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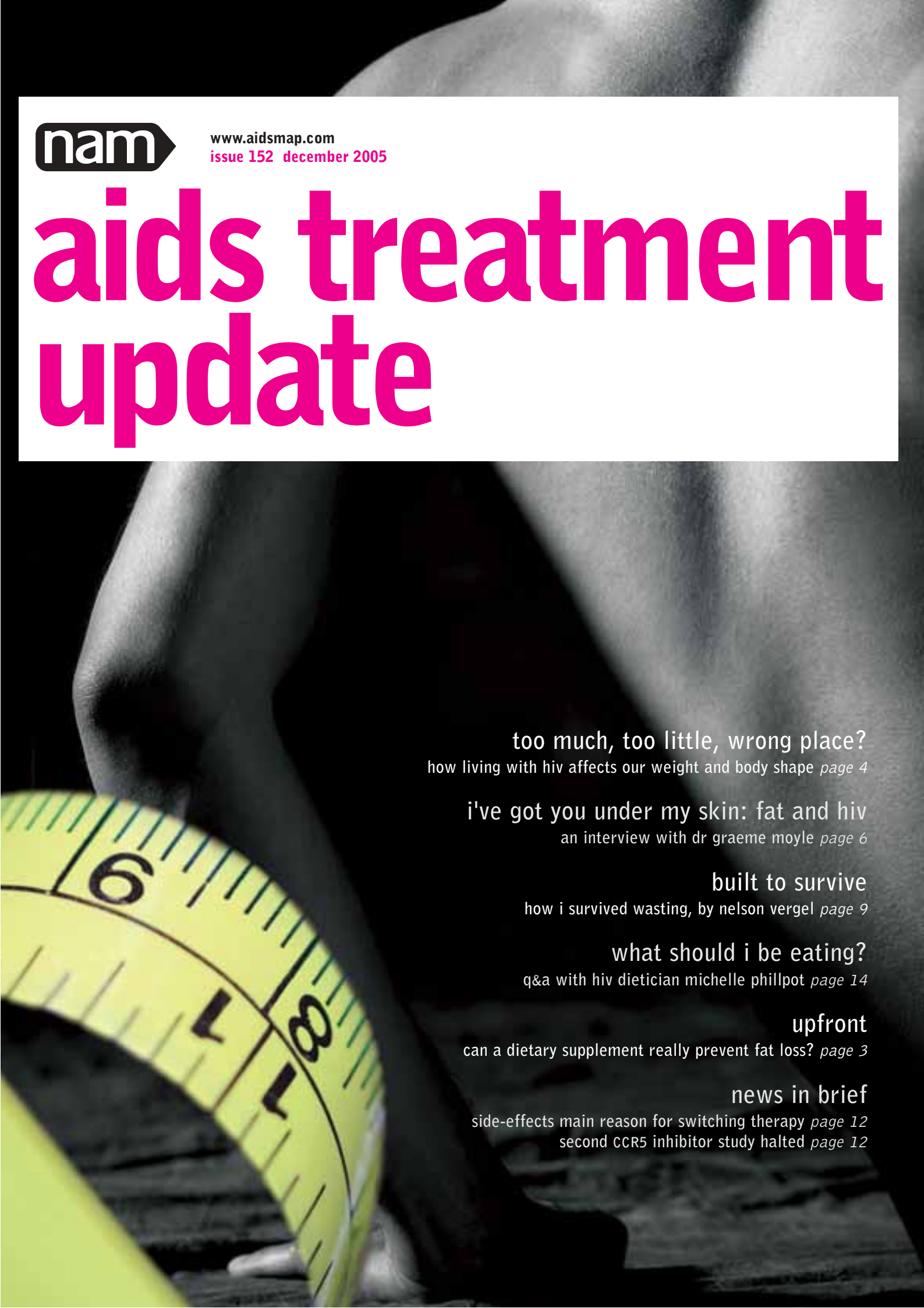
aids treatment update



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in this issue

December is the festive month when we traditionally indulge in rich food and drink. This is, not coincidentally, followed by the New Year when we often resolve to eat better, start exercising and generally live healthier lives.

Thanks to the complications of wasting and lipodystrophy, managing our body shape and weight are major issues for people living with HIV, but finding accurate, HIV-specific information can be difficult.

Is mainstream healthy eating advice the best advice for us? Do we need to exercise more, less or differently than our HIV-negative counterparts? Does diet and exercise even matter? That's what this issue is about. If this is something you don't feel like digesting right now, keep it in a safe place and read it when you're making those New Year's Resolutions, or just before next seeing your HIV doctor.

If you have noticed that your body shape or weight is changing, it's important to remember that you have every right to raise your concerns with your HIV doctor, because this might be something that affects your long-term health, not just your looks or waistline. In addition, if you can access one, a specialist HIV dietician can provide a wealth of information about diet, exercise and other general health issues for people living with HIV.

page 3 In *upfront*, NAM's senior editor, Keith Alcorn, reports from the Lipodystrophy Workshop held in Dublin last month on a possible new way to restore lost fat due to anti-HIV therapy.

page 4 *Too much, too little, wrong place?* examines HIV's effects on weight and body shape, and asks what we can do about it.

page 6 In *I've got you under my skin: fat and HIV* Dr Graeme Moyle, Associate Director of HIV Research at London's Chelsea and Westminster Hospital, explains why the amount of fat we have matters, and how best to deal with lost fat.

page 9 US writer and activist, Nelson Vergel, explains how he survived wasting and went on to become an extremely well-informed expert patient specialising in wasting, lipodystrophy, diet and exercise.

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upfront

a spoonful of sugar

could a dietary supplement really restore lost fat?

by Keith Alcorn

Although the causes of fat loss (lipoatrophy) in people receiving antiretroviral treatment are still under investigation, there is increasing agreement that the nucleoside analogues d4T (stavudine, *Zerit*) and AZT (zidovudine, *Retrovir*; also in *Combivir* and *Trizivir*) are major contributors, and that their use is best avoided wherever possible. Fat restoration as a result of switching from d4T or AZT to abacavir (*Ziagen*; also in *Kivexa*) or tenofovir (*Viread*; also in *Truvada*) is very slow and often imperceptible to people who have experienced the fat loss during the first year after the treatment switch.

Until recently, no one had identified a method of blocking the fat-destructive properties of d4T or AZT, which seems to be related to toxicity to mitochondrial DNA within the cells, leading to a complex process of fat cell shrinkage and destruction that is quite distinct from the fat loss caused by dieting or starvation.

Eighteen months ago German researcher Dr Ulrich Walker published a report suggesting that a supplement made from sugar cane called *NucleomaxX* could raise levels of a natural nucleoside called uridine in the body, and that this might block some of this toxicity and give fat cells a chance to regenerate. In fact he has since applied for a patent for uridine and the use of its precursors in the treatment of lipodystrophy.

Last month, the first results of his collaborations with Finnish and US researchers to evaluate *NucleomaxX* were presented at the Seventh International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV, in Dublin, Ireland. In the Finnish study[1] 20 people with lipoatrophy on anti-HIV therapy containing AZT or d4T for an average of 18 months were randomised to receive *NucleomaxX* or a placebo three times daily for ten days each month for three months.

After three months DEXA scans found that the group that had received *NucleomaxX* gained a significant amount of limb fat under the skin (approximately 900g), and that the fat gain was significantly greater than any fat gain seen in the placebo group. This improvement in limb fat seen after three months of *NucleomaxX* is similar to the improvement seen after more than one year in patients who switched from d4T to abacavir in the Australian MITOX study.

The US study[2] involved 14 individuals with lipoatrophy on d4T who knew they were getting *NucleomaxX*. They took the supplement three times daily every other day for 16 weeks. This study relied on less accurate doctor/patient reports of visual improvements rather than DEXA scans, but after 16 weeks significant improvements were reported.

It remains unclear at this early stage whether this treatment will provide long-term sustained fat restoration, and it may not be appropriate for all people with lipoatrophy, particularly for those who switched to other drugs in order to limit or repair the fat loss. In addition, people receiving ddI (didanosine, *Videx EC*) are unlikely to benefit since test-tube studies have found that uridine does not affect ddI toxicity.

NucleomaxX, a dietary supplement made from sugar cane, may help reverse fat loss

Neither study reported any significant side-effects apart from the one person withdrawing due to the taste of the supplement, but after 12 weeks *NucleomaxX* recipients in the Finnish study had significantly lower HDL ("good") cholesterol levels, due both to a slight decline in HDL among *NucleomaxX* recipients and to an HDL increase in the placebo group. Lipid effects in the US study were not reported.

NucleomaxX is available through an internet pharmacy for approximately £590 for the three month course of treatment used in the Finnish study but anyone considering the use of this product as a treatment for lipoatrophy should consult their HIV doctor. Self-medication is not recommended, and since studies so far have only been in individuals receiving AZT or d4T, the benefits and toxicities are unknown in individuals not currently taking AZT or d4T. For people who have already suffered fat loss as a result of their treatment only *New-Fill* is licensed in Europe and North America for facial fat loss repair.

too much, too little, wrong place?

How living with HIV affects our weight and body shape, by Edwin J Bernard

As a nation, the UK is getting fatter. In 1993, according to the Association of the Study of Obesity, 38% of men and 44% of women had a body mass index (BMI) within the ideal range (20-25) and the BMI of the average UK man and woman was 25.9 and 25.7, respectively. Ten years later, only 30% of men and 38% of women had an idea BMI, and the average BMI had increased to 26.9 and 26.7 for men and women, respectively.

It should come as no surprise that according to a survey reported by the BBC last year, more than one in four adults in the UK are trying to lose weight most of the time. Those 13 million people are being fed a constant diet of conflicting information about how best to lose weight: sensible eating habits and regular, moderate exercise recommended by health professionals are often eschewed for the latest, often dangerous 'advice' fuelled by the multibillion pound fitness, supplement and weight loss industry.

Fat is an issue for people living with HIV, too. Some of us might be overweight and need to lose weight, ideally fat not muscle. Some of us are likely to be underweight and need to gain weight, ideally as muscle not fat.

Some of us might also experience body fat redistribution or loss of lean body mass, and others might have a combination of some or even all of these.

Lipodystrophy-associated fat issues include fat loss from the face, arms and legs; fat gain in the belly, breasts or back-of-the-neck; and the metabolic problems (increased blood fats and sugars) that often accompany body shape changes which can lead to an increased risk of diabetes and heart disease.

Although the dramatic declines in weight loss of 10% or more, characterised by HIV-related wasting before highly active antiretroviral therapy (HAART) appeared in 1996,

what is my BMI?

The Body Mass Index (BMI) can be used to determine if you are at a healthy weight (BMI 20-25), overweight (25-30), or obese (over 30).

It is calculated by taking your body weight (in kgs) divided by your height (in metres) times your height.

weight [kg] ÷ (height [m] × height [m])

For example:

72[kg] divided by (1.83[m] multiplied by 1.83[m]) is a BMI of 21.5

However, BMI is not as accurate if you are an athlete or very muscled (muscle weighs more than fat), as it can push you into a higher BMI category despite having a healthy level of body fat. It is also not accurate for women who are pregnant or breastfeeding, or people who are frail.

Remember, though, that BMI is only one guide about your overall health. Waist measurement, body fat level, blood pressure, blood fats, physical activity, and whether you smoke, drink and eat a balanced, healthy diet are also important to get the whole picture.

are rarely seen today, more subtle - but still worrying - involuntary weight loss (the loss of muscle, or lean body mass, rather than fat) still occurs. A recent study by Alice Tang and her colleagues at Tufts University in Boston found that the proportion of HIV-positive individuals who lost 5% or more of their weight over a six month period increased significantly between 1995 and 2003[1]. This weight loss was not connected with lipodystrophy. What concerned Dr Tang was that her earlier research had found that even losing 3% of weight unintentionally could lead to a higher risk of death[2]. Her latest study found that weight loss was associated with HIV- and anti-HIV drug-related symptoms, like diarrhoea, nausea, thrush, a CD4 cell count below 200 cells/mm^3 and a viral load above 100,000 copies/ml, as well as with recreational drug use and living in poverty.

But another recent study from the US city of Philadelphia suggests that HIV-positive people can be overweight, too, and that, in the city of brotherly love at least, obesity is now much more common than wasting amongst HIV-positive people. Over there, 58% of HIV-positive women and 42% of men were either obese (a BMI over 30) or overweight (a BMI between 25-30). Risk factors for obesity in women included African-American ethnicity and a CD4 cell count above 200 cells/mm^3, with a CD4 cell count over 200 cells/mm^3 also being associated with obesity in men[3].

However, the study also found that HIV-positive people were still less likely to be obese than the average man or woman in Philadelphia, and recent unpublished data from the Chelsea and Westminster[4] suggest that their predominantly white HIV-positive gay male patients are much less likely to be overweight or obese and much more likely to be struggling to keep weight on. In contrast, two out of three HIV-negative men between 35-44 in the UK are overweight or obese. Although the picture may well be different for women or people of African ethnicity, what this suggests is that even though it is possible for HIV-positive people to be too fat, we may have different fat issues than our HIV-negative counterparts wherever we live.

so what can we do about it?

In the July/August 2005 issue of AIDS Treatment Update, we examined the latest recommendations from the British HIV Association (BHIVA) regarding lipodystrophy. There was plenty of information on medical interventions - including switching away from d4T (stavudine, *Zerit*) and possibly AZT (zidovudine, *Retrovir*) and having lost facial fat replaced via *New-Fill* or other facial fillers, if access was available to you - but there was very little information on what individuals with HIV could do for themselves regarding diet and exercise, or how to safely deal with weight loss or gain that isn't lipodystrophy-related.

True, the guidelines say that HIV healthcare workers should assess and then recommend changing lifestyle choices that may increase the risk of cardiovascular disease and diabetes, such as "smoking, diet, possibly dietary supplementation and exercise", but their advice on diet and exercise, although helpful, is not very detailed.

Over the next six pages (as well as our Q&A with specialist dietician Michelle Philipot at the back of the newsletter) various experts will explain why both too much and too little fat and weight is critically important to people with HIV and how diet and exercise could make a difference to both quality and quantity of life.

further information

NAM produce two booklets in our award-winning Patient Information Series that cover diet and exercise for people with HIV: 'Nutrition' and 'Lipodystrophy.' These can be read online or downloaded from our website, aidsmap.com. People living with HIV can also order free copies of these booklets by visit our online Publications Centre, by emailing info@nam.org.uk or by telephoning 020 7840 0050.

i've got you under my skin fat and hiv

ATU: Recently, we have seen data from several different studies regarding fat, weight and HIV. Whereas one suggested that many HIV-positive people are still wasting, another found that obesity is more common than wasting. And last month, the FRAM study[1], which was set up to define HIV-related lipodystrophy, confirms in men what had been found in women: fat loss rather than central fat gain is the defining body-shape change associated with lipodystrophy. Which fat and weight changes do you think we should be concerned about the most?

GM: First of all, I think it's important to point out that involuntary weight loss is a concerning event. Even a small amount of involuntary weight loss, in the HAART era, has been associated with increased risk of illness and death. Alice Tang and colleagues[2] found that if you involuntarily lost between 3-5% of your normal weight even once, it doubled your risk of dying. If you lost between 5-10%, you had a fourfold increased risk of death. And if you lost more than 10% it was nearly sixfold. And that's in predominantly HAART-treated patients. So weight loss remains a relevant phenomenon. And one of the things that HIV clinics continue to do poorly is measure weight in a reliable and consistent way. It's important to know what's happening with your weight, and it's particularly relevant when people are experiencing altered body shape.

ATU: How does lipodystrophy fit in with involuntary weight loss?

GM: A typical way in which people notice they've lost weight is that their trousers don't fit. But with lipodystrophy your trousers could still fit, or even get tighter, whilst you're actually losing weight. But there isn't a quick and easy way to measure lean body mass or fat loss, which makes it difficult in terms of providing routine assessment of whether involuntary weight loss is going on. So people could be experiencing loss of fat or loss of lean body mass, or most commonly, a mixture of both lean and fat loss.

ATU: Who is most likely to be affected?

GM: There are a few studies that point to the idea of a relationship between disease factors and clinical fat loss. In a recent study by Dube and colleagues[3] you see that there is an initial rise in limb fat as a result of going onto therapy. What that reflects is that people who go onto HAART gain weight because they'd lost some weight when they had untreated HIV infection, probably due to a marginally increased metabolic rate but maybe also because the quality of nutrient absorption isn't as good when you have HIV. What happens over time, depending on what drug you take, is that you may then start to lose limb fat, or it may stay the same.

glossary

body mass index (BMI)
a measure of body weight relative to height, used to determine if people are at a healthy weight, overweight, or obese.

CT scan
computerised tomography is a sophisticated x-ray procedure in which a computer is used to generate a three-dimensional image.

DEXA
dual energy X-ray absorptiometry is a method of scanning the body to determine bone density and fat distribution.

highly active antiretroviral therapy (HAART)
a term used to describe anti-HIV combination therapy with three or more drugs, where at least one is either a protease inhibitor or a non-nucleoside reverse transcriptase inhibitor.

insulin resistance
when the amount of insulin needed to maintain glucose (sugar) levels in the body is greater than usual; can lead to type II diabetes.

Edwin J Bernard chews the fat with Dr Graeme Moyle, the Associate Director of HIV Research at London's Chelsea and Westminster Hospital, whose specialisms include body shape changes and the metabolic consequences of HIV therapy.

ATU: How much fat is being lost?
GM: Well, patients entering the MITOX study[4] had on average about 4kg of limb fat, and patients entering the RAVE study[5] had on average about 3kg of limb fat. And limb fat in the general population is around 8kg. So we're looking at people who have lost 50-60% of normal limb fat. But, remember, people entering those studies were selected for moderate-to-severe changes, obvious changes. There's a spectrum of fat loss depending on your individual characteristics, and there's a range of time when it becomes clinically obvious. For example, if you're female you have relatively more subcutaneous fat than if you're male, so lipoatrophy usually becomes noticeable later than in men. And there are also going to be variations based on your genetics and ethnicity.

ATU: There's no denying the psychological effects of fat wasting from under the skin, particularly in the face. New research is suggesting that there may be other reasons to be concerned about this lost subcutaneous fat. What's it there for, and what happens when it's lost?
GM: There are many different hypotheses regarding the role of subcutaneous fat. A few things are fairly clear from animal studies, as well as studies of people who have an inherited form of lipoatrophy, in that it clearly plays a role in the management of lipids and insulin sensitivity.

ATU: So fat loss, and not just fat gain, as has been thought, could be linked with the metabolic side-effects that we see with lipodystrophy?
GM: That's a reasonable conclusion to make. The evidence seems to suggest that there's a link between the metabolic side-effects and fat loss. There may well be some contribution, depending on the extent of fat loss in that particular individual. But if we take, for example, the recent FRAM study, we'll see the separation of lipoatrophy from all of the other abnormalities. What it's saying is that we have two things going on in the population that we're evaluating here. We have metabolic syndrome - raised blood fats and sugars - which is a common phenomenon in the general population, and we have a second phenomenon of fat wasting that is exclusive to the HIV population.

ATU: What do you think are the long-term ramifications of the loss of subcutaneous fat?
GM: It's reasonable to assume that those individuals are going to have a greater challenge managing their lipids and glucose.

> "the evidence seems to suggest that there's a link between the metabolic side-effects and fat loss"

lean body mass
body weight minus body fat; primarily muscle, bone and other non-fat tissue.

lipids
fat or fat-like substances found in the blood, such as cholesterol.

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.

mitochondrial DNA
the building blocks of energy production within cells.

New-Fill
the UK brand name for poly-L-lactic acid, a facial filler used for the treatment of facial wasting in people with HIV-related lipodystrophy.

non-nukes
non-nucleoside reverse transcriptase inhibitors (NNRTIs), the family of antiretrovirals which includes efavirenz and nevirapine.

nucleoside analogues
nucleoside reverse transcriptase inhibitors (NRTIs), the family of antiretrovirals which includes AZT, ddI, 3TC, d4T and abacavir.

ATU: So far, even the most successful strategies for restoring lost fat - which have come from switching from d4T and AZT to abacavir or tenofovir - have only restored a tiny amount of lost fat even after two years. And studies with the diabetes drug, rosiglitazone, haven't produced very exciting results, have they?

GM: No, they've produced decidedly disappointing results! But the big news from the Lipodystrophy Workshop should be about uridine. My understanding of the small randomised study to be presented by Jussi Sutinen from Finland is that there were quite substantial differences between changes in limb fat in the placebo group relative to the intervention group. And the levels of fat recovery in the small numbers on uridine were much more substantial than found when simply switching from a thymidine analogue. There's also a larger ongoing study of uridine by the AIDS Clinical Trials Group in the United States. [Editor's note: this interview took place prior to the Workshop, but see our *Upfront* article on page 3 for more on this].

ATU: What do you think happens first when people have both central fat gain and lipoatrophy as well as the metabolic side-effects?

GM: It's not clear which comes first. In general there is a common association between insulin resistance and central fat accumulation. But weight gain around the middle might happen because you can't store it under the skin if you have lipoatrophy, or it might be the other way around. But, either way, in the end you can still get lipid problems and insulin resistance.

ATU: Aside from switching away from d4T or possibly AZT – which not everyone can or should do – and using lipid-lowering drugs, when appropriate, it does seem that diet and exercise appear to make the most sense.

GM: They are also the lowest-risk things to do. If you fiddle with your combination it could be a triumph of hope over benefit, or it could actually lead to a disastrous outcome.

ATU: It seems to make sense to do weight training, in order to reshape your body with muscle and reduce the obviousness of the appearance of fat wasting. But if you do cardio exercise to try and lose your central fat and/or increase your cardiovascular health, how do you not make subcutaneous fat loss worse?

GM: The problem is that any kind of exercise is fat burning regardless of whether you are doing weights or doing cardio. To make up for that you should eat more calories, and I don't just mean lots of cheese! I think in general it would be best to follow a cardio-friendly diet. Whilst it's not clear if changes in diet alone can affect body shape in HIV-positive individuals, we do know that diet can affect your future risk of heart disease.

ATU: What is the best exercise regime?

GM: There's no simple answer to that but some studies have tried to look at it by adding exercise to other interventions, including anabolic steroids. Bhasin and colleagues[6] showed that weight training alone was as beneficial as using a testosterone supplement in HIV-positive men with weight loss and low testosterone. But other studies have shown that a mix of cardio and weights is beneficial. My suggestion is to do whatever exercise suits you best and that it's reasonable to consider doing a mixture of cardio and weights. Just remember that all this exercise is going to be fat burning and, therefore, weight-losing, and that you need to eat more to make up for the risk of fat loss in those circumstances.

ATU: Finally, what's your opinion on using anabolic steroids?

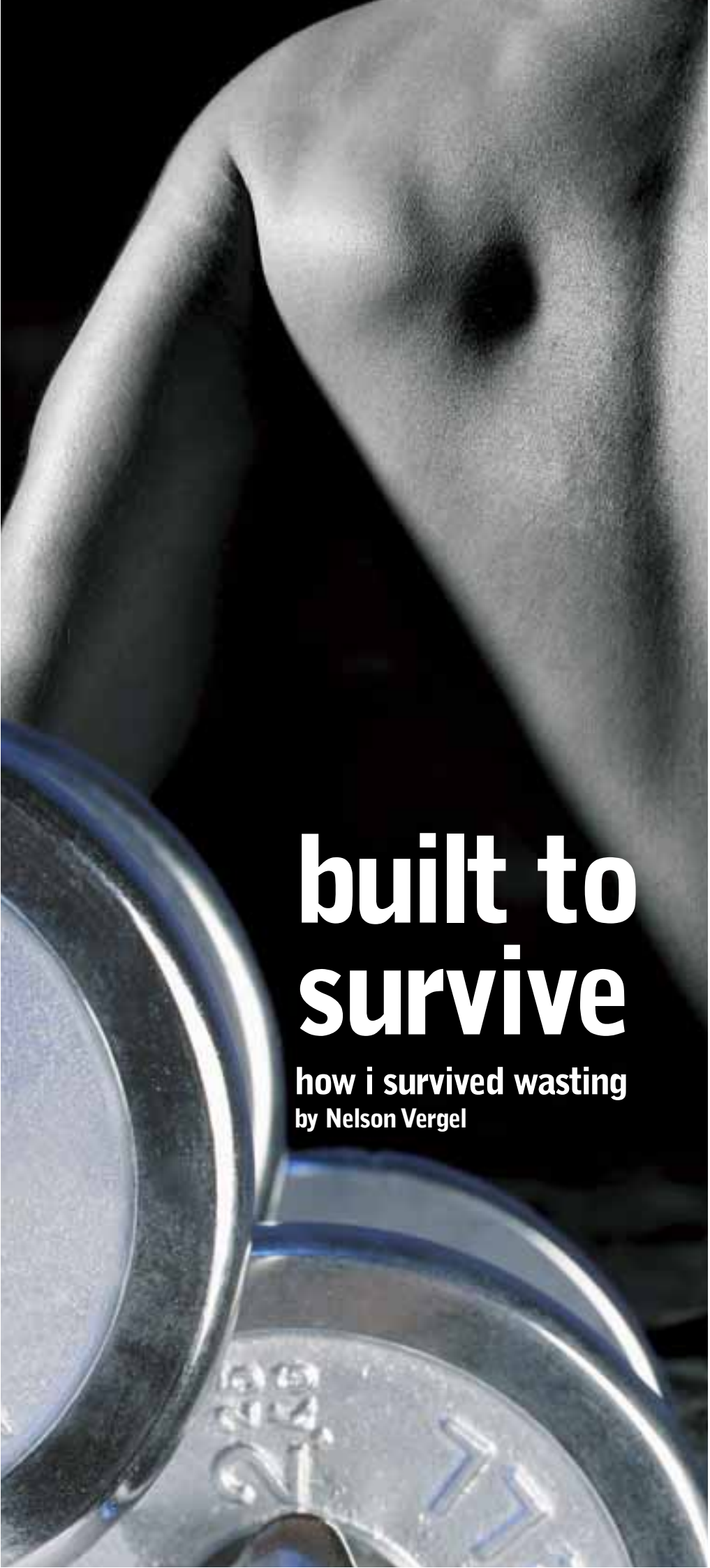
GM: The use of testosterone replacement is appropriate for someone who has low or low-ish testosterone levels, and it can have benefits in terms of reducing fatigue and increasing libido. Although we used to prescribe nandrolone for wasting at the Chelsea & Westminster, we don't any more. As well as there being issues of abuse and dependence, there is also evidence that if you have lost subcutaneous fat, using anabolic steroids may make it worse, not better, since it will replace muscle at the expense of fat.

glossary continued

placebo
something which looks and tastes exactly like a real drug, but contains no active substance.

protease inhibitors
family of anti-HIV drugs which target the protease enzyme. Includes atazanavir, fosamprenavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir, and tipranavir.

thrush
a fungal infection of the mouth, throat or genitals, marked by white patches, also called candidiasis.



built to survive

how i survived wasting

by Nelson Vergel

US writer and activist Nelson Vergel explains how he survived wasting and went on to write a book about it. Nelson is the founder of the Body Positive Wellness Clinic in Houston, Texas; moderator of one of the largest HIV health discussion groups on the internet, Yahoo's pozhealth; and a lay expert on lipodystrophy, diet and exercise.

It was 1993 and I was losing weight fast. Whilst I and my friends were dying of wasting syndrome I had just read reports of the horrible conclusion of the Concorde study that found that people with HIV were dying faster on high dose AZT than those not taking it. Back then we had not heard about protease inhibitors and non-nukes, new drugs that were only a few years away and which would prove to be life savers. I felt that there was nothing that I and my friends could do to survive. All doctors and dieticians could tell us was to eat higher calorie foods like doughnuts and ice cream, and to put peanut butter and mayonnaise on everything!

As there were no guidelines to treat involuntary weight loss, and no agreement on the best treatment or diagnosis, many of us in the community took matters into our own hands to try to prevent our deaths from what was then known to be among the top three killers of people with HIV.

I was lucky enough to live in Los Angeles and there I met up with other HIV-positive patients who were trying all kinds of complementary therapies out of desperation. I started hearing about anabolic steroids and testosterone supplementation as an effective way of putting on lean body mass and buying time until better therapies came come along. I decided to try it myself, got hold of some nandrolone and testosterone, did weight training at the gym, and after just four months reversed my wasting, gaining

16 kilos. My energy levels jumped, my libido returned, and my AIDS-related symptoms disappeared.

I decided that I needed to bring this approach out of the closet and started researching the clinical use of anabolic steroids to combat wasting. I found a wealth of information that had been suppressed in the mainstream medical community thanks to bad publicity due to bodybuilding and athletic abuse.

With Michael Mooney, I summarised all the research I had uncovered in the book *Built to Survive,* now in its fourth edition, and started lecturing on a comprehensive approach of using proper nutrition, exercise, supplementation and anabolic therapies, where appropriate, to combat wasting syndrome through my charity, Program for Wellness Restoration, PoWeR.

The idea behind this work is that, in order to prevent wasting, it is advisable to have an 'insurance pad' of extra lean body mass (i.e. muscle) in case of weight loss due to illness, infections, diarrhoea, or the other still-unknown causes of involuntary weight loss in people with HIV. As Graeme Moyle notes, a well-respected study found that losing even 3% of normal body weight doubles your risk of dying. Although there have been no studies to determine if the 'insurance pad' theory is a valid risk management measure, I strongly believe that having extra lean body mass to prevent falling into the 'danger zone' has kept me alive.

Once we were able to advocate for studies showing that using proper nutrition, exercise, supplementation and anabolic therapies, where appropriate, was not only safe but effective if monitored by a physician, it achieved mainstream acceptance amongst many HIV doctors in North America. I am glad to see many doctors in the US treating and preventing wasting proactively by helping their patients to stay muscular and strong while fighting this disease.

Of all the anabolic steroids, 150mg nandrolone decanoate (injected into muscle every seven or 14 days) has been shown to help HIV-positive people with involuntary weight loss gain lean body mass with few side-effects, at least in the short-term. In fact, there are more than a dozen studies documenting its safe use in HIV-positive men and women, and one in people with kidney dysfunction. However, anabolics work better with regular exercise and proper nutrition, and need to be provided with testosterone replacement since they decrease testosterone levels in the body. I am saddened to see that many doctors outside of North America are still against providing anabolic steroids to patients who need help, even though they are a cheap and effective way to reverse wasting.

When the era of highly active antiretroviral therapy (HAART) began in 1996, and we started living longer, I began to hope that wasting would soon disappear and I could start spending my energies on other advocacy issues. Then lipodystrophy happened and I realised that the more things change, the more they remain the same.

In 1997, I attended a conference where doctors started to report body shape changes that were disfiguring the same people who were having

12345 nelson's top five tips for gaining weight

1. If you have diarrhoea, make sure it is diagnosed correctly, and treat it aggressively.
2. Talk to your doctor or dietician about ways to improve your appetite or reduce nausea.
3. Ask you doctor to check your hormone levels and your thyroid function, and supplement testosterone and/or the thyroid hormone, thyroxin, in case these levels are low.
4. Increase your protein intake to at least half a gram per half kilo of bodyweight per day if you can. This is a moderate level not found to tax the kidneys in those with kidney dysfunction; those with healthy kidneys could possibly double this. Exercise with weights, but minimise aerobic exercise. One hour 3-4 times a week is enough if done correctly.
5. Try and persuade your doctor to prescribe anabolic steroids if nothing else works.

12345

great responses to HAART. Protruding bellies, flat butts, increased breasts and neck size, 'buffalo humps', and protruding veins on thinning arms and legs and sunken cheeks were being reported. I knew then that my work was not over!

A lot has been learned since then, even though researchers cannot agree on a definition and treatment for this multi-factorial syndrome. I personally have learned a lot through my years of treatment advocacy for wasting syndrome and now for lipodystrophy. The situation with lipodystrophy today reminds me of the early days of wasting syndrome.

Five years ago a US study[1] found that close to 25% of people on HAART were experiencing unintentional weight loss and wasting. Although differentiating between loss of muscle (true wasting) and lipoatrophy-related fat loss is difficult without the use of body scans like DEXA or CT, scientists now think that those who start HAART when they are overweight tend to lose more fat than muscle, while those who start HAART when they are lean tend to lose more muscle.

And people are still wasting today. A recent US study[2] found that the proportion of HIV-positive individuals who experienced unintentional weight loss of 5% or more increased significantly between 1995 and 2003. Wasting may be a less obvious problem today, but it still can affect people's long-term survival.

It is obvious that managing body shape and metabolic changes when you have HIV is not an easy task. It is still imperative for the HIV community to search for ways to deal with body shape changes until clinicians agree on what standard guidelines should include. Like the days of rapid wasting, we really cannot just sit and wait for answers!

Eating right and going to the gym are things we can do for ourselves. I wish there was a pill that had all the benefits of exercise since so many people have such a difficult time adhering to a routine in the long term. It takes a strong commitment to adhere to diet and exercise programmes, but the benefits can be the best motivators to many. My main motivator is the fear of falling apart as I age with HIV!

Exercise your mind as well. Keeping yourself informed through HIV information providers like NAM, internet discussion groups, lectures, newsletters, support groups, and learning from other diseases, like diabetes, will keep us empowered with the latest information to not just survive, but also to age well while coexisting with this virus, and hopefully buy us some time until we have a cure. ■

further information

For comprehensive resistance exercise tips, including short videos showing the correct form for each exercise, Nelson Vergel recommends: www.exrx.net/Lists/Directory.html

For more information on the US approach to the medical use of anabolic steroids, visit http://www.medibolics.com

nelson's top five tips for losing fat 12345

1. Cut calories and fill yourself up with fruits, vegetables, grains and lean meats. Eat small frequent meals.
2. Exercise with weights/machines 3-4 times a week for an hour, and also do cardiovascular exercise (fast walking, light jogging, etc.) for at least 30 minutes a day after weight training. Make sure that you sweat!
3. Ask you doctor to check your hormone levels and your thyroid function since low levels of testosterone or thyroxin can make you prone to gaining more fat.
4. Get your lipids and blood sugar under control with a healthy diet, regular exercise, and medicines if necessary.
5. Beware of companies that claim their weight loss/appetite suppressant supplements or "growth hormone precursors" work. They don't. Most weight loss supplements have stimulants that can affect mood and increase blood pressure and cardiovascular risks.

12345

news in brief

side-effects

Side-effects main reason for switch from first anti-HIV regimen

The reason more than half of people on their first anti-HIV therapy regimen switch to another combination is because of side-effects, according to a new report from the British HIV Association (BHIVA). This compares with a third who changed regimens due to 'virological failure'.

The most common side-effects seen were metabolic problems, including fat loss (lipoatrophy), high blood pressure, high triglycerides, and central fat gain; central nervous system-related side-effects, due to efavirenz (*Sustiva*); gastrointestinal problems and peripheral neuropathy.

Of those who switched due to the fact their viral load was no longer 'undetectable' (termed 'virological failure'), worringly, one in four did not obtain a resistance test result before switching therapy, which is recommended in BHIVA guidelines, and many waited too long before switching, increasing the risk of resistance.

The key messages from BHIVA were that "clinical centres should reassess their practice so as to minimise delay before changing therapy in patients with virological failure", and that they should "ensure appropriate use of resistance testing".

drug development

Second company halts CCR5 inhibitor study

Schering Plough has halted a phase II study of its experimental CCR5 antagonist, vicriviroc, in treatment-naïve patients due to early viral load rebound in patients receiving the drug. A study in treatment-experienced patients will continue, but the omens are not good for the further development of this drug, or for the whole CCR5 antagonist class. In September, Glaxo SmithKline (GSK) halted a phase IIb study of its CCR5 anatagonist, aplaviroc, in treatment-naïve patients due to two cases of serious liver enzyme elevation. A week before Schering Plough's announcement, GSK also called a halt to its phase III studies of aplaviroc in treatment-experienced patients, due to a case of liver toxicity. However, Pfizer recently announced that clinical trials into its CCR5 inhibitor maraviroc will continue.

latest research

Fish oils can reduce triglyceride levels

A prescription-only fish oil supplement containing much higher levels of the omega-3 fatty acids, EPA and DHA than can be bought over the counter can significantly reduce triglyceride levels in HIV-positive people taking antiretroviral therapy, according a recent US study. The US data confirm a similar French study that was reported at the Retrovirus Conference in Boston earlier this year. However, whilst the French study reported no increases in LDL ("bad") cholesterol, the US study found that there were some LDL increases in some of the study participants. This is due to the fact that fish oils reduce triglyericides by interfering with LDL production, and, in some individuals, this can lead to LDL increases.

The fish oil supplementation reductions averaged 20% after 16 weeks, and are similar to those seen in people taking fibrates, the lipid-lowering drug class that is prescribed to some HIV-positive people with high triglycerides. Fibrates may also increase LDL cholesterol levels. People taking boosted protease inhibitors like *Kaletra* are more likely to have high triglycerides, usually over 200mg/dl. Reducing triglycerides levels by even 20% can significantly reduce your risk of future heart disease.

Although the US and French brands of high EPA/DHA fish oils that were studied are not available in the UK, another brand, *Omacor*, is available here on prescription. Four capsules of *Omacor* daily would provide similar EPA/DHA levels to those used in these trials, compared with around ten over-the-counter fish oil supplements. Eating around 250g of oily fish, like salmon or mackerel, daily, would also provide these EPA/DHA levels.

new drugs

Tipranavir now available in the UK

European approval has now been granted for tipranavir, Boehringer Ingelheim's protease inhibitor (PI), which is marketed under the trade name *Aptivus*.

The anti-HIV drug is taken in two daily doses of 500mg (two 250mg capsules) and boosted with 200mg (two 100mg capsules) of ritonavir (*Norvir*). It should also be taken in combination with other anti-HIV drugs. It is only approved for patients who have extensive previous experience of antiretroviral therapy and have HIV which is resistant to other PIs.

New data suggest that patients who need so-called 'salvage therapy' should probably use boosted tipranavir together with the injectible fusion inhibitor, T-20 (enfuvirtide, *Fuzeon*), since this is much more effective than boosted tipranavir alone at reducing viral load and improving CD4 counts. However, tipranavir is likely to cost more than other boosted PIs, and T-20 is currently the most expensive antiretroviral available, and this may limit its availability at some clinics now or in the future.

Side-effects of tipranavir include raised liver enzymes and increased levels of blood fats, and tipranavir is known to interact with statins, a class of drugs used to lower blood fats, requiring the dose of tipranavir to be increased. Some antacids can affect tipranavir in this way, too. Tipranavir can also interact with other PIs and with some drugs used to treat infections, such as fluconazole and rifampicin, requiring careful monitoring.

latest research

Measuring *Sustiva* levels can predict side-effects

Spanish researchers have found that patients who have been taking long-term antiretroviral therapy, including the non-nucleoside transcriptase inhibitor (NNRTI) efavirenz (*Sustiva*), are much more likely to keep experiencing central nervous system side-effects, such as depression or sleeping problems, if they have high blood concentrations of efavirenz. Using therapeutic drug monitoring (TDM), which measures the concentration of efavirenz in the blood, they found that those with levels above 2.74µg/ml were almost six times more likely to develop efavirenz-related side-effects. These side-effects can include sleep disturbances such as insomnia and vivid dreams or nightmares, poor concentration, dizziness, depression, or even suicidal thoughts. Generally, central nervous system side-effects caused by efavirenz tend to become mild and disappear or become less intense after the first few weeks or months of treatment, but some people are prone to having higher levels than normal, including women, people who are underweight, and people of African ethnicity. The researchers suggest that TDM would allow for doses of efavirenz to be adjusted and this should reduce or prevent further side-effects.

the new hiv news update from nam

news from *hiv weekly*

St John's wort

An American laboratory study has found that a protein in the herbal antidepressant St John's wort is able to inhibit the replication of HIV.

The results of this study were picked up by some of the popular media and misrepresented. In particular, it should be noted that St John's wort has an interaction with protease inhibitors resulting in low levels of anti-HIV drugs in the blood which could lead to the development of drug resistant HIV.

The American researchers who conducted the study also warn against taking St John's wort tablets bought over the counter as an HIV treatment. They emphasise that their study was conducted in a laboratory and the same results might not be produced in humans. They also caution, "even if the [anti-HIV] protein were available in [St John's wort] tablets, we don't know how much might be present and whether the protein would be effective."

It makes good sense to talk to your HIV doctor or another member of your HIV healthcare team about any drugs you are taking in addition to drugs prescribed by them. This includes complementary, herbal and alternative treatments, medicines bought over the counter from chemists, and recreational drugs.

subscribe to *hiv weekly*

NAM has launched a new, weekly email bulletin, *HIV Weekly*, that provides people affected by HIV with a concise, plain English digest of the very latest HIV news. The bulletin is edited by Michael Carter, NAM's patient information and news editor. One of the unique benefits of *HIV Weekly* is the inclusion of hyperlinks within the stories so that you can quickly and easily access further information on NAM's website, aidsmap.com, with the click of a mouse. Information and news about the latest NAM treatment information resources will also be included in the bulletin.

To receive your free weekly news digest visit www.aidsmap.com/hivweekly

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what should i be eating?

Michelle Phillpot, specialist dietician at London's Chelsea & Westminster Hospital, answers Edwin J Bernard's questions about HIV, food and weight.

What are the critical issues for people living with HIV when it comes to being a healthy weight?

It's important to be, or at least know, your usual body weight, so that if you lose or gain weight then you know what your usual weight should be. That's because weight loss is usually an indication of illness or an infection, and gaining too much weight, especially around your middle increases your risks of diabetes and heart disease, which is also increased with HIV, particularly if you are on anti-HIV treatment.

You used to only need to see a dietician when you were wasting. Who needs to see a dietician these days?

We still see patients with wasting, but we now also see people with body shape changes, and blood fat and sugar metabolism problems. We're focusing more these days on health promotion, trying to prevent long-term chronic diseases, rather than simply saying, 'You need to get fat', as we used to. We are in the business of trying to get people to adopt healthy lifestyles. So

Low GI diet basics

- Use breakfast cereals based on oats, barley and bran.
- Use "grainy" breads made with wholegrains such as pumpernickel, rye or granary.
- Eat potatoes in their skin to reduce the GI.
- Enjoy all types of fruit and vegetables.
- Eat plenty of salad vegetables with a healthy oil (walnut, pumpkin seed, hazelnut, olive) and vinegar dressing.

we look at smoking cessation, regular exercise, and healthy eating to prevent diabetes and heart disease, illnesses that are happening increasingly more frequently in people with HIV. Some of our patients are having heart attacks in their late 30s and early 40s.

How can you tell if someone has lipodystrophy, is too fat, or has lost lean body mass, when these three weight issues could actually all be happening at the same time?

Lipodystrophy can be hard to diagnose. When you gain weight around your belly or breasts we need to know if it's 'middle-age spread' [fat gain beneath the skin associated with eating too much and not exercising], or if it's HIV-associated fat gain in the abdomen [increased fat around the organs, known as visceral fat]. It's important to get the right diagnosis, to know if your fat has moved around your body, or whether you are also losing weight. Body fat measurements or DEXA scans [expensive and not routinely available at some clinics, however] can help to figure this out, but also photographs of how you used to look can help, too.

Should everyone with HIV spend time reviewing their diet, no matter how fat or thin, or well or ill they may be?

I think it's really important. The Government's healthy eating guide, *The Balance of Good Health,* is applicable to everyone, whether or not you are living with HIV. Basically your diet is considered to be healthy when you base your meals on higher fibre starchy foods, like wholegrain cereals, wholemeal breads and pastas, or potatoes in their skins; eat five or more portions of fruit and veg; eat more fatty fish and less fatty meat; cut down on sugary and salty foods; drink plenty of water; and don't skip breakfast.

Is your advice different for people who need to lose or gain weight?

Basic healthy eating advice is the same. I would say if you want to gain weight, eat more calories, but don't get them from animal fats (like fatty meat or butter) or from fried foods, and do some kind of resistance exercise training, like weights, which builds muscle. If you want to lose weight, burn the calories you are eating by doing exercise, probably a combination of aerobics and weights. Also, try not to be fooled by so-called low fat foods that the supermarkets try and sell you. Fat is usually replaced by sugar, ending up with the same or sometimes even more calories. And remember that something that is 90% fat free still means there's 10% fat! And do you really need a 'low fat' biscuit or chocolate bar? Have a piece of fruit if you need to snack.

If people do want to follow a mainstream diet in order to lose weight, which ones do you recommend?

Well, the current 'fad' diet, *The Low GI Diet* – a ranking of carbohydrates based on their immediate effect on blood glucose (blood sugar) levels – is actually all about healthy eating and isn't so different from what the Government suggests in *The Balance of Good Health.* Unlike the Atkins Diet, there's nothing unhealthy about it. Another healthy diet that can help to normalise your weight, as well as being heart-healthy, is the Mediterranean diet. The Mediterranean diet has always included more cereals, less meat, more fish, more fruit and vegetables, and more olive oil than countries in northern Europe.

the balance of good health

mediterranean diet basics

- Eat lots of vegetables, fruits and cereals.
- Increase the amount of fish you eat.
- Reduce the amount of meat and dairy products.
- Reduce saturated fats (found in fatty meat and dairy products and coconut, palm or hydrogenated oils) and increase unsaturated fats, such as olive oil, nuts, seeds, and avocados.
- Drink red wine in moderation, reduce other alcoholic beverages.

thanks to our funders

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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 ' HIV in 2006: *the future now*', and will be held on 30th January 2006. For more details, go to www.aidsmap.com/forums.

- **www.aidsmap.com**
  Visit our website for the latest news about HIV & AIDS and a fully searchable treatments database and a complete list of HIV treatment centres in the UK.

- **THT Direct Phoneline**
  Offers information and support to help you take decisions about testing and treatment
  0845 1221 200
  Mon-Fr 10am-10pm Sat-Sun, 12pm-6pm

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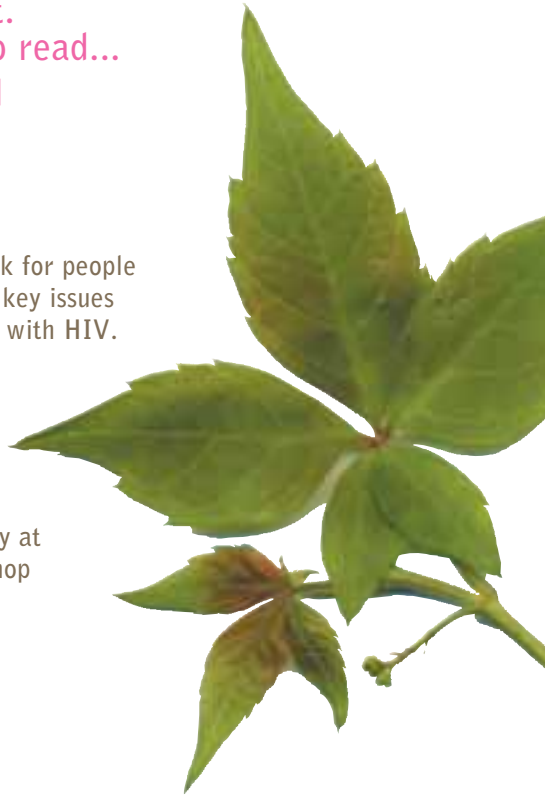

If you would like further information about any of NAM's resources, please call us on +44 (0) 20 7840 0050 or email info@nam.org.uk

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