depression, sadness and unhappiness - which can happen at almost any stage of their life with HIV.

However, the numbers of people we are seeing now are greater than ever. In 1990 we had 123 new referrals. Five years later that grew to 306. By 1999, we had 360. And by 2005, we had 406 new referrals. Now, quite clearly, this may well be because there are more people living with diagnosed HIV infection than ever before, but something else may be happening too.

You see, the issues that we are dealing with today are very different from those we dealt with in the past. What's very striking is that the diagnosis of chronic depression has increased very substantially. In 1990, just 17% of our referrals were thought to be suffering from depression. In 2005, 40% of referrals - 162 people - were thought to be dealing with chronic depression. Anxiety, too, has increased from 3% in 1990, to 12% in 2005. So, too, has the issue of sexual dysfunction: we had one person in 1990 and in 2005 57 were referred to our clinic, which is more than one a week.

On the other hand, 'adjustment disorder' - being very distressed by an

HIV diagnosis - has fallen dramatically, from 27% in 1990, to 13% in 2005. And HIV-related brain syndromes - such as mania or dementia - are hardly ever seen now.

ATU: You said that depression might happen at any stage in an HIV-positive person's life. Are there any specific triggers that people can watch out for?

PC: Obviously, the longer you are living with HIV, the greater your chances of experiencing depression. We tend to see two different types of HIV-positive people here, and the person who is more likely to suffer from chronic depression is someone who was diagnosed before effective treatments, before 1995. This would be the kind of person who gave up their work or career because they thought they were going to die soon, because that was the expectation that they had at the time. They are now experiencing a sort of 'existential angst', trying to make sense of their life. People who have been diagnosed more recently tend to have different issues - often issues that predated their HIV diagnosis - but fewer are suffering from long-term, chronic depression.

ATU: How do you help people who are trying to make sense of their life with HIV?

PC: We all have to find meaning in our life, in all kinds of ways. Some find it easier than others. Mental health intervention may have a role if someone has a number of troubling experiences to process and needs to solve these issues in order to move forward. But I think quite often it's more about social change, engaging with people, and taking part in activities that engage you, whether it's about going back to college, or doing voluntary work or paid work. We often see quite a change in people who had very conventional jobs before their diagnosis, who, by exploring all kinds of options and finding activities that engage them, move into more creative things that they had wondered about, but never took up. We see people go back to college, or take up photography or creative writing, things they'd always

wanted to do, but which they previously had considered to be, perhaps, too frivolous or too selfish. Fulfilling past dreams is often just what people need in order to have a sense of direction and a purpose.

ATU: We know that the people most at risk of HIV are people who are already at a higher risk of mental health problems. How important is it to know which came first?

PC: Although we find that HIV often is a trigger, it's not always the main problem: often HIV-positive people have all types of unresolved issues. So we tend to look at the whole picture, and we don't assume that it's all 'just' HIV. So, in a way it doesn't matter; as long as we can identify the problem, we can work on helping the person.

ATU: How can an individual determine whether the main cause of their problem is unresolved issues from the past; the effects of HIV itself on the brain; or anti-HIV drug side-effects, particularly, problems with efavirenz (*Sustiva*)?

PC: First of all, today the question of whether HIV is doing something to the brain is much less of an issue. However, I think the issue of treatment side-effects is much more relevant; some people feel very strongly that their medication is doing things to them, and I am sure many are right.

ATU: How, then, can someone tell if they're really depressed or not and if it's serious enough to ask for help?

PC: We all have bad days where we feel down. But depression at a psychiatric level has to be much more persistent than that - usually something which lasts at least four weeks. So, you are probably depressed if:

- You are experiencing a low mood that is not responsive to good news or to cheery events.
- You feel a lack of hope, and think that things aren't ever going to get any better
- You don't enjoy the things that used to cheer you up and give you pleasure.

When sadness, loss of hope and loss of enjoyment happens every day - whether it comes out of the blue or it has very obvious cause - that's when you should seek some help. Then the whole question of antidepressant medication and/or psychological interventions can be considered.

ATU: Is it still possible to be depressed and not realise it?

PC: I think that if you also rely on what people around you are telling you, then that should help you understand what is happening to you. If you aren't spending time with the people you usually spend time with; or if people close to you tell you that you've changed in some way - become grumpy or difficult - or if you find you're falling out with your friends all of a sudden. You don't necessarily have to be sad or tearful to be suffering from depression: being grumpy and isolated and not engaged in life are also symptoms. So clearly, what others say would be an important factor in understanding your symptoms.

ATU: Some people might react to those feelings by 'self-medicating' with alcohol, recreational drugs, or even sex, rather than seeking outside help. When can self-medication cross the line from being something that helps you cope to being something that's harmful?

PC: That's sometimes quite difficult to know. Traditionally, someone who drinks too much often says they do so because they're depressed or because they were sexually abused, or for some other reason. Although that may be true, unless you stop the recreational alcohol or drug use you can't tackle those things: it can't work the other way round because it requires some clarity of mind. This is one of the big problems that we see with substance abuse. Drinking, taking drugs, having lots of sex, is part of the culture. For many people, it's part of the joy of life and they can manage it, and it doesn't interfere with their lives. However, you need to address this behaviour when it becomes a habit, a way of coping, a

way to avoid pain, particularly if it no longer masks the pain but instead you pay the price of the side-effects of the alcohol or drugs. You need to ask yourself, 'Am I really helping or hurting myself by escaping with drugs and alcohol?'

ATU: The ultimate escape, of course, is suicide. A recent study from the United States¹ found that one in five HIV-positive individuals had experienced suicidal thoughts in the previous week, although far fewer had actually planned their suicide or would kill themselves. Do those statistics sound realistic to you?

PC: We see many people who get referred to us because of suicidal thoughts, and actually, suicidal thoughts are very common in people with chronic illnesses, including HIV. Whether you should be concerned about them is a question of degree. It may be that occasional suicidal thoughts - where you think about a way out but do not consider acting upon your thoughts - work as a kind of 'safety valve', to help you feel in control of a difficult situation. However, if they become a troubling experience, if they keep coming back to you repeatedly and you begin to think about what you might do, and how you might do it, and it begins to take up a lot of space in your mind, then that's cause for concern and it's worth seeking help. In fact, if these thoughts go on for too long you may begin to feel that there is no point in talking to anybody, so when in doubt, talk to somebody sooner rather than later. If you're beginning to have these thoughts I suggest you talk to your GP, or your HIV clinic health adviser; if your concerns are urgent, then go to A&E.

ATU: You mentioned GPs as a possible first port of call for someone concerned about their mental health. Some HIV-positive individuals still don't have GPs or aren't happy to disclose their status to them - what then?

PC: I think many GPs these days are usually good in terms of recognising mental health problems. However, if you don't have a GP, the doctors and the nurses working in HIV clinics are usually very sensitive to

“ It’s important to remember that there are effective treatments, so you shouldn’t have to suffer in silence, or feel despair about the future. ”

Dr Pepe Catalan

psychological and social issues in general and they should have access to mental health specialists. Of course, there used to be a lot of voluntary organisations that offered specialised HIV counselling services, but the range of services is now shrinking, which is a tragedy.

ATU: Finally, what take-home messages do you have for our readers?

PC: With the extended life expectancy of people with HIV in the UK and elsewhere in the developed world, issues around aging with HIV are likely to become a new and pressing problem. In our clinic we are already seeing a substantial proportion of older people with HIV with psychological and social needs. These needs - as well as the more obvious medical needs - will have to be addressed throughout the developed world.

But clearly we’re seeing the flip side of good news: people are now living longer because anti-HIV treatments are working, and so it is important to keep things in perspective. If you are experiencing symptoms of depression or anxiety - or any other mental health problems - it’s important to remember that there are effective treatments, so you shouldn’t have to suffer in silence, or feel despair about the future. ■

NAM’s booklet, *HIV and mental health*, is available to download from www.aidsmap.com, in the ‘patient information booklets’ area of the ‘treatment & care’ section.

THT Direct (0845 1221 200) can help you access local counselling services provided by THT or other agencies. Alternatively, search the ‘organisations’ area of www.aidsmap.com for ‘counselling’ or ‘mental health services’ in your area.

Samaritans (08457 90 90 90) provides confidential non-judgemental support, 24 hours a day for people experiencing feelings of distress or despair, including those that could lead to suicide.

To find a private short-term counsellor or long-term therapist in your area, use the ‘find a therapist’ searches provided by the British Association for Counselling and Psychotherapy (www.bacp.co.uk) or the United Kingdom Council for Psychotherapy (www.ukcp.org.uk).



starting treatment

Two studies conclude starting treatment much earlier is better

Two more studies have concluded that starting anti-HIV therapy before CD4 counts drop below 350 cells/mm³ provides the best possible outcome, making it even more likely that treatment guidelines will recommend earlier HIV treatment when they are revised later this year.

First, the International Antiretroviral Therapy (ART) Cohort Collaboration revised its calculations regarding the risk of progression to AIDS or death in individuals taking antiretroviral therapy for the first time, using data from over 20,000 individuals. The study looked at progression risk at the time someone starts therapy for the first time, and also after six months of therapy.

Individuals aged under 30 who started anti-HIV therapy with a CD4 cell count above 350 cells/mm³, and a viral load below 100,000 copies/ml, were found to have the lowest risk of five-year progression to AIDS or death. However, individuals who had a good response to anti-HIV therapy (viral load below 500 copies/ml) and were under 50 when they started treatment and who achieved a CD4 cell count higher than 350 cells/mm³

after six months were found to have an even lower risk of five-year progression to AIDS or death.

The study also found that people who injected drugs, were older than 50, and who started with very low CD4 cell counts had the highest risk of AIDS or death after five years.

Meanwhile, the ATHENA study from the Netherlands has found that it is possible to restore CD4 cell counts to 'normal' levels within seven years if individuals begin antiretroviral therapy at CD4 counts above 350 cells/mm³.

In fact, study participants who began treatment with CD4 counts in the 350-500 cells/mm³ range were almost three times as likely to achieve 800 CD4 cells/mm³ (the average 'normal' number of CD4 cells for gay men) within seven years compared to those who started according to current guidelines, at 200-350 cells/mm³.

An accompanying editorial by Canadian treatment expert, Dr Julio Montaner, called for a "broader re-evaluation of the ideal time to start therapy, incorporating outcomes other than survival, such as the level of immune reconstitution".

HIV policy

Campaign launched to stop deportation of HIV-positive failed asylum seekers

The African HIV Policy Network (AHPN) has launched a campaign calling on the UK government to halt the deportation of failed HIV-positive asylum seekers to countries where HIV treatment is not readily available or affordable.

The AHPN campaign, called Destination Unknown, asks people to contact their MP and request that they support an Early Day Motion that "notes that there is a clear contradiction between the UK's policy aim of universal access to treatment for all

those who need it by 2010 and the deportation of people living with HIV who are on treatment to countries where treatment is not readily available or affordable."

Although Early Day Motions have no chance of being debated in the House of Commons, they are used by MPs to bring issues to the attention of the government.

More information about the campaign and the Early Day Motion can be found at: www.ahpn.org/campaigns.



hiv and illness

Increased lung cancer risk found, even in non-smokers

American researchers have found that people with HIV have an increased risk of dying from lung cancer, and they found that these risk couldn't be entirely explained by smoking.

Lung cancer is not considered an AIDS-defining cancer, although there is increasing evidence that the cancer is seen more often in people with HIV. It has been suggested that the increased risk of lung cancer seen in people with HIV is largely because people with HIV are much more likely to smoke.

Researchers from the ALIVE study in Baltimore have now found that HIV-positive injecting drug users were much more likely to die of lung cancer than HIV-negative injecting drug users. Smoking was almost universal in both groups, but smoking alone could not explain the increased risk of lung cancer observed in people with HIV.

People with HIV are more vulnerable to lung disease and the researchers found that those with lung problems such as asthma were more likely to develop lung cancer.

The findings of this study are very similar to those of another American study published earlier this year. It found that people with a prior AIDS diagnosis had an increased risk of lung cancer and that smoking alone couldn't explain this. The researchers in that study speculated that chronic lung disease could cause long-term inflammation that could increase the risk of cancer.

However, both of these studies included people who are already considered to be at the highest end of the risk of disease progression of death. It's not clear whether this risk is increased in people who do not inject drugs, or who have never received an AIDS diagnosis.



side-effects

New-Fill alternative finally studied

The first published study looking at whether *Bio-Alcamid* (polyalkylimide gel) is suitable for treating HIV-related facial wasting has found that it was safe and effective.

Although *Bio-Alcamid* has been promoted by private clinics in the UK for several years as a viable treatment for facial wasting, very little information has been available on its effectiveness in HIV-positive people despite it being used on over 2000 HIV-positive individuals worldwide. In contrast, data have been available on *New-Fill* (polylactic acid) since 2001, leading to its limited availability at some NHS HIV clinics in the UK since 2002, with more widespread use from 2004.

In this small, open-label study from Canada, 31 individuals with moderate-to-severe facial wasting received between one and four injections of *Bio-Alcamid*. No infections, nodules, or other serious events were seen. Side-effects were limited to mild swelling, redness, bruising and pain, and lasted a median of three days. After a year, all participants experienced measurable improvements in quality of life, anxiety and depression.

The results are very similar to early studies of *New-Fill*; however, as of yet there are no reliable long-term comparison studies to see which lasts longer.

hiv treatment

Anti-HIV treatments increase testosterone

Levels of the hormone testosterone increase significantly in men after they start anti-HIV treatment, a US study has found. Increased testosterone levels helped the men gain an average of 1kg of muscle 18 months after starting anti-HIV drugs.

Before starting treatment, only 6% of men in the study had abnormally low levels of testosterone, much lower than the level observed in previous studies, but many of the men in those earlier studies were very unwell and had wasting syndrome.

The researchers found that increases in testosterone were linked to the anti-HIV drugs taken. Men who took AZT (zidovudine, *Retrovir*) with 3TC (lamivudine, *Epivir*) had a greater increase in testosterone than the men who took d4T (stavudine, *Zerit*) with ddI (didanosine, *Videx*). Greater increases were also seen in men who took efavirenz (*Sustiva*) compared to nevirapine (*Viramune*).

The study did not look at any other anti-HIV drugs.

what do you need?

how filling in this survey helps shape the future of hiv services,
by Peter Keogh

Included with this month's *ATU* is a survey about living with HIV, appropriately called 'What do you need?' ('WDYN' for short). Peter Keogh, of Sigma Research - a social research group specialising in all aspects of HIV and sexual health which developed the survey (funded by the Terrence Higgins Trust with the support of the Department of Health) - explains why filling it in is an especially important opportunity to help others understand the needs of people living with HIV.

Who is the WDYN survey for and who wants to see the results?

The survey is for all people living with HIV in the UK. To take part in the survey, you need to be over 16, currently live in the UK and be diagnosed HIV-positive. We're doing the survey for two reasons. First, many services for people with HIV are being withdrawn or are under threat. We want to show the real picture of need among people with HIV in the UK so that existing services can be improved and expanded and new services funded. Second, people with HIV often suffer from discrimination and stigma. By describing this, we can help to reduce the discrimination faced by people with HIV.

What did you learn from the last WDYN survey in 2001 and how did it make a difference?

The last WDYN was the most comprehensive description of the needs of people living with HIV in the UK to date. We found that psycho-social needs predominated. That is, people with HIV were most concerned about their quality of life, such as their

mental, emotional and sexual well-being. Practical concerns (such as money, housing, employment etc.) tended to come second. The survey's results have been used extensively by AIDS organisations to improve their services for people with HIV. It has also been used to make the case for more funding for services. Finally, the data from the survey have been used to fight stigma and discrimination against people with HIV.

Why are you doing another WDYN survey now?

The size and nature of the population of people with HIV has changed dramatically since we carried out the original survey in 2001. Back then, it was predominantly gay and bisexual men. Today, the population of people with HIV has become more diverse, especially as many African women and men with HIV have joined that population. So, the needs of HIV-positive people are likely to have changed and it's time to get a more up-to-date picture of these needs. In addition, highly effective treatments for HIV had arrived quite recently in

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What kind of things are you asking about and will my details be completely anonymous?

The survey covers 20 'key life areas' ranging from how well you sleep, whether you have enough money to live on, what your housing is like, whether you would like more training, whether you are having a good sex life and much more. Although it looks long, the way the survey is designed means it's

quick and easy to fill out (it shouldn't take more than 20 minutes). Your responses will absolutely be anonymous because we do not ask you anything that could identify you (such as your name or where you live). You can fill the survey out in two ways: either by filling in the paper survey included with *ATU*, completing it yourself in confidence and sending it back to us yourself (it's FREEPOST and self-sealing so you don't even need an envelope or a stamp), or you can fill it out online via a link from www.aidsmap.com. We have ensured that we have no means of tracing you or the computer you used to fill out the survey.

When will the results be published?

We have a very quick turnaround time for this survey. In January 2008, we will produce a full report of the findings. In addition, we will publish a shorter (two page) summary of this report. Both are available FREE.

You can order a copy by calling 0207 820 8022 or online at www.sigmaresearch.org.uk.

You will also be able to download the report free as a pdf (Acrobat Reader) document on the same web address. In addition, copies of the final report will be sent to Local Authorities, AIDS service organisations and other key individuals and groups throughout the UK.



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where to find out more about hiv

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- **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 'sexual health' on 30th July 2007. For more details, go to www.aidsmap.com/forums.
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