

aids treatment update

heart disease & fat wasting

First this month a little history. My earliest encounter with lipodystrophy was at an infectious diseases conference in Toronto in 1997. Hidden between the endless lanes of poster presentations was a short collection of case studies, oddities amongst a forest of good news about HAART.

Now the buffalo humps, abdominal paunches and wasted limbs have a conference of their own, and whilst it's a small meeting, it packs quite a punch. This month our coverage concentrates on new information from the Second International Lipodystrophy Workshop, held recently in Toronto. As our lead article describes on page 2, projected estimates of the future risk of heart disease in people taking anti-HIV drugs could have far-reaching implications for the care of people with HIV. Further on, we feature two more unwanted accessories to life with HIV – facial wasting and osteoporosis.

Looking over the responses to our readers survey which have begun to tumble in, it's already clear that many of you want more information on the side-effects of HIV treatments. Mindful of the need to balance bad news with good, our Factsheet this month is about the positive effects of exercise on health and well-being.

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HIV drugs & heart disease

2 anti-HIV treatment can raise the blood fats which contribute to heart disease: how great a risk does this pose to people taking or considering HAART? by keith alcorn

In the past two years concerns have begun to emerge about the long term impact of Highly Active Antiretroviral Therapy (HAART) on the risk of heart disease. Many things, including smoking and genetic factors, contribute to heart disease, but high levels of cholesterol and triglycerides are major culprits, and many people on HAART have experienced big increases in levels of these fats in their blood since starting therapy. Given that HAART is for life, what could these lipid increases mean for life expectancy? And if you are already at risk for heart disease, is the risk great enough for you to delay starting treatment?

Dr Matthias Egger of Bristol University has worked extensively in tracking both HIV disease and coronary heart disease (CHD) in Switzerland and the UK. *AIDS Treatment Update* spoke to him after he posed some difficult questions for the HIV community at the Second International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV, held in Toronto in September.

How do we answer the questions?

In order to establish what the risk might be, it's necessary to look at several questions:

- What is the existing risk of heart disease, and which metabolic changes predict heart disease, in the general population?
- What patterns of metabolic changes occur in people taking HAART?
- Using this information, what can we conclude about the effects of HAART on coronary heart disease risk?

- How do we decide whether heart disease could pose a greater risk than HIV infection for someone considering whether to start or continue treatment?

Matthias Egger presented data on CHD risk in the HIV-negative male population from the Caerphilly Heart Disease study. The factors that predicted the risk of death from heart attacks, or of non-fatal heart attack over 15-20 years of follow-up were as follows:

- Ever smoked: 2.3-fold increased risk compared to non-smokers
- Diabetes: 2.3 fold increased risk
- Triglycerides above 2.0mmol/L (175mg/dL): 1.8-fold increased risk
- High blood pressure (above 140/90): 1.5-fold increased risk
- Cholesterol above 5.2mmol/L (200mg/dL): 1.5-fold increased risk
- Reduced HDL ('good') cholesterol (below 1.0mmol/L): 1.4-fold increased risk

What happens when these figures are compared with metabolic changes on HAART? Matthias Egger used data gathered by Andrew Carr in Sydney to assess the severity of metabolic changes in HAART patients, and used the Caerphilly study to calculate relative risks (how much more likely people with this particular risk factor were to develop CHD). The purpose of this exercise was to create a mathematical model which would predict the



How might metabolic changes due to HAART affect future risk of heart disease?

Cholesterol above 5.5mmol/L?	Triglyceride above 2.0mmol/L?	Impaired glucose tolerance?	Diabetes?	Relative risk of heart disease compared to people of same age without these problems
YES	No	No	No	1.4
No	YES	No	No	1.7
No	No	YES	No	1.3
No	No	No	YES	2.3
YES	YES	No	No	2.0
YES	No	YES	No	1.8
YES	No	No	YES	3.1
No	YES	YES	No	2.1
No	YES	No	YES	3.3
YES	YES	YES	No	2.4
YES	YES	No	YES	3.9

key to table

The table on the left shows Dr Egger’s projected estimates of how metabolic changes might affect future risk of CHD. For example, looking at the first line, Egger estimates that a person taking HAART whose cholesterol rose above 5.5mmol/L, but whose triglycerides did not rise over 2.0mmol/L, and who did not have impaired glucose intolerance or diabetes, would have a 1.4-fold higher risk of CHD than someone of the same age and lifestyle. Remember these are estimates only.

glossary

- antiretroviral**
A substance that acts against retroviruses such as HIV.
- cardiovascular**
Pertaining to the heart and blood vessels.
- CD4**
A molecule on the surface of some cells onto which HIV can bind. The CD4 cell count roughly reflects the state of the immune system.
- cholesterol**
A waxy substance, mostly made by the body and used to produce steroid hormones. Popularly associated with hardening and narrowing of arteries.
- cohort**
A group of people who share at least one common factor (e.g. being HIV-positive) and are studied over a long period of time.

degree to which HAART may add to an individual’s risk of CHD, over and above the influence of age and lifestyle.

A number of different patterns of metabolic changes were seen in the Sydney HIV cohort, and different combinations of anti-HIV drugs have also been linked with different patterns. The results are shown in the table above.

Balancing benefits & risks of HAART

Epidemiologists use two concepts when measuring the potential risks and benefits of a medical intervention. The first is the number of people who need to be treated for one patient to benefit, and the second is the number of people who need to be treated for one patient to be harmed.

For example, 22 women need to be treated with the drug tamoxifen in order to prevent one death from breast cancer, but 97 women

need to be treated with tamoxifen in order to cause one case of endometrial cancer.

Egger used data from the Swiss HIV Cohort which looked at the risk of death after beginning HAART at various CD4 and viral load levels, and compared this with the risk of developing AIDS within three years if HIV infection is left untreated.

“You need to treat only one patient for one death to be prevented where the risk of progression is very high”, said Egger, “but in people with a CD4 count of 350 to 500 and viral load up to 10,000, you would reduce the risk from 2% to 0%, so you would have to treat 50 patients in order to prevent one death. The other 49 [might] get adverse effects, including lipodystrophy.”

So, if the other 49 people in Egger’s example were at risk of developing lipodystrophy, how

HIV drugs & heart disease continued

many would develop metabolic changes? Studies show that anywhere from 20% to 74% of people starting protease inhibitor (PI)-containing HAART will have developed significant lipid increases within a year of starting treatment, and the problem is not restricted to PIs – a study at the Chelsea and Westminster Hospital found that 32% of those who started an efavirenz-containing regimen had raised cholesterol after nine months.

Matthias Egger used data from the Framingham model (a study of heart disease risk in a US town) to calculate the risk of CHD within five years if serious lipid increases occur. The Framingham data is routinely used by doctors to assess the risk of heart disease, but it is important to realise that risk of CHD is not the same in all countries.

- A male smoker aged 50 in the US has a 14% risk of CHD within five years, compared to an 8.3% risk in France. UK levels of risk are broadly similar to those in the US, but the level of risk is likely to be higher in Scotland and Ireland.
- A female non-smoker aged 30 has a 0.5% risk of CHD within five years, and a 50 year old male non-smoker has a 9.1% risk.

These absolute risks need to be balanced against the risk of developing AIDS or dying if HAART is not started, and the risk of dying despite starting treatment, argues Egger.

For example, the MACS cohort (a study of HIV disease progression among 1604 symptom-free American gay men, who were not taking anti-HIV treatment), shows that the risk of developing AIDS within three years doesn't climb above 10% until viral load rises above 41,000 copies. Once it hits this level, a CD4 cell decline below 750 cells is associated

with a 16.1% risk of developing AIDS within three years, climbing to a 40% risk in those with CD4 cell counts below 350.

In contrast, according to the Framingham model an individual with a CD4 count between 201 and 350 has an 8% risk of developing AIDS within three years if their viral load lies below 41,000 copies. If this individual were an overweight 50 year old male smoker, he might decide that a deferral of anti-HIV therapy is worth the risk, given the higher five year risk of CHD noted above.

If these figures are translated into the number of people who need to be treated in order to cause harm, only 18 non-smoking 50 year old men would need to start treatment and develop lipodystrophy for one death to occur as a result of CHD within five years.

Amongst 50 year old male smokers starting treatment, only 10 would need to start treatment and develop lipodystrophy for one death to occur within five years due to CHD. However, among non-smoking 30 year old women, 217 women would have to start treatment and develop lipodystrophy for one death to occur within five years due to CHD.

Egger stressed that "This is a worst case scenario – we are looking at people with severe lipodystrophy in metabolic terms".

Others agree that Egger's predictions may be overly pessimistic, and don't in themselves provide a clear way forward on the question of when to begin HAART. Tony Pinching, of St Bart's Hospital argues: "People don't just have to consider taking or not taking HIV therapies. They can lose weight, stop smoking or reduce cholesterol levels with diet or drugs.

"Do people really want to go back to pre-1996 [when HAART was introduced], when we can count cardiovascular episodes attributable to HAART on the fingers of one hand?"

AIDS Treatment Update (ATU): These figures look at people's risk of CHD based on the

baseline cholesterol levels. What effect does treatment have?

Matthias Egger (ME): What you're asking, essentially, is should I start treatment and just treat the metabolic complications? The problem is that this is more complicated in HIV disease. An increase in pill burden may reduce adherence, there are drug interactions between the statins [lipid-lowering drugs] and protease inhibitors, and hypoglycaemic drugs may cause lactic acidosis. But if the risk of HIV-related complications is high then I would definitely recommend antiretroviral therapy and deal with the complications as they arise.

On the other hand, if you don't have a high risk of AIDS but you are male, obese, a smoker, or have high cholesterol levels, we must realise that treatment could do more harm in the short term, because we're unlikely to gain much in terms of preventing HIV complications [as the risk was low anyway].

ATU: You said that geographic location is important in assessing the risk of CHD.

ME: Yes. The variations between England and France, and the US and France for example, are not explained by much higher levels of cholesterol in the US. The French like their *frites* and steak and have similar cholesterol levels to the US, [yet CHD risk is lower].

ATU: What happens if you move from one country to another?

ME: It depends who moves from where to where. But in general, people tend to adopt the risk of the new country, although this may take a generation or so to happen.

ATU: What is known about CHD risk in people from Africa living in the UK?

ME: Very little is known because there are no cardiovascular cohort studies in Africa. But we do know that populations in Africa are in the process of making the transition from high mortality due to infectious disease to a pattern

of mortality that is more similar to industrialised countries. In many countries the more affluent people living in the cities have a relatively high risk of CHD.

ATU: What problems arise when using the Framingham model in HIV disease?

ME: It was developed based on data from people not infected with HIV. The situation could be different in people with HIV, though there is no evidence to support this. The Framingham model doesn't take into account the difference between impaired glucose tolerance and diabetes. Most people on HAART don't develop overt diabetes, so we need better information on the importance of insulin resistance and impaired glucose tolerance that falls short of diabetes. The great advantage of the Framingham equation is that it includes both women and men. Many other cohorts only included men.

ATU: What about the impact of interventions like stopping smoking, exercise or reducing alcohol intake?

ME: Stopping smoking is really important. If someone has mild or intermediate metabolic complications, but they stop smoking they will reduce their CHD risk considerably, perhaps to the level before starting HIV treatment.

Exercise can also reduce CHD risk. A study among HIV-infected people that was presented in Toronto showed a reduction in lipid levels and improvements in body fat distribution following resistance exercise.

Drinking moderately is probably not harmful and there is even some evidence of benefit of, say, one glass of wine a day.

ATU: Does drinking alcohol have a harmful effect on triglycerides that ought to be taken into account?

ME: I'd be more concerned about high blood pressure and the risk of stroke in people who drink more than that glass of wine.

glossary

diabetes

A condition characterised by raised concentration of sugar in the blood, due to problems with the production or action of insulin.

glucose

An end product of the metabolism of carbohydrates, and the chief source of energy for the body.

HAART

Highly Active Antiretroviral Therapy, a term used to describe anti-HIV combination therapy with three or more drugs.

insulin

A hormone produced by the pancreas which tends to lower blood sugar levels.

insulin resistance

A failure to respond to insulin, resulting in increased levels of insulin and sugars in the blood.

lipid

A general term for fats.

lipodystrophy

A disruption to the way the body produces, uses and distributes fat.

metabolism

The mechanisms which sustain life, turning sugar and fat into energy.

triglycerides

The basic 'building blocks' from which fats are formed.

viral load

Measurement of the amount of virus in a sample. HIV viral load indicates the extent to which HIV is reproducing in the body.

facial wasting

6 what can be done to repair lost facial fat? by anna poppa

In Toronto last month, four hundred delegates gathered at the 2nd International Lipodystrophy workshop to exchange ideas and research on why this syndrome of abnormal fat handling has emerged, and what can be done to manage it. The range of ill-effects being attributed the label 'lipodystrophy' – fat gain, fat loss, high cholesterol, high triglycerides, insulin resistance, bone problems – is growing. Each addition seems to strengthen the view that the syndrome is caused by multiple factors, suggesting multiple therapeutic options will be required to manage it.

Treating body fat changes

Briefly, fat accumulation, high cholesterol levels and lean body mass may be improved in people with lipodystrophy through exercise (see this month's Factsheet) and dietary changes. Human growth hormone may be effective in reducing abdominal girth, though

its effect appears short-lived, and treatment is associated with a relatively high level of side-effects. Switching anti-HIV drugs, for example exchanging a protease inhibitor for nevirapine or efavirenz, may regulate abnormal blood fat and sugar levels, but there is little evidence that it will improve changes in body shape. The diabetes drug metformin may reduce insulin resistance, and perhaps reduce fat accumulation.

Reports of restored facial fat are rare. As members of the internet-based discussion groups which focus on HIV treatment and lipodystrophy will know, this is a subject which comes up frequently. Though it's impossible to place a figure on it, the sense is that a growing number of people with HIV in industrialised nations are taking the cosmetic surgery route to re-fill the wasted fat pads of their face.

Popularly conceived as an indulgence of the wealthy, the vain and the unhinged, it's

perhaps not surprising that getting a request for cosmetic surgery taken seriously has been hard work for some positive people. This is not a universal experience though, and many HIV doctors are strongly concerned about the emotional impact which visible body changes may have on their patients' quality of life and their attitude to taking HIV treatment. For people whose antiretroviral therapy is otherwise successful, knowing how best to deal with a constant physical reminder of 'illness' which may represent one's positive HIV status not only in the bathroom mirror but to the outside world as well, can be a wearing psychological challenge.

Stevie, from Manchester, told *AIDS Treatment Update*: "I had photos taken recently where people felt I looked closer to 60 instead of 49 which is my true age. The 'haggard' appearance is reminiscent of photos of HIV-positive people with late-stage illness from the 80's, and this is psychologically important for the effect it generates within the Gay Community. Sunken cheeks and hollow-looking eye-sockets serve to reinforce an unhealthy appearance, and affect personal feelings about self esteem and confidence in public."

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New product arouses interest

According to a report from French researchers at the Lipodystrophy meeting, facial fat loss may be cosmetically improved with injections of a substance called poly-lactic acid¹. Thirty-three people who had been taking HAART for

an average of 64 months were treated with an average of four injections below the surface of the skin over a six month period. Twenty four had severe fat loss (defined as a thickness of less than one millimetre on the cheeks).

Seven patients had experienced an improved facial appearance by the third injection, and a further six experienced maximum improvement by the fifth injection. However, all patients had some degree of improvement by the end of the treatment period, though the facial fat pad itself was not significantly restored. Poly-lactic acid works by stimulating the growth of collagen (a structural component of the skin and other body tissues), and the development of a thicker layer of skin which fills out the wasted regions of the cheeks. This thickened layer remains after the poly-lactic acid has been broken down and dispersed.

Poly-lactic acid is a preparation already used in cosmetic surgery as treatment for fine lines, wrinkles and furrows. In the European Union it's licensed under the brand name *New-Fill* as a Class 3 Medical Device rather than a pharmaceutical, the chief difference between the two categorisations being that medical

devices do not have a systemic effect; their effect is local to where they are placed rather than occurring throughout the whole body. Poly-lactic acid is described as 'immunologically inert', meaning that it does not stimulate an allergic or inflammatory response from the immune system. Having

glossary

See glossary words on pages 3 and 5.

peer support

Terrence Higgins Trust Lighthouse (formerly London Lighthouse) offer a monthly support group for people with lipodystrophy. Contact 020 7792 1200 for details. Ask your local HIV organisation if they provide a similar group.

facial wasting continued

been administered to over 250 HIV-positive people within studies so far, there have been no reports of allergic reactions.

Medi-Phill Ltd, the UK distributors of *New-Fill* say the effects last around two years on average, and that most people with facial fat loss require two to three treatment sessions, one month apart. The approximate cost is around £250, though cases will be evaluated on an individual basis and costs may vary in different private clinics. Gaining access through the NHS however, may not be impossible. *New-Fill* is under investigation in people with HIV in eight sites in France and Switzerland, and we understand that at least one UK centre has expressed interest in being added to this list.

What are the alternatives?

The options available to people with facial wasting currently fall into three broad categories: injections, implants and face lifts. The common hazard of all three is that, unless you have a sympathetic consultant who will argue that the NHS should meet the costs of your treatment, they will cost you quite a lot of money. The surgery involved in face lifts and implants makes these procedures much more expensive than injected substances.

Remember also, that a mention in these pages does not constitute a recommendation – anecdotally, many of these techniques have failed to meet the expectations of some individuals who've paid large sums of money to try them. Most have not been formally studied in people with lipodystrophy, and even those which have are at very early stages of investigation. This means that it's too early to say whether any of these interventions will really prove worthwhile over the longer-term. It's also worth considering that the skill and

experience of the practitioner who performs the treatment are also likely to be important, as is their understanding of lipodystrophy.

Collagen is an injectable liquid made from the connective tissues of cows or pigs which is used in cosmetic surgery to fill in wrinkles or fine lines. The effects of treatment last between a few months and about a year and a half, whereupon treatment may be repeated. About 3% of the population are allergic to collagen and so a skin test must be performed before any treatment course is begun. People with connective tissue disorders such as rheumatoid arthritis may be at particular risk of a severe allergic reaction, and some doctors believe that collagen should never be given in these circumstances.

Fascian works in a similar way to collagen injections but is made from human connective tissue called fascia. It has only recently become available in injectable form and so its safety and effects are less well-understood than those of collagen. It is claimed to be more effective in filling larger hollows than collagen, and should last longer, but also requires skin testing beforehand.

Hylaform is another injectable filler which is used cosmetically. It is made from hyaluronan, a naturally occurring polysaccharide. It cannot be used by people who are allergic to eggs or chicken. *Restylane* is similar, and both it, and *Hylaform* don't require allergy testing.

Silicone injections are banned in the US but licensed for cosmetic purposes in the European Union. Possible adverse effects include the movement of silicone to other parts of the body, discolouration and inflammation of the areas surrounding the injected site, and the formation of nodules

called granulomas – hence the tough line taken in the States. Despite being illegal there, it's very much available and is being taken up by the HIV-positive community, with some positive anecdotal reports.

It's also possible to have one's own fat injected into the face (assuming you have fat to spare elsewhere), through a procedure known as fat transfer. Whilst this is more expensive, it avoids the risk of allergic reactions as you'll be using your own body tissue. Once again, though, it is not expected to be anything other than a temporary measure – cutting fat from one area and placing it in another will do nothing to alter the underlying mechanisms of facial fat loss, and would be expected to be 'reabsorbed' in time.

At the lipodystrophy meeting in Toronto, a doctor from Brazil reported that methacrylate injections, an adhesive used in hip transplants, had a beneficial effect on sunken cheeks in a group of sixty people with HIV². Information presented in this paper is quite limited, but all patients reported improved quality of life, and there were no allergic reactions during eighteen months of follow-up. Treatment usually involves two sessions costing \$350 each, (plus the fare to Rio).

Implants & face lifts

Surgical implants are a second method which some people with HIV have pursued in an attempt to fill out their cheeks. Implants may

be made from organic material such as *Alloderm*, which is made from human collagen, or from artificial products such as *Goretex*. Implants are inserted through an incision made in the mouth, so there is no facial scarring. Surgical procedures may pose infection risks, however, particularly for people with weakened immune systems. Results are likely to be dependent on the surgeon's skill in fitting the implant with the hollow. Initial swelling, and the use of implants in a face which is very wasted, can leave a 'chipmunk' look. And whilst the effect should be permanent (assuming they don't move), implants are expensive.

The term 'face lift' is used to describe what may be a series of surgical procedures designed to remove loose skin and thereby 'tighten' a sagging face. This may not be suitable for a very wasted face, and can be a very laborious and costly venture. Incisions are made behind the ears and in the hairline, so scarring may be visible.

Papering over the cracks?

One thing all of the procedures described in this article have in common is that they do nothing to address the underlying causes of body fat changes affecting people with HIV. These changes are unexplained, and according to some critics in the HIV community, the adoption of cosmetic solutions may be a distraction from the need to find a more permanent answer.

key conclusions

- Lipodystrophy, a syndrome of body fat and metabolic changes affecting people with HIV, remains unexplained and hard to treat.
- Body fat changes can have a significant impact of quality of life.
- Fat which is lost from the face seems particularly hard to regain. Some people with HIV are considering cosmetic surgery in response to this.
- A range of cosmetic options are available. All of these are expensive, though some people may gain access through the NHS. Individual experiences with cosmetic surgery vary however, and there is no guarantee that positive results will last.

costs

The cost of techniques and products mentioned in this article will vary according to the work undertaken, and between practitioners. Most injectable substances are priced according to the volume injected. As a rough guide, most injectable products will cost less than £1000 for a course of treatment, but may require 'topping up' periodically. Surgical procedures, including fat transfer, are much more expensive. Plastic surgery is available on the NHS, but only if your doctor is willing to refer you, and your trust is willing to pay. Waiting lists may be fairly long. We understand that several HIV treatment centres are negotiating individual arrangements, so the situation may change in the future.

references

- 1 Amard P et al. *Antiviral Therapy* 5 (Supp 5): 79, 2000.
- 2 Serra M. *Antiviral Therapy* 5 (Supp 5): 76, 2000.



New ddI capsules

A new capsule formulation of ddI, known as *Videx EC*, was launched in the UK last month following its full approval in the European Union. *Videx EC* is the first once daily, one pill anti-HIV drug to be licensed for use in combination therapy. 'EC' stands for enteric-coated, which is the term many people use to describe this formulation.

Advice on the timing of meals for people taking the new capsule differs to that which accompanied the old, tablet formulation of the drug. Manufacturers Bristol-Myers Squibb have been asked to complete further studies to confirm exactly how soon after taking *Videx EC* it is safe to eat or drink.

The AIDS Pharmacists Group have issued a patient factsheet on *Videx-EC*, which says: "The new recommendation is to take the enteric-coated ddI at least two hours after food, preferably before bedtime, or as best suits your lifestyle.

"Until further studies have been done, the company cannot give a precise recommendation about how long a gap must be left after taking the ddI EC before eating. This is why they are recommending that it is taken at bedtime, at least 2 hours after food, and not to eat again until the morning. However, based on what is known about ddI itself and also about the way that drugs are absorbed into the body, it is reasonable to

assume that leaving a gap of at least 2 hours after the ddI EC before eating would be safe.

"In other words, you should not eat or drink (except water) for at least 2 hours before and at least 2 hours after taking your ddI EC."

Osteoporosis

Osteoporosis is a condition where the bones lose mass and density. It is commonly referred to as 'thinning of the bones' and occurs mostly in older, post-menopausal women. It is not an AIDS-defining condition and was rarely seen among people with HIV until recently.

Osteoporosis is caused by a lack of bone calcium and protein, but its appearance in relatively young, mostly male, HIV-positive people, remains unexplained.

In 1999, the Royal Free Hospital in London reported two cases of sudden onset osteoporosis in young African women on anti-HIV treatment. Both women had lower back pain and irregular periods. Bone scans showed a number of bones had collapsed and bone mineral analysis confirmed osteoporosis.

Since then, several studies have reported a spectrum of changes in bone mineral density:

- Osteopenia, a less severe form of bone mineral loss, is relatively common, affecting around 30% of people taking anti-HIV treatment in the investigations

into its frequency which have been conducted so far.

- When bone mineral density reduces further, the risk of fracture is increased. When the bone mineral density has fallen so low that an individual has a fracture risk four to five times higher than the average for the population, that condition is known as osteoporosis. Osteoporosis has been reported in between 3 and 21% of HIV clinic populations investigated.
- Avascular necrosis has been reported rarely. This condition refers to the death of the bone in the hip joint, requiring hip replacement.

Protease inhibitor treatment has been associated with a significantly greater incidence of osteoporosis according to researchers from Washington University, St Louis, who found that 21% of a group of 64 men receiving protease inhibitors (PI), compared with 6% of an age-matched HIV-negative control group, had severe osteoporosis. Fifty percent of the PI group had some evidence of reduced bone mass, compared to 29% of the control group. Although some researchers have speculated that reduced levels of the male sex hormone testosterone might be linked to reduced bone mass, the St Louis group found no link.

An Australian group has reported reduced bone mass in 28% of 80 patients with lipodystrophy. However, researchers do not know what is causing this high prevalence of osteoporosis given that the proportion with reduced bone mass did not increase during six months of follow-up, and switching from a PI-containing regimen to a PI-sparing regimen did not improve bone mass. The loss of bone mass was most pronounced in the legs and spine, increasing the possibility of broken bones among PI recipients.

However, two further Australian studies have identified a number of factors other than protease inhibitor treatment which may be associated with reduced bone mineral density:

- More rapid loss of subcutaneous fat correlated with a greater reduction in bone mineral density in 171 patients, regardless of PI therapy. However, indinavir therapy was associated with higher bone mineral density compared to nelfinavir.
- Higher lactate levels, (which in this group were associated with current ddI or d4T treatment and the magnitude of CD4 increase since starting treatment). The authors suggest that bone-derived calcium may be used to buffer high levels of acid in the blood.
- Lower weight prior to starting antiretroviral therapy (low body weight is a well known risk factor for osteoporosis).

Reduced bone mass has also been identified in people receiving nucleoside analogues without a protease inhibitor, and in treatment-naïve patients. Forty five male patients (average age 35) were evaluated by Spanish researchers; 62% had osteopenia. A French study of 85 consecutive patients attending an HIV clinic found that 20% of treatment-naïve patients had osteopenia, and 45% of PI-naïve patients had osteopenia. Only the duration of HIV infection was found to be significantly associated with osteopenia.

In the UK, a comparison of 52 untreated HIV-positive patients with 22 men on protease inhibitor therapy, and 10 men receiving nucleoside analogues only, found no significant difference in bone mineral density between the three groups. Indeed, antiretroviral therapy of any sort seemed to reduce the severity of bone mineral loss when patients were matched for duration since HIV diagnosis, and there was a trend towards reduced risk in those with lower viral load regardless of risk. These findings suggest that bone mineral loss may be a consequence of long-term HIV infection and immune activation.

For a more detailed review of this subject, and references for the studies noted above, see coverage on the NAM/BHIVA website aidsmap.com.

nam forum

This month's forum is on *HIV Drugs and Heart Disease*. Our guest speaker is Dr Matthias Egger, who is interviewed about his work on this subject on pages 2 to 5 of this issue. The forum takes place at the University of London Union, Malet Street, London WC1 on November 27th, 7-9pm. Entrance is free, and a sign language interpreter will be available. All are welcome.





credits

editor
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AIDS Treatment Update
founded by Peter Scott

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design
Alexander Boxill

printing
Cambrian Printers

ISSN
0969-4706

charity number
1011220

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NAM's treatments information for people living with HIV is provided free thanks to the generosity of:

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any questions

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This 600 page book, published twice a year, is a comprehensive guide to the medical aspects of HIV. Available at only £9.95 to people with HIV, £57.50 to professionals.

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NAM's resources are also available online at aidsmap.com. These include our extensive and searchable treatments database, the latest news on treatment developments, our online directory of AIDS organisations, hundreds of links to recommended HIV-related sites, and free downloadable resources.

Monthly NAM information forums in London
Each month an expert speaker discusses a treatment-related topic. Entry is free. Future forums are advertised inside this newsletter.

AIDS Treatment Phonenumber 0845 9470 047
From Terrence Higgins Trust: Mon& Wed 3-9pm, Tue 3-6pm.

NAM recommends that you discuss all your treatment decisions with your doctor.



subscriptions

Free to individuals in the UK affected by HIV or AIDS.
Professional/organisational rate: £69/year.
Voluntary organisation rate: £50/year.
Overseas rate: within EU add £10/year;
outside EU add £15/year.

AIDS Treatment Update is available on audio tape, and can be emailed to you as a pdf file for viewing with Acrobat Reader. Telephone 020 7627 3200 for details.

The publishers have taken all such care as they consider reasonable in preparing this newsletter. But they will not be held responsible for any inaccuracies or mis-statements of fact contained herein. Inclusion in this newsletter of information on any drug or clinical trial in no way represents an endorsement of that drug or trial. This newsletter should always be used in conjunction with professional medical advice.

Donations towards production costs are welcomed.