

aids treatment update

Matters of the heart

Here in the UK, the annual incidence of heart attack in the general population is about 300,000, leading to around 140,000 deaths per year and, according to the British Heart Foundation, "coronary heart disease remains the single most common cause of death of both men and women in the UK."

Since living with HIV now appears to increase the risk of coronary heart disease – especially in the young – experts in the field are trying to ascertain what they can do about it, looking at switching us to more heart-friendly HAART, or treating the underlying fat and sugar metabolism problems that have become part of living with HIV.

American experts suggest that first-line interventions should be patient-led: stopping smoking, eating a more heart-friendly diet, losing excess weight and exercising. These require a collaborative approach between those of us living with HIV and our doctors. This is in line with the latest MEDFASH recommended standards for NHS HIV services, which suggest that "expert patients" with HIV can be empowered through "joint-decision making and support to adopt and maintain a healthy lifestyle."

If you are living with HIV and reading *ATU*, you probably already recognise that there may well be things we can do outside of taking our pills on time that can keep us healthier for longer, and you may feel an added responsibility to make sure that diabetes and heart disease aren't added to your growing list of ailments. However, it is important for all of us to remember to put all risk into perspective and to find a balance between taking HAART and taking care of our heart, both literally and figuratively.

managing metabolic syndrome 2

diet & lipodystrophy 6

news in brief 11

managing metabolic syndrome

2 can changing your lifestyle or switching antiretrovirals help lower your cardiovascular risk? by edwin j bernard

Since we last reported on metabolic abnormalities and HIV (*ATU 123*), evidence continues to accumulate that HIV does indeed increase the likelihood of coronary heart disease (CHD) and stroke, with HAART a contributing, but not sole, factor.

Today, HIV clinicians are increasingly concerned with managing lipodystrophy's metabolic syndrome, since it can be life-threatening, particularly in regards to the risk of cardiovascular disease.

These include:

- high total cholesterol (over 5 mmol/l)
- increased LDL (low density lipoprotein, the so-called 'bad' cholesterol)
- reduced HDL (high density lipoprotein, the so-called 'good' cholesterol)
- high triglycerides (another type of blood fat, or lipid; over 4.4 mmol/l)
- hyperglycaemia (high blood sugar, or glucose; over 5 mmol/l)
- insulin resistance (when more insulin is needed to control blood sugar)
- diabetes (when the pancreas can no longer make enough insulin)

The logic behind their concern is this: even if HAART doesn't actually increase the risk of heart attack by 26% for each year of exposure to antiretroviral therapy, as was estimated by the authors of the DAD study¹, HAART's uncanny ability to keep us alive means that as an increasingly ageing population living with HIV we are, *at the very least*, subject to the same cardiovascular risks as everyone else.

Who is at risk?

Several factors contribute to the risk of coronary heart disease (CHD) in HIV-negative populations, some of which can be modified (like smoking) and some of which cannot (like gender and age). Back in 1985, the British Regional Heart Study identified the relative risk of factors associated with CHD in middle-aged men drawn from general practices in 24 British towns [see TABLE: *Relative risk factors for Coronary Heart Disease in British males aged 40 -50 years*²].

HIV disease now means that CHD is no longer simply a problem that comes with middle age. A recent impressive study from California³ found that, compared with their HIV-negative peers, CHD incidence more than doubled in HIV-positive men aged 25–34 years and was a staggering six-times higher in HIV-positive men aged between 18–25.

HIV-positive women were also found to have a significantly increased risk of heart disease, more than double the risk for women aged 18–24, and about one-and-a-half times the risk for women aged between 25–44. This, concluded the study's authors, put younger HIV-positive people at a risk of CHD "comparable in magnitude with the increase associated with ageing."

Interestingly, when the investigators looked for evidence of a link between HAART and heart disease they found that 18–33 year olds on HAART had double the risk compared to their peers who did not receive antiretroviral therapy, but that once they reached 34, other factors (like smoking and ageing) overshadowed HAART's risks.

First change your lifestyle?

In August, the Infectious Disease Society of America published guidelines⁴ recommending that all adults with HIV be evaluated and treated to reduce their risk of heart disease and stroke, and included detailed discussion of how to do just that.

“Clinicians will need to weigh the risks of new treatment-related toxicities and possibility of virological relapse when switching antiretroviral drugs to the risks of potential drug interactions and new treatment-related toxicities from lipid-lowering agents that are added to existing regimens,” the guidelines’ authors warned.

Consequently, these US guidelines prioritise lifestyle changes over drug switching or lipid lowering therapy. Surprisingly, however, stopping smoking was only mentioned in passing, despite the fact that smoking is the single most significant modifiable lifestyle choice in the prevention of CHD. Diet and exercise were given most space in the guidelines and this month’s accompanying article explores these options in more detail.

However, given the UK’s penchant for fried and sugary foods, high smoking rates and perversely proud coach-potato status, can we afford to be as conservative with lipid interventions on this side of Atlantic?

In June, the Royal Society of Medicine organised a round table meeting on the subject

of lipid management that will be turned into a booklet later this year. Whilst smoking, diet and exercise interventions were discussed, and considered to be equally, if not more important than medical interventions, there did appear to be a consensus amongst the experienced clinicians that it was up to doctors to make the most heart-friendly choices in terms of drug therapy – and to monitor the correct metabolic parameters regularly – since many patients are simply not motivated enough to make lifestyle changes until it is too late.

Assessing the risks

The US guidelines review the latest information on the prevalence and incidence of high total, lowered HDL and increased LDL cholesterol, and high triglycerides, and their relationship with cardiovascular disease in people with HIV on HAART, and recommend that antiretroviral drug switching and/or lipid lowering therapy should be initiated, depending on an individual’s 10 year-risk of CHD, which they base on the Framingham Heart Study risk assessment tool⁵.

However, this may not be sensitive enough for CHD risk assessment in people with HIV, according to Dr Devi Nair, the Royal Free’s lipid specialist who manages many HIV patients with metabolic disorders, and one of the round table participants. “One of the problems with assessing cardiovascular risk in patients with HIV is that because they are mostly young, even though they might have high

Relative risk factors for Coronary Heart Disease in British males aged 40 -50 years²

Risk factor	Relative risk
Older age	4.7
Total cholesterol	3.1
Low HDL	2.0
High triglycerides	Disappeared on correction for total cholesterol and HDL
High systolic blood pressure	3.0
High diastolic blood pressure	3.1
Number of smoking years	5.1 (smokers and no-smokers 3)
Body mass index	1.8
Alcohol	No association

bhiva hiv treatment guidelines and lipodystrophy

The four major conclusions regarding lipodystrophy are:

- Insulin resistance should be treated with metformin.
- Abnormal lipid profiles should be treated by switching drugs wherever possible and by the use of both statins and fibrates.
- Exercise and diet may have a modest effect on both body habitus and lipid abnormalities.
- Controlled trial evidence exists for the use of New-Fill injections in established lipodystrophy.

The full guidelines are available online at: <http://www.bhiva.org/guidelines/2003/hiv/index.html>

web links

Several interactive tools are available from the Clinical Care Options For HIV website that may help assess cardiovascular risk factors due the metabolic complications of HIV and HAART. Visit <http://clinicaloptions.com/hiv/manage/cardio/> Free registration is required to access the site.

when to use lipid-lowering drugs

A future ATU will feature a discussion of the use of lipid-lowering drugs in managing metabolic disorders. Visit www.aidsmap.com for the latest information on all aspects of lipodystrophy.

Key conclusions

Metabolic abnormalities are part of lipodystrophy syndrome and are a cause for concern, since the greater the metabolic changes, the higher the risk of heart disease and stroke.

Both HIV, and some HIV drugs, particularly protease inhibitors, increase these risks, along with certain lifestyle choices and some unchangeable factors like how old you are, what gender and ethnicity you are, and whether cardiovascular problems run in the family.

It is possible to change some aspects of your lifestyle to reduce these risks. The most important of these is stopping smoking, but also eating a heart-healthier diet and exercising regularly can make a difference.

Being unable to metabolise blood sugar – known as insulin resistance – or getting diabetes, is probably more of a cardiovascular risk than having high blood fats alone. Medication, diet and exercise can help reduce these risks.

If you are starting on anti-HIV medication for the first time, or want to change from your first combination, it should be relatively easy to find HAART that packs a powerful anti-HIV punch without adding significantly to your cardiovascular risk.

If you have been on several HAART combinations and you or your doctor are concerned it may be adding to your cardiovascular risk, there are lipid-lowering drugs that may help reduce the risk. Additionally, a new protease inhibitor, atazanavir, is now available that may reduce the risk if you switch from another protease inhibitor, although more studies are needed to know how successful this will be in the long-term.

cholesterol, low HDL and high blood pressure and smoke, they would not be considered at risk according to the Framingham calculation, which weights age as an important factor. In HIV patients, because risk factors cluster at a very young age, we have to be more proactive," she argues. "I do not use the Framingham calculator; if a patient has a lipid problem, I count up the risk factors. If they have more than one risk factor, I take the problem seriously. If they have insulin resistance, I take it a little more seriously. If they have three or four risk factors, I treat them."

Are high sugar levels more of a concern than high fat levels?

Although the US guidelines focus on cholesterol and triglycerides, there is a growing concern amongst UK clinicians that hyperglycaemia, insulin resistance and diabetes (increasingly severe stages of the same disease process – an inability to metabolise blood sugar or glucose) are more risky than increased lipids in terms of CHD risk. "It is important to realise that insulin resistance is not a sugar disease; rather it is a cardiac problem," says Dr Nair. "Lipid metabolism is linked with insulin resistance and both go hand-in-hand with HAART."

Dr Nair takes elevated glucose levels very seriously in terms of CHD risk, since fasting glucose levels above 5 mmol/l signifies insulin resistance. "The clock starts ticking for cardiovascular disease before people become hyperglycaemic," she says. "The quality of LDL is also different in the presence of insulin resistance: the LDL particles are small, dense and more atherogenic."

"The prevalence of insulin resistance is much higher in HIV patients who take HAART," adds Dr Nair. "Infection with HIV itself does not make people insulin resistant, in fact insulin sensitivity is better if the patient is not treated and has infection with HIV that is not controlled. Only when patients start taking drugs and get better does insulin resistance develop."

Insulin resistance will eventually lead to diabetes, which adds considerably to the risk of CHD: people diagnosed with diabetes have a similar level of heart attack risk to people who have suffered a heart attack in the past eight

years. "In addition," notes Dr Nair, "the inflammation which is part of insulin resistance adds to their risk further because the cytokines produced contributes to atherogeneity."

The latest US Guidelines don't shy away from the issue, but see it as secondary to high lipids. The latest British HIV Association (BHIVA) Guidelines⁶ take it more seriously, however, and include the recommendation that "insulin resistance should be treated with metformin", as the first of only four conclusions in their section on lipodystrophy.

Is switching from PIs the best option?

A recent systematic review of both the published literature and conference abstracts on the relationship between protease inhibitor (PI) use and cardiovascular risk has found that with the exception of atazanavir, all currently available PIs do appear to elevate risk factors for heart disease⁷. The US guidelines note that "lipid abnormalities tend to be most marked with ritonavir and lopinavir/ritonavir (*Kaletra*). Amprenavir and nelfinavir tend to have intermediate effects, whereas indinavir and saquinavir tend to have the fewest effects." Preliminary reports suggest that atazanavir, the latest PI, currently only available in the UK to a limited number of people through an expanded access scheme, "appears to have little, if any, effect on lipid concentrations."

The NNRTIs efavirenz and nevirapine also cause alterations in lipid levels, "although generally to a lesser degree than has been observed with PIs," according to the US guidelines. However, the recent 2NN study appeared to favour nevirapine over efavirenz regarding cholesterol and triglyceride levels⁸ although many clinicians still have concerns about the potency of nevirapine compared with efavirenz as well as nevirapine's liver toxicities.

The recently completed NEFA study compared the effects of switching from a protease inhibitor to abacavir, nevirapine or efavirenz⁹. Although this study found a trend towards a higher virological rebound rate in those who switched to abacavir, failures were almost entirely confined to people who had received dual nucleoside analogue treatment in the past. Abacavir-treated patients were significantly less

likely to require lipid-lowering medication by the end of the study and had significantly lower total cholesterol after 48 weeks.

Less is known about the differing effects of PIs on insulin resistance: a 2000 review found that indinavir appeared to have more of an effect on insulin levels than nelfinavir or saquinavir, but pointed out that the statistical standards of the study were weak¹⁰. The NEFA study found that after switching from a protease inhibitor, glucose levels fell in nevirapine and abacavir-treated patients, but not in the efavirenz group.

Heart-friendlier HAART

Are some antiretrovirals less atherogenic? Is it possible to switch to these and/or use them as first-line therapy in the treatment-naïve?

Preliminary data suggest that both tenofovir and atazanavir may permit the use of more atherogenic agents as part of HAART, on the assumption that either drug exerts a benign effect.

Two years into a three year study comparing tenofovir with stavudine, alongside lamivudine and efavirenz, the only significant differences between the two arms of the study appear to be higher fasting cholesterol and triglyceride levels in the stavudine-treated patients¹¹. Given efavirenz's tendency to increase lipids, and a lack of previous evidence that stavudine raises lipid levels¹² these results suggest that efavirenz could be the agent affecting lipids, and tenofovir may actually be exerting a moderating effect, rather than stavudine a negative effect. More data is needed before this theory is proved, or disproved, however.

The only switching study using atazanavir reported so far, found that after switching from nelfinavir to (unboosted) atazanavir, significant reductions in total cholesterol (16%), LDL cholesterol (21%) and triglycerides (28%) and a significant increase in high density lipoprotein (HDL) "good" cholesterol (5%) were seen. Prior to receiving nelfinavir, however, the study population were drug-naïve, and appeared to continue to sustain low viral load without the need for boosting¹³. A Bristol Myers Squibb (BMS)-sponsored Phase IIIB study is currently recruiting in the US looking at the effect of serum LDL cholesterol when switching from other protease inhibitor regimens to atazanavir.

Professor Brian Gazzard suggests that given current evidence switching from a PI-based regimen to atazanavir – rather than nevirapine or abacavir – may well be the best option, because "even if resistance testing does not suggest NNRTI or nucleoside analogue resistance, the possibility of resistance must be relatively high. I would usually opt for atazanavir in the majority of patients who had previously failed an NRTI/NNRTI-containing regime but have not failed a PI."

It is still a little early to come to any firm conclusions, but atazanavir (at least when boosted with ritonavir) may also help reduce lipids in the PI-experienced, whilst keeping viral load under control. The 045 study found that ritonavir-boosted atazanavir was equal to lopinavir/ritonavir in terms of anti-HIV potency and still reduced total cholesterol significantly, whilst keeping fasting triglycerides stable. The same study found that combining atazanavir with saquinavir also appears to be lipid friendly, but is not as potent in terms of sustained viral load compared with atazanavir/ritonavir or lopinavir/ritonavir¹⁴.

It should be noted, however, that atazanavir and tenofovir should not be combined without ritonavir-boosting, according to an August 2003 'Dear Doctor' letter from BMS, since this may risk treatment failure, due to an interaction that reduces atazanavir levels by up to 40%. They suggest that doctors consider boosting atazanavir levels with ritonavir, using the 300/100 mg dose, if atazanavir and tenofovir must be used together.

Do you want to prove them wrong?

The news that HIV alone can increase cardiovascular risk needs to be taken, if you pardon the pun, to heart by everyone living with HIV. Simply being young no longer appears to protect people with HIV from diseases previously associated with middle age. Can we afford to rely on only one head-in-the-sand strategy – let the doctors deal with it – when it is becoming clear that changing to lipid-friendlier HAART or adding lipid-lowering medications is probably not enough to make up for this increased risk? Are the round table clinicians right about our lack of motivation to take better care of ourselves? Do you want to prove them wrong?

references

1. Law M. *HIV Med* 4:1-10, 2003.
2. Shaper AG. *J Epi & Com Health* 39: 197-209, 1985.
3. Currier J. *JAIDS* 33: 506 - 512, 2003.
4. Dubé MP. *CID* 37: 613-27, 2003.
5. see <http://hin.nhlbi.nih.gov/atpii/calculator.asp>
6. see <http://www.bhiva.org/guidelines/2003/hiv/index.html>
7. Rhew DC. *CID* 37: 959-72, 2003.
8. van Leth F. 10th CROI, Boston, abs 752, 2003.
9. Martinez E. *NEJM* 349: 1036-46, 2003.
10. Dubé MP. *CID* 31:1467-75, 2000.
11. Staszewski S. 10th CROI, Boston, abs 564b, 2003.
12. Matthews GV. *JAIDS* 24: 310-5, 2000.
13. Murphy R. 10th CROI, Boston, abs P555, 2003.
14. Badaro R. 2nd IAS Conf, Paris, abs 118, 2003.

glossary

atherogenic Producing the most degenerative changes in artery walls.

buffalo hump A mass of fat and connective tissue on the back of the neck.

cardiovascular Relating to the heart and blood vessels.

cardiovascular disease Includes CHD (about 50%), stroke (about 25%), and other circulatory system diseases.

cholesterol A waxy substance, mostly made by the body and used to produce steroid hormones.

continued on page 7



diet & lipodystrophy

6 is the currently chic carb-free Atkins diet beneficial for lipodystrophy, or is moderation the key? asks megan nicholson

Despite the recent emphasis on dietary interventions to improve the metabolic disorders associated with lipodystrophy, few studies have explored whether the same diets recommended to improve lipids and insulin sensitivity – which are based on evidence largely drawn from HIV-negative population studies – can help with certain physical features of lipodystrophy, particularly central fat (abdominal) accumulation.

Of course, the jury is still out as to whether the fat gain reported by many people on HAART can even be called lipodystrophy. Although increased abdominal fat is regarded as a core feature of lipodystrophy according to the HIV Lipodystrophy Case Definition Group¹, recent reports from the ongoing Fat Redistribution and Metabolism (FRAM) Study suggest that HIV-positive men and women with lipodystrophy actually have less visceral abdominal fat than their HIV-negative counterparts².

Dietary strategies for managing metabolic disorders

Both the UK³ and American⁴ guidelines on the management of lipodystrophy-related metabolic disorders stress the importance of dietary advice.

The American guidelines generally recommend eating more fibre and reducing fat intake. When high triglycerides are an issue, saturated fats should be replaced with monounsaturated fat or omega-3 polyunsaturated fats (eg fish oils). When

wasting and lipid disorders occur together, however, wasting should be addressed first (ie fat may need to be increased to add calories), since it is riskier in terms of HIV disease progression.

The latest British HIV Association (BHIVA) guidelines also suggest that dietary advice may play a role in the prevention and management of lipodystrophy. The guidelines authors suggests a 'Mediterranean diet' rich in omega-3, fibre, and fruits and vegetables. This diet is known to reduce risk factors for cardiovascular disease in the general population.

There is some evidence that this low-fat, omega-3-rich, high-fibre diet can improve metabolic function in people taking anti-HIV treatments. A UK study, which compared lipid lowering agents with dietary advice found that the latter showed modest effects⁵. But a Spanish team reported that whilst a low-fat diet in people on HAART with high lipids had moderate success in lowering lipids it had almost no impact on central fat accumulation⁶. A U.S. study of 62 men and 23 women with lipodystrophy found that, on average, people who consumed more dietary fibre had lower insulin levels^{7, 8}. And a laboratory study reported that omega-3 polyunsaturated fats may have a protective impact on fat cells exposed to protease inhibitors⁹.

But will these strategies really help you reduce your risk of cardiovascular disease as well as help

you lose (apparently) lipodystrophy-associated excess fat without worsening fat loss elsewhere?

Unfortunately, more than six years after the first reports of lipodystrophy, there are no reliable studies comparing different dietary strategies in people with HIV. Alternative weight loss strategies such as the Atkins diet¹⁰ and the low glycemic index diet (the GI diet) have not been studied. However, current theories about the causes of central fat accumulation seem to suggest that diets which target insulin sensitivity and sugar metabolism may play a role in reversing this part of lipodystrophy syndrome.

How HIV meds interfere with metabolism

The factors driving body fat changes and metabolic abnormalities in HIV-positive people have not been definitively established. Two classes of anti-HIV drugs – protease inhibitors (PIs) and nucleoside analogue reverse transcriptase inhibitors (NRTIs) – are known to contribute to the syndrome but exactly how remains the subject of speculation and research.

There are several theories regarding how HIV and/or anti-HIV drugs might be causing peripheral fat loss (lipoatrophy), fat gain (lipohypertrophy) and metabolic disorders.

- Mitochondrial toxicity. Damage to mitochondrial DNA by NRTIs, particularly stavudine (d4T), may disrupt energy metabolism, damage cells and hasten programmed cell death (apoptosis). This theory can account for a range of symptoms including loss of fat tissue, high lactate levels and peripheral neuropathy.
- Disruption to fat metabolism. PIs disrupt lipid metabolism, leading to excess production of triglycerides, cholesterol and lactate. PIs and/or NRTIs may interact to undermine the making of fat cells and increase programmed cell death, as well as disrupting production of energy from fatty acids. Possible mechanisms include the disruption of certain cytokines (chemical messengers eg TNF alpha) and the effect of PIs on transcription factors (eg SREBP1).
- Inhibition of insulin. Inhibition of some glucose transporters by most protease inhibitors may be one element causing insulin resistance. This may be compounded by disruptions to fat cells and fat metabolism. Insulin resistance may be driving central fat accumulation and 'buffalo hump' by causing reduced uptake of sugar, triggering a release of fatty acids into the blood.
- Chronic immune activation due to HIV may contribute to some or all of these mechanisms.

all you can eat?

The best way to feel good about your body and your blood fat levels is to pick and choose – buffet-style – what suits you best. General sound advice includes:

- Eat more fibre (eg whole grains, beans, pulses, most fruits and vegetables).
- Eat fewer refined carbohydrates (eg white bread, cakes, pizza).
- Reduce and replace consumption of saturated fats (eg all fat derived from animals and coconuts) and trans fats (eg processed cakes and biscuits, snack foods, takeaway food) with more beneficial monounsaturated fats (eg olive oil, avocado, almonds, macadamia nuts) and polyunsaturated fats (nuts and seeds, sunflower oil, safflower oil, soybean oil, and foods rich in omega-3).
- Eat more fish, which contains omega-3 fatty acids (eg salmon, tuna, sardines, mackerel).
- Do regular exercise – either moderate aerobic exercise (like brisk walking or swimming) or resistance exercise (like weight training) which strengthens your muscles – but don't overdo either.
- Quit smoking!

glossary contd

coronary heart disease (CHD) Occurs when the walls of the coronary arteries become narrowed by a gradual fatty build-up. Heart attack and angina are main symptoms.

diabetes Raised concentration of sugar in the blood, due to insulin production or action (insulin resistance, or reduced insulin sensitivity, are also known as pre-diabetes).

glycogen Glucose stored in cells, predominantly found in the liver.

HAART Highly Active Antiretroviral Therapy: anti-HIV combination therapy with 3 or more drugs.

hyperglycaemia High blood glucose level.

insulin Pancreatic hormone that lowers blood sugar levels.

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

lipid General term for fats.

metabolism The mechanisms which sustain life, turning carbohydrates and fat into energy, and protein into muscle.

mitochondrial toxicity Mitochondria are structures in human cells responsible for energy production. When damaged by anti-HIV drugs, this can cause a wide range of side-effects, including possibly fat loss.

myopathy A disorder of muscle tissue or muscles.

continued on page 11

diet & lipodystrophy continued

Can the Atkins diet help with lipodystrophy?

The fashionable Atkins diet has four phases: a strict two-week induction period where carbohydrate (carb) intake is limited to 20 grams each day; an ongoing weight loss phase where you can eat up to 100 grams of carbs daily, and the pre-maintenance and maintenance phases where carb intake remains restricted but you maintain a stable weight. Carbohydrates include all foods made up of sugar or starch, including bread, pasta, fruits and vegetables.

Two studies published in the *New England Journal of Medicine* earlier this year found that this low-carb strategy does lead to weight loss and improves metabolic parameters in HIV-negative people. In one of the studies, 132 obese people with a high prevalence of diabetes or pre-diabetes (insulin resistance) were randomised to either a low-fat, calorie-restricted diet or a low-carbohydrate diet. Average weight loss was 5.8 kg in the low-carb group and 1.9 kg in the low-fat group – a statistically significant difference. Measures of metabolic function also improved significantly in the low-carb group – triglycerides fell irrespective of medication and insulin sensitivity improved^{11, 12}.

However, despite some anecdotal success stories from HIV-positive people with central fat accumulation, experts unanimously agree that the Atkins diet may have serious health consequences for HIV-positive people in both the short- and long-term.

According to Dr Devi Nair, a lipidologist from London's Royal Free Hospital, and two specialist HIV dieticians – Pip Greenop and Simon Sadler from Australia, where the Atkins diet is also currently in vogue – Atkins is an unbalanced and restrictive diet which is not sustainable or safe in the longer term, despite some apparently attractive short-term benefits.

The Atkins diet raises many specific concerns for people with HIV infection:

- The Atkins diet is high in saturated fats, and thus may contribute to elevated cholesterol and the long-term risk of artery disease. Dr Nair suggests that a modified Atkins diet – which reduces, but does not eliminate carbs (replacing extra carbs with more protein and fats that are heart-healthy, like olive and fish oils) – may be a healthier alternative.
- The body needs glucose. When glucose consumption is dramatically restricted, the body accesses its glycogen stores. If glycogen stores are not replenished through dietary glucose, fatigue may occur and contribute to muscle wasting. Maintaining muscle is known to preserve immune function and slow disease progression in people with HIV.
- Low consumption of fibre may have negative effects. In people with HIV, treatment with soluble fibre is often recommended to help control cholesterol, relieve treatment-associated diarrhoea, and maximise gut health.
- Low consumption of carbs may alter calcium metabolism, causing kidney stones (already a risk in people taking indinavir) or reducing bone mineral density, which is already a problem for certain people with HIV, due to either HIV itself or HAART.
- A high-protein diet may be difficult for people with kidney damage to tolerate, and since tenofovir has been associated with kidney toxicity, caution should be taken if on this drug and eating a high protein diet.
- A low-carb diet may remove many B vitamins and antioxidant nutrients from the diet. Low vitamin and mineral consumption may compound these deficiencies in HIV-positive people.

The nature of the weight loss seen in people on Atkins is also suspect. Initial weight loss comes from fluid (water) loss, as the body raids its stores of glycogen.

The low GI diet: a healthier alternative?

Dietician Jennie Brand-Miller from the University of Sydney points out that a randomised study comparing four diets has shown that people on a low glycemic index diet lose more fat than people on a high protein diet, even though overall weight loss is comparable. The low GI diet also aims to reduce blood glucose and promote insulin function and weight loss. Could this way of eating be a less radical alternative to Atkins?

A case study published last year reported successful treatment of lipodystrophy and metabolic improvements using a high-fibre, low GI diet plus regular aerobic exercise and weight training. The man's diet was made up of 15% protein, 30% fat and 55% carbs including at least 25 grams of dietary fibre daily. After four months, the man had experienced a 52% reduction in visceral fat and his weight had fallen by a total of 8 kg. His LDL or 'bad' cholesterol had fallen by 30%, fasting insulin by 3.5% and insulin resistance by 15%¹¹.

Key elements of the low GI strategy have been successfully incorporated into the management and prevention of diabetes, insulin resistance and hyperglycaemia.

The glycemic index is a way of comparing foods in terms of how quickly sugar is absorbed into

the blood stream. Some foods such as potatoes, white flour products and rice cakes are processed quickly, producing a rapid and dramatic peak in blood sugar levels. These simple carbohydrates are called high GI foods. Other foods are turned into blood sugars more slowly, and produce a less dramatic and more enduring rise in blood sugar. These are complex carbohydrates, or low GI foods. Examples include *al dente* pasta, brown rice, wholegrain bread, apples, chickpeas and porridge.

A detailed list of GIs for over 750 types of food can be found free on the internet in the *American Journal of Clinical Nutrition* at <http://www.ajcn.org/cgi/content/full/76/1/5>¹⁴.

A low GI diet involves reducing your intake of refined foods, potatoes and rice, and eating more fibre and unsaturated fats. Simple changes such as replacing white bread with wholemeal bread, or making sure that you never eat simple carbohydrates on their own (by adding unsaturated fat and/or protein), can help reduce blood sugar levels after eating. This may help with sugar metabolism and improve insulin sensitivity.

The glycemic index of food also influences hunger and weight loss. The rapid peak in blood sugar associated with high GI foods is followed by a drop in blood sugar which produces hunger. In contrast, low GI foods delay the return of hunger: which is

what kind of exercise is best?

The ability of frequent aerobic exercise (30 minutes, three times a week) to lower cholesterol levels and improve insulin sensitivity in the general population is well established. However, two recent studies show that moderate resistance and aerobic exercise together may have more benefits.

A small study presented at the Fifth International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV involved 37 people with high insulin levels and/or impaired glucose tolerance and physical signs of lipodystrophy. Participants were randomised to exercise (one hour of aerobic and strength training, three times a week) plus the anti-diabetes drug metformin or metformin alone. Data on 25 people who completed 3 months of treatment found that the exercise/metformin group had a significantly greater reduction in waist-to-hip ratio, lower blood pressure, more thigh muscle, and significantly greater reductions in fasting insulin levels than the group who took medication only¹⁶.

There is also evidence that whilst regular aerobic exercise or combined aerobic and resistance training appears to lower triglycerides and may reduce insulin resistance in people with lipodystrophy, it may also make facial or limb fat loss worse.¹⁷.

references

1. HIV Lipodystrophy Case Definition Group. *Lancet* 361: 726-35, 2003. http://www.ti3m.com/hiv/default_id.htm
2. Zolopa A. 10th CROI, Boston, abstract 774, 2003.
3. Dubé MP. *Clin Infect Dis* 37:613-627, 2003.
4. available at <http://www.bhiva.org/guidelines/2003/hiv/index.html>
5. Moyle G. *AIDS* 15(12):1503-1508, 2001.
6. Barrios A. *AIDS* 16(15):2079-2081, 2002.
7. Hadigan C. *Clin Infect Dis* 33(5):710-7, 2001.
8. Hadigan C. *Clin Infect Dis* 37 (supp 2) 101-104, 2003
9. Domingo JC. 5th Intl Lipodystrophy Workshop, Paris, abstract 27, *Antivir Ther* 8:L24, 2003.
10. Atkins, RC. *Dr Atkins' New Diet Revolution*, Vermilion; ISBN: 0091867835
11. Samaha FF. *NEJM* 348(21):2074-2081, 2003.
12. Foster GD. *NEJM* 348(21): 2082-2090, 2003.
13. Roubenoff R. *Clin Infect Dis* 34(3):390-3, 2002.
14. Foster-Powell K. *Am J Nutrition* 76:5-56, 2002.
15. Sears B, *The Zone Diet*, HarperCollins; ISBN: 0722536925
- 15a. *Am J Clin Nutr*. 2003;78:671-672, 734-741
16. Driscoll SD. 5th Intl Lipodystrophy Workshop, Paris, abstract 4, *Antiviral Therapy* 8:L7, 2003.
17. Gavrilu A. *Clin Infect Dis* 36: 1593-1601, 2003.



diet & lipodystrophy continued

why porridge is a long-lasting morning fuel, compared with toast and jam. By controlling hunger, low GI foods can contribute to weight loss.

Enter the Zone

Another alternative is The Zone diet¹⁵, which is popular in North America, and which essentially consists of eating meals that contain approximately 30% protein, 40% carbohydrates and 30% fat – with an emphasis on unsaturated fats – at every meal. To lose weight, you combine this strategy with restricting calories (typically 800-1200 calories/day), but by not restricting calories it can also be used to simply control sugar and insulin levels in the blood, as a recent study observed^{15a}. Here, 12 HIV-negative people with adult onset diabetes consumed a zone-like diet followed by a standard diet for five weeks each, separated by a two- to five-week washout period. The ratio of protein to carbohydrate to fat was 30:40:30 in the zone-like diet and 15:55:30 in the standard diet. Although weight remained stable throughout the study, the zone-like diet improved glycemic control and lipid profiles without adversely affecting kidney function, or increasing risk factors for cardiovascular disease.

Food for thought

At this stage, there is no clear scientific evidence that any particular dietary strategy will help you lose your belly whilst keeping your facial or limb fat loss to a minimum. If you are considering changes to your diet, discussion with your doctor and/or a dietician is recommended. Standard lipid-lowering or fat loss advice is not always appropriate for everyone with HIV.

Additionally, no diet can work in isolation: exercise and other lifestyle changes, particularly stopping smoking, are known to be other key elements in maintaining a healthy heart.

It is also crucial that dietary changes (eg reducing fat intake) do not reduce absorption of your HIV medications, or cause you to lose weight if you are already wasting.

The final point to bear in mind is that attempts to lose your central fat accumulation through regular intense aerobic exercise may worsen fat loss in your face and limbs. Although weight training to build muscles may help to offset this problem, adding anabolic steroids to your muscle-building regime can actually worsen facial lipoatrophy.

key conclusions

- Dietary strategies and exercise may help lower blood fats and improve insulin function but there is little evidence that any particular dietary strategy will reduce central fat accumulation or other manifestations of lipodystrophy.
- Evidence that a low-carb or low GI strategy can improve lipodystrophy in HIV-positive people is anecdotal.
- Many factors can influence an appropriate diet for people with HIV – stage of disease, metabolic measures, lipodystrophy or fat wasting, individual food preferences, and disposable income. Consultation with a specialist HIV dietician is recommended before embarking on a new dietary strategy.

MEDFASH Guidelines published

The Medical Foundation for AIDS and Sexual Health (MEDFASH) - a charity that promotes excellence in the prevention and management of HIV - have published their 'Recommended standards for NHS HIV services'. This timely publication outlines 12 broad areas where the NHS could improve in the provision of HIV services. These include earlier HIV diagnoses, empowering people with HIV, and ameliorating care from GPs, in the GUM clinic, from dentists, and in hospitals. By including standards regarding the support of women with HIV who wish to become pregnant, and the inclusion of families affected by HIV, they also bring to the forefront the issue of the changing demographics of people living with HIV in the UK, which is now affecting almost as many heterosexuals as gay men. A free copy of the standards is available directly from MEDFASH, BMA House, Tavistock Square, London WC1H 9JP, 020 7383 6345, www.medfash.org.uk.

Vitamin C and PIs

Taking 1000 mg of vitamin C a day reduces indinavir concentrations in the blood by up to 32%, according to research conducted amongst HIV-negative volunteers and presented in Chicago at the 43rd ICAAC Conference in September. This was based on the 800 mg three times daily dose of indinavir, however, and should have no effect on ritonavir-boosted indinavir. According to the researchers, vitamin C appears to have some relationship with both the P450-3A4 enzyme and p-glycoprotein - both of which affect levels of all PIs - but as yet the clinical significance is unknown. However, "our findings would suggest that high doses of vitamin C could lead to a reduction of PI effectiveness," say the authors. The study

only lasted seven days, and it is possible that chronic vitamin C consumption and/or higher doses may make an even larger difference. Given that many people with HIV take vitamin C this time of year to help avoid or reduce severity of colds and flu (the effectiveness of which is unknown), it might be prudent to rethink this strategy, particularly if you are on a PI that is not boosted with ritonavir. A future ATU will examine the significance of interactions between antiretrovirals and the other medications, drugs, food and drink that we consume. Visit www.aidsmap.com and search for 'drug interactions' or enter the name of the individual antiretroviral for further information.

Slain D. 43rd ICAAC, abstract A-1610, 2003.

Tenofovir warning

Gilead, the manufacturer of the nucleotide analogue tenofovir (Viread) has written to doctors in the US warning them not to use the drug in combination with the NRTIs ddI and 3TC after a 24 week pilot study showed that patients using this combination experienced a high rate of virological failure and NRTI resistance.

Free 'flu jab available

Everyone with HIV in the UK is entitled to the influenza vaccine free of charge, and if you want one, you should book an appointment with your GP before the end of November. Although there is conflicting evidence regarding the benefits of the 'flu jab in people with HIV, 'flu can lead to serious illnesses such as bronchitis and pneumonia. The factsheet included with this month's ATU provides more information. For detailed research on the pros and cons of 'flu vaccination visit www.aidsmap.com and enter the search term 'vaccinations and immunisations.'

glossary contd

National Cholesterol Education Programme US programme aimed at reducing high blood cholesterol.

www.nhlbi.nih.gov/about/ncep/index.htm

NNRTI Non nucleoside reverse transcriptase inhibitor.

NRTI Nucleoside analogue reverse transcriptase inhibitor.

PI Protease inhibitor. triglycerides The basic 'building blocks' from which fats are formed.

viral load The amount of virus, usually from a blood sample, indicating the extent to which HIV is reproducing in the body.

virological relapse When viral load can be measured after previously being undetectable.

wasting Muscle and fat loss.

nam forum

Mental health and HIV is the subject of the next NAM forum on Monday 27th October, 7-9 pm at University of London Union, Palms Room, 4th Floor, Malet Street, London WC1. The last forum of 2003 will take place on Monday December 1st and will focus on hepatitis and HIV co-infection.

news in brief



credits

editor

Edwin J Bernard

founded by Peter Scott

typesetting & layout

Thomas Paterson

design

Alexander Boxill

printing

Cambrian Printers

ISSN

0969-4706

copyright

©NAM Publications 2003
All rights reserved

charity number

1011220

medical advisory panel

Dr Fiona Boag
Dr Ray Brettle
Professor Janet Darbyshire
Dr Martin Fisher
Professor Brian Gazzard
Dr Diana Gibb
Professor Frances Gotch
Professor Paul Griffiths
Dr Margaret Johnson
Dr Jacqueline Mok
Dr Graeme Moyle
Dr Barry Peters
Dr Gareth Tudor-Williams
Professor Jonathan Weber
Dr Ian Williams
Dr Mike Youle

about NAM

NAM is a charity that exists to support the fight against HIV and AIDS with independent, accurate, up-to-date and accessible information for affected communities, and those working to support them.

For more information, and details of our other publications and services, please contact us, or visit our website, www.aidsmap.com.

disclaimer

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.

thanks to our funders

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

African HIV Policy Network, British HIV Association, International HIV/AIDS Alliance, Scottish Voluntary HIV & AIDS Forum, The European Commission, Government of the United Kingdom - Department of Health, London HIV & GUM Commissioning Consortium, Birmingham area PCTs, East Surrey area PCTs, East Sussex, Brighton & Hove area PCTs, Manchester area PCTs, Manchester City Council, Newcastle PCT, Norfolk area PCTs, Salford Primary Care Trust, South West Essex PCTs, South East Essex PCTs, Stockport Social Services, Trafford North PCT, Trafford South PCT, West Sussex area PCTs, The Allan & Nesta Ferguson Charitable Trust, Crusaid, The Elton John AIDS Foundation, Lloyds TSB Foundation for England & Wales, M-A-C AIDS Fund, Peter Moores Foundation, St Stephen's AIDS Trust, Abbott Laboratories, Boehringer Ingelheim (UK & International), Bristol-Myers Squibb Pharmaceuticals, Delphic Europe (for Tibotec Virco), Gilead Sciences, GlaxoSmithKline, Merck Sharp and Dohme, Positive Action GlaxoSmithKline, Vertex Pharmaceuticals, Visible Genetics, Roche Hepatitis C, Roche Molecular Diagnostics, Roche Products, Serono.

order form

Please set up my subscription to AIDS Treatment Update at the following rate:

- free (for personally affected individuals)
 £75 (professional rate)
 £55 (voluntary organisations rate)

format required

(please tick the format you require):

- paper email (pdf) audio tape

overseas postage costs

(for paper and audio subscriptions only)

within EU please add £10/year

outside EU please add £15/year

name _____

address _____

postcode _____

email address (if applicable) _____

signature _____

total payment due: £ _____ (if applicable)

Payment can be made by cheque (payable to NAM), or call +44 (0) 20 7840 0050 with your credit card details.

- NAM publishes a complete range of information resources about HIV and AIDS. Please tick this box if you would **not** like to receive information about them.
- NAM occasionally undertakes fundraising campaigns to help support its work. Please tick this box if you would **not** like to receive information about them.

subscriptions

free subscriptions for individuals

AIDS Treatment Update is available free to individuals in the UK affected by HIV or AIDS. We ask individuals from overseas to contribute to postage costs.

costs to professionals and organisations

professional/organisational rate:
£75/year
voluntary organisation rate:
£55/year

To begin your subscription simply complete the form opposite and return it to NAM, or call or email us.

AIDS Treatment Update is also available on audio tape, and can be emailed to you as a pdf file. Call NAM on +44 (0)20 7840 0050 for details.

any questions

for an introduction to HIV treatment issues

NAM's information booklets are free to people with HIV. Titles include: **adherence, anti-HIV drugs, clinical trials, glossary, HIV & hepatitis, HIV therapy, lipodystrophy, nutrition, resistance, and viral load & CD4**. Please contact NAM for your copies.

HIV & AIDS Treatments Directory

This is a comprehensive guide to the medical aspects of HIV. Available at only £12.95 to people with HIV and £64.95 to professionals. Please contact us to order your copy.

www.aidsmap.com

Visit our website for the latest news and conference reports, a fully searchable treatments database, and The Wheel – your personal pill planer.

information forums in London

Each month an expert speaker discusses an HIV treatment-related topic. Entry is free. Future forums are advertised inside this newsletter and on our website.

THT Direct Phoneline

0845 1221 200

Mon-Fri 10am-10pm Sat-Sun 12-6pm

i-Base Treatment Phoneline

0808 8006013

Mon-Wed 12-4pm

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