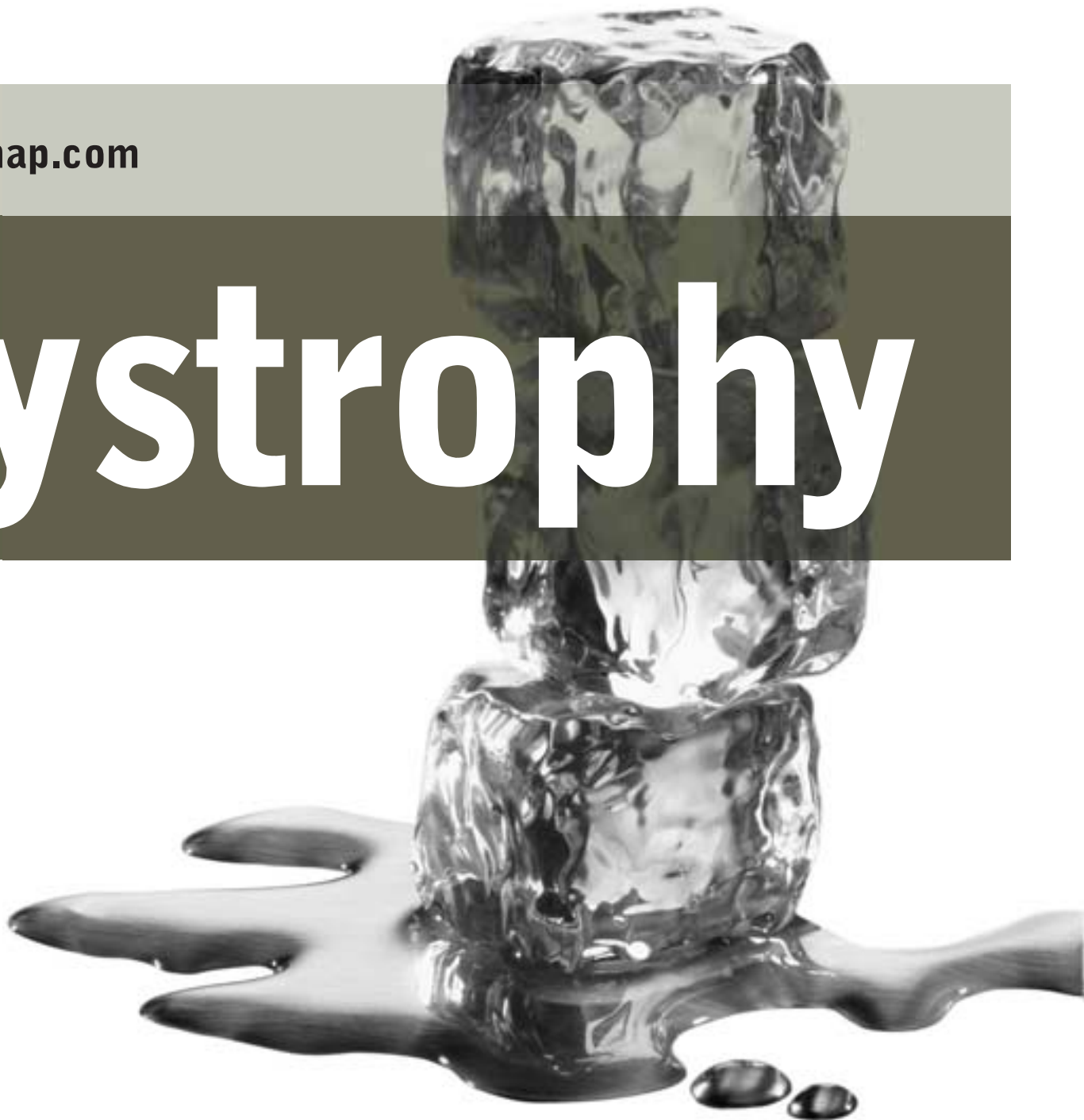


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lipodystrophy

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lipodystrophy

This booklet covers two problems that you may experience when taking combination therapy: changes in body fat and changes in your metabolism, also known as lipodystrophy. It looks at what may cause or contribute to these changes, what the long-term consequences might be, and what can be done to treat these problems. The first part covers body fat changes and the second part covers metabolic changes, but the two problems often occur together. This booklet is not intended to replace discussion with your doctor about your treatment. However, it may help you to decide what questions to ask about any course of treatment you may be considering.

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What is lipodystrophy?

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Body fat changes in HIV are also known as lipodystrophy. Three patterns of body fat changes are being seen in people with HIV who are taking potent combinations of anti-HIV drugs (often called Highly Active Antiretroviral Therapy or HAART for short). These are:

- Gaining fat on the abdomen/belly (central fat), between the shoulder blades, or around the neck or in the breasts (mostly in women).
- Losing fat from under the skin which becomes most obvious in the arms, legs, buttocks and face, resulting in facial wasting, shrunken buttocks and prominent veins on the arms and legs.

Only this particular kind of fat loss is specific to HIV infection. Fat gain may be caused by metabolic changes that also occur in HIV-negative people.

- A mixture of both fat gain and fat loss.

The fat gain is not sub-cutaneous fat (the squidgy fat directly under the skin). Central fat gain is within the abdomen. This makes the belly feel harder; some people have described it as feeling taut, like a football or like pregnancy. This fat accumulation may also interfere with food intake.

The majority of people who develop these changes experience a mixture of both types of body fat change. You may

often hear these fat changes referred to as 'fat redistribution'.

The body fat changes can be accompanied by metabolic changes (rises in levels of fats and sugar in the blood).

A few people will also develop small, unusual fat deposits on other parts of the body, usually the limbs and trunk. These are called lipomas.

Who will develop body fat changes?

3

People taking protease inhibitors and nucleoside analogues (NRTIs) together seem more likely to develop some or all of these changes than people taking these drugs alone. There is also evidence that people who take non-nucleoside analogues (NNRTIs) and certain NRTIs are at risk of developing body fat changes. People with very low CD4 counts before starting treatment are more likely to experience fat loss, regardless of which drugs they take.

There is some evidence to suggest that if you are taking anti-HIV treatment, the following might increase the risk further:

- Most research shows that the longer you take anti-HIV treatment, the more likely you are to have changes in your body fat. Studies have shown that after three years on a combination of nucleoside analogues and a protease inhibitor, 30 to 40% of people will develop body fat changes. It is not yet clear whether the risk carries on growing after this point, or whether most people who will eventually get lipodystrophy can expect to do so within three years of starting treatment with a protease inhibitor and NRTIs.

- People who are overweight are more likely to complain of an increase in central fat.
- Fat loss is more commonly reported in men than women, although women with average or low body weight are more likely to observe loss of fat than women who are overweight.
- Older people are more likely to experience both central fat gain and fat loss from the arms, legs and face. It may be that some of these changes are being confused with the usual body fat changes that occur with ageing – because the syndrome is new it will take time to be sure.
- The extent of immune system damage before starting treatment and the recovery after treatment also seems to influence the risk of body fat changes. A large CD4 cell rise and a past CD4 cell count below 200 have been associated with more severe fat loss (but these may be an indication of very successful treatment or the length of time you have been on treatment, both of which have been suggested as causes of the body fat changes. See HIV treatment and body fat changes on page 5).
- Body fat changes have been less common in children, but tend to become more noticeable in teenagers.

HIV treatment and body fat changes

5

The causes of body fat changes in people with HIV still aren't known for certain. This makes it very difficult to give clear advice about how to avoid lipodystrophy and how to treat the problem.

At first people with HIV and doctors thought body fat changes were caused only by protease inhibitors. In fact, the changes have also been seen in some people who have never taken protease inhibitors – but not as often.

It's not yet clear whether taking a boosted protease inhibitor (a protease inhibitor, such as lopinavir (*Kaletra*), fosamprenavir (*Telzir*), atazanavir (*Reyataz*) or tipranavir (*Aptivus*) which are boosted by

adding a small dose of ritonavir) will increase your risk compared to taking a single protease inhibitor.

6 Do particular drugs cause body fat changes?

We know that some protease inhibitors cause changes in the body's handling of fats and sugar when they are given to people without HIV. This shows that in HIV-positive people, it is the drugs themselves, and not just the disease or the effects of the drugs on the immune system, which are contributing to the problem.

There is now a lot of evidence that two drugs from the NRTI class, d4T (stavudine, *Zerit*), and to a lesser extent, AZT (zidovudine, *Retrovir*) cause fat loss. Because of this it is not recommended that you take d4T or AZT (either by itself or in the combination pills *Combivir* or *Trizivir*) as part of

your first anti-HIV combination. If you are currently taking either d4T or AZT you should be offered the chance to change to either abacavir (*Ziagen*) or tenofovir (*Viread*). Neither of these drugs has been associated with fat loss (in fact, there is evidence that fat loss very slowly improves in people who have switched to them), but they do have other side-effects.

The importance of protease inhibitors to body fat changes is still uncertain. When body fat changes were first noticed in people taking potent combinations of anti-HIV drugs, protease inhibitors were initially blamed and studies have shown

that protease inhibitors do cause both fat changes. It is hoped that newer protease inhibitors which appear to be less toxic will not cause body fat changes, but it is too early to say for certain that this is the case. It is also possible that particular effects of drugs used in combination therapy could be amplifying a problem which might be caused by the recovery of the immune system from long-term suppression. Similar fat and sugar disturbances and weight gain have been seen in HIV-negative children and young people who received bone marrow transplants and subsequently recovered.

8 **Should I be worried about body fat changes?**

Body fat changes alone do not appear to substantially contribute to poor future physical health. However, they may be stigmatising, uncomfortable or embarrassing and so worry many people when they occur. Persistent changes in fat and sugar metabolism, together with central fat increases however, could increase the risk of heart disease if you also have other risk factors for heart disease (such as smoking or a family history).

Body fat changes may have a serious effect on your quality of life. The next section deals with treating body fat changes to improve your quality of life.

More is being learnt about the causes and treatment of body fat changes, however they still aren't fully understood. Strategies to prevent and treat lipodystrophy are therefore evolving all the time and it is important to remember that they may involve side-effects or other consequences which might be as unpleasant or even more serious than the problem that you are trying to correct.

Can lipodystrophy be prevented by choosing particular drugs?

There is now very good evidence that combinations which contain d4T, and to as lesser extent, AZT, are associated

with an increased risk of fat loss. It is also clear that people who start with an NNRTI-containing combination seem less likely to have lipid increases (see page 10).

Lipodystrophy will be delayed by not starting HIV treatment, but this must be balanced against the real risks of illness if you do not take anti-HIV therapy, and by the fact that fat loss is more common in people who started treatment with CD4 counts below 200.

Treating body fat changes by switching treatment

There is no strong evidence from big studies to show that switching from a protease inhibitor to an NNRTI-containing or triple nucleotide combination improves body fat loss. Small improvements in abdominal fat accumulation have been reported in some small studies. The rate of fat loss may slow down after switching. It has been shown that switching from d4T or AZT to abacavir or tenofovir can halt fat loss and result in a very slow improvement in fat loss.

Studies have shown that lipid, glucose and insulin levels usually fall after switching from a protease inhibitor to an NNRTI-based combination, especially to nevirapine (*Viramune*), although they may not return to normal levels. The same pattern has also been seen with switches to an abacavir-based triple NRTI combination.

However, the use of this combination isn't recommended because it's not as powerful as NNRTI or protease inhibitor-based treatment.

Your choice of new drugs will be influenced by your previous treatment experience.

Treating body fat changes by stopping treatment

Some people choose to deal with body fat changes by stopping treatment. At the moment there is no clear proof from studies that this will reverse the body fat changes, but lipid and insulin levels are reduced within a few months.

If you are thinking about doing this, it is important to be aware of the general risks of stopping treatment, and to talk to your doctor about regular monitoring to reduce the risk that your CD4 count will fall to a level at which you could develop AIDS-related illnesses.

- Your CD4 cell count is likely to fall back to its pre-treatment level within six months or less, regardless of how high it is now, and it will continue to fall after that point.
- If you had an AIDS-defining illness before you started HIV therapy, you are five times more likely to experience a CD4 decline back below 200 cells (the at-risk level for further AIDS-related illness) than someone who didn't have AIDS and who started treatment with a higher CD4 cell count.
- If you stop treatment with a CD4 count below 200, you are at risk of

developing AIDS-defining illnesses immediately and should discuss with your doctor whether you need to take medicine to prevent infections (prophylaxis) before you stop combination therapy.

- If you are taking a drug such as efavirenz (*Sustiva*), 3TC (lamivudine, *Epivir*) or nevirapine which takes a long time to clear out of the body, you run the risk of developing resistance during the withdrawal period. If you want to start treatment again with the same drug, it may no longer work.
- If you start treatment again your lipid levels are likely to return to their previous levels.

At the moment there is no treatment that will reverse all the body fat changes. Some people who stop treatment altogether report improvements, but may not return to normal, and most people with body fat changes are not in a position to stop taking anti-HIV drugs.

Dietary changes have not been shown to improve body fat changes, so eating less fat is not likely to help (although it may help reduce cholesterol levels). See page 36 for further advice on diet and managing lipid levels.

Human growth hormone

Fat deposits on the abdomen and between the shoulder blades may be reduced by taking human growth hormone, but you have to keep taking the hormone for the improvement to last, and the correct dose is not known. Side-effects such as joint pain and swelling in the hands and feet are common, and the development of diabetes has been reported in a small number of people with lipodystrophy who received this treatment.

Anabolic steroids

Anabolic steroids have been suggested by some people as a treatment for body fat changes because gains in abdominal fat in older men have been linked to declining testosterone levels. Anabolic steroids encourage the growth of muscle tissue at the cost of subcutaneous fat and so may increase the rate of fat loss from the face and limbs. Anabolic steroids may also cause further increases in cholesterol levels and could harm the liver. Various anabolic steroids are being tested in clinical trials for weight loss at the moment.

Metformin

A drug used to treat diabetes, called metformin, may be effective in reducing abdominal fat deposits. It also reduces triglyceride levels and improves glucose metabolism. Metformin often triggers some weight loss and so it may not be suitable for people with fat loss. It may cause nausea and diarrhoea and requires monitoring for lactic acidosis.

Metformin is available only through diabetes specialists.

Both central fat deposits and lipid levels in people with HIV have been improved by a programme of resistance exercise and aerobic exercise. Resistance exercise builds muscles which burn triglycerides stored in body fat, and regular exercise of any sort increases levels of HDL cholesterol (the form which protects us from heart disease). People with fat wasting from the arms and legs may find that they lose more fat.

Recommended exercise levels in order to modify fat gains

A combination of both aerobic (oxygen burning) and resistance (weight training) exercise is best for people with HIV and for tackling body fat changes.

Aerobic exercise

Aerobic exercise improves both your heart's ability to pump and your muscles' ability to use oxygen. It includes activities like brisk walking, running, swimming, cycling, rowing, even vigorous sex and dancing.

Aerobic exercise should be at a level where you are puffing but could still talk. A total of 30 minutes of any of these activities per day at this level will reduce your risk of heart disease. If you maintain your heart rate within a training range for at least 20 to 30 minutes three times per week you will improve your fitness from your current

level. You can calculate your training heart rate range with the following formula:

- You should aim to exercise between 60% - 75% of your maximum heart rate.
- To find out your maximum heart rate subtract your age from 220, e.g. $220 - 39 =$ maximum heart rate of 181.
- Multiply 181×0.6 to get the lower end of your training heart rate and by 0.75 to get the upper end.
- Therefore the training heart rate of a 39 year-old is between 109 and 136 beats per minute.

Progressive resistance training

The most efficient way to improve your muscle strength and size is by resistance or weight training. Activities like yoga and swimming do provide some resistance but the most efficient way is to use free weights or weight machines in a gym. You need to work on large muscle groups to gain the most benefit.

To improve muscle strength you need to load your muscles quite heavily. Therefore do a small number of repetitions using relatively heavy weights.

Always do a warm-up of ten repetitions on a light weight before starting.

Your training weight needs to be increased as your strength increases to make sure your muscles continue to experience resistance. Do three sets of 8-12 repetitions.

How does exercise affect the different body fat changes?

Central fat accumulation

Doing lots of sit-ups will not reduce central fat. The most efficient way of using up your central fat is with progressive resistance training. By increasing your total percentage of muscle, you burn off more fat even at rest. You will lose more central fat than peripheral fat when larger muscles begin to burn fat.

Peripheral fat loss (arms, legs)

Weight training may lead to slightly less peripheral fat. However by building up more muscle you can balance changes in the appearance of your limbs. If you feel you are losing too much fat reduce your exercise regime slightly.

Blood fat and sugar control

Improving your heart's fitness tends to reduce your blood fats. However this depends on consistent regular exercise. By reducing central fat and increasing muscle you are able to control your blood sugar levels more efficiently.

Plan for exercise

- Build up your exercise regime gradually; if you haven't exercised for years, don't expect to reach all the targets described here in the first few weeks or even months.
- Find somewhere to exercise where you feel comfortable. Your HIV clinic or local voluntary organisation may be able to recommend somewhere, and some clinics are able to provide access to free facilities.
- Warm up (10 mins of aerobic activity at a low level below your training range to warm your muscles).
- 20 to 30 minutes of aerobic activity keeping heart rate in the range described.
- Progressive resistance exercise at an appropriate level.
- Warm down (same as warm up).
- Stretch all muscles trained (this reduces muscle tears and injuries).
- Have 3-4 aerobic sessions and 2-3 progressive resistance sessions per week. Most people will have to build up gradually to this amount of exercise. You can vary your programme, for example, by doing two gym sessions with both aerobic and resistance components and one swimming or cycling or yoga session per week.

Cautions

- Always consult your doctor before starting a new exercise programme.
- Ensure you have an appropriate orientation to any gym – make sure that you know what you are doing, or you risk injuring yourself.
- Do not exercise if you have a fever as this can cause significant stress on your heart.
- If you have high blood pressure, make sure that you don't hold your breath when weight training, as this will further increase your blood pressure.

- Free weights require much more strength and stability, so starting on weight machines may reduce injuries.
- For further information contact your local gym or physiotherapist, and also contact your local authority for schemes for people on low incomes.

Positive Health

The YMCA has launched a scheme called Positive Health to provide gym access for people with HIV.

Call 020 7343 1720/21 to see if there is a centre near you.

Drugs to treat body fat loss

Studies are underway to see if any medicines can help prevent or reverse fat loss.

Creatine

Creatine is a dietary supplement often used by body builders. Some small preliminary studies have suggested that it can improve lean muscle mass in HIV-positive men. However, creatine can damage the kidneys, and people who are taking tenofovir and indinavir (*Crixivan*) should be particularly cautious about using creatine.

Uridine

Some studies suggest that uridine supplementation may be able to block the harmful effects of d4T and AZT while they are being taken and prevent and partially reverse fat loss. Uridine is available in a supplement called *NucleomaxX*. Unpleasant taste is its most widely reported side-effect and it interacts with ddI (*Videx*).

It can be bought from online pharmacies but if you are thinking of taking it you should discuss its potential benefits and risks with your doctor first.

Statins

Pravastatin is widely used in HIV-positive people with increased lipids. There is some evidence that the use of pravastatin can also help restore limb fat lost whilst taking d4T or AZT.

Treatment of facial wasting

Injections into the facial tissue can help restore a more normal facial appearance, but cannot regenerate facial fat cells.

Several forms of surgery have been used, with varying success, to repair body fat changes.

The use of polylactic acid, better known as *New Fill* has received a lot of attention.

Studies in the UK and abroad have shown that *New Fill* can reverse the appearance of facial wasting, leading to an improvement in people's self esteem and confidence.

New Fill is administered by a course of injections into the cheeks, normally spaced over six weeks. The injections encourage tissue growth and fill-out the sunken areas. Most people have three to five sets of injections.

It is uncertain how long the effects of *New Fill* last. So far, it seems that a single course of treatment will remain effective

for at least two years in the majority of people. However, it may last longer in some people, and there have been reports of others needing treatment on an annual basis or even more frequently.

Treatment appears to be safe, with the most commonly reported side-effect being soreness and swelling in the area where the injections were administered.

Access to *New Fill* from the NHS is becoming more widely available, but it is not universal. If you cannot get *New Fill* from the NHS, it is possible to obtain private treatment, cost varies from £800 – £1,200, depending on who you receive treatment from and how many treatments you need.

Other cosmetic treatments for facial wasting that are being examined include fat transfer, collagen injections, and hyaluronic acid.

Other injectable cosmetic treatments are becoming available; further information will be available from www.aidsmap.com or through NAM's treatment newsletter, *AIDS Treatment Update* (see the order form at the back of this booklet).

Metabolism refers to the way that our bodies process all the things that cells need in order to work properly. If metabolism is abnormal, this means that some of these processes are out of balance.

Metabolism – the basics

The general term for blood fats is lipids. There are two main types of lipids: cholesterol and triglycerides.

Cholesterol

Cholesterol comes in two main sorts – ‘good’ and ‘bad’.

- Good cholesterol is called HDL. It is a measure of protection against heart disease and is often reduced in people

with HIV and other chronic illnesses. Levels of HDL cholesterol may rise after starting combination therapy.

- Bad cholesterol is called LDL. A high level of LDL cholesterol and a low level of HDL cholesterol increase your risk of heart disease. Anti-HIV therapy – and lipodystrophy – have been associated with high LDL and high total cholesterol levels. Rises in LDL levels may occur after starting therapy, particularly with combinations including several of the PIs.

If you have high LDL cholesterol levels, certain risk factors increase your risk of heart disease further:

- Smoking.
- High blood pressure.
- A family history of heart disease.
- Physical inactivity.
- Age over 45 years if male or 55 years if female.
- Diabetes mellitus or insulin resistance.
- High triglycerides.
- Lack of regular exercise.
- Obesity, especially central fat accumulation.
- Use of cocaine or amphetamines.

For people on most protease inhibitors, it is especially important to monitor levels of 'bad' cholesterol (LDL).

Triglycerides

Triglycerides are fatty acids derived from fat, sugar and starches in food, and from excess alcohol, which travel through the bloodstream to be stored in tissues or the liver.

Glucose

Glucose is a form of sugar found in the blood. High levels of glucose may increase the risk of heart disease.

Insulin is the substance produced in order to control glucose levels in the blood. Some people on combination therapy need to produce more insulin to keep their blood levels of glucose normal. This is called insulin resistance. It may also be necessary to test insulin levels in some individuals.

How will I know if I have metabolic changes?

Abnormalities in sugar and fat levels and in the processing of fats and sugars can occasionally cause physical symptoms such as:

- Tiredness.
- Dizziness (due to high blood pressure).
- Loss of concentration.
- More frequent urination.
- Feeling thirsty most of the time.

However, many people do not notice any problems for a long time even when they have levels of fats and/or sugar in the blood that put them at risk of heart disease in the future.

How do I know if my blood test results are normal?

Metabolic test	Target level	When should I talk to my doctor?
Total cholesterol	5.2mmol/l or below	Above 6.5mmol/l
LDL cholesterol	Less than 3.4mmol/l	When the ratio of LDL to HDL is greater than 4:1 or LDL is above 3.4mmol/l, risk of heart disease increases
HDL cholesterol	More than 0.9mmol/l	As above
Triglycerides	Less than 2.2mmol/l when fasted	Above 8-10mmol/l may raise risk of pancreatitis. High triglyceride levels in the presence of high cholesterol levels and other risk factors further increase the risk of heart disease.

Metabolic test	Target level	When should I talk to my doctor?
Glucose	<ul style="list-style-type: none"> ■ 4-7mmol/l before meals ■ Less than 10mmol/l one and a half hours after meals ■ Around 8mmol/l at bedtime 	<p>Above 6.1mmol/l before meals indicates impaired glucose tolerance, increased risk of heart disease.</p> <p>Above 7mmol/l before meals indicates type 2 diabetes</p>
Insulin	15-17 mU/L or below	Any elevated level

Cholesterol levels can vary from day to day so you should not place too much emphasis on a single high measurement. It's the trend over time that is important. The same goes for other measurements discussed in this section.

The main influence over cholesterol levels is genetic whereas diet choices are particularly important for managing triglycerides and may help glucose and insulin levels. Measuring fasted levels is the most accurate way to assess lipids and glucose.

The level of fats in your blood (lipids) may rise when you start treatment, particularly with some ritonavir-boosted protease inhibitor-based treatment.

Sometimes they rise far above normal levels and need to be treated by changes in diet, exercise or drugs. An increase to a very high level is especially likely if your levels are already quite high.

Protease inhibitors have been shown to increase cholesterol and triglyceride levels, usually within weeks of starting the drug, although atazanavir (*Reyataz*) seems less likely to cause lipid increases. Cholesterol levels may increase on efavirenz and nevirapine too, but much

of this cholesterol appears to be 'good' (HDL) cholesterol.

Should I be concerned?

There is evidence that people taking protease inhibitors may have an increased risk of heart disease.

The following information on monitoring your risk of heart disease and what action you can take should prove useful.

If you have existing heart disease or diabetes, your treatment should be carefully chosen to ensure that it does not increase the risk of further complications.

If you have several of the risk factors listed in the table below, and your cholesterol level rises as a result of combination therapy, this may increase your long-term risk of heart disease if your cholesterol stays at this level for a number of years. This is why your doctor will suggest treatment to lower your cholesterol levels.

If you do not have any of these risk factors apart from an increase in cholesterol when you start treatment, it is unlikely that a change in cholesterol levels will have a significant impact on your long-term risk of heart disease.

Risk factors for heart disease

Risk factors	How the risk can be reduced
Smoking	Stop smoking - your clinic can help
A family history of heart disease	Address all other risk factors

Risk factors	How the risk can be reduced
Cholesterol levels (any)	Use drug treatment if diet and exercise adjustment are not sufficient to reduce cholesterol levels and improve LDL: HDL ratio, and/or consider switching to a protease inhibitor-sparing regimen if taking a PI
High blood pressure	Exercise regularly and reduce alcohol intake, reduce stress. May require medication.
Age over 45 years for men, 55 for women	Address all other risk factors
Elevated blood glucose (6.1 - 6.9mmol/l)	Use drug treatment if diet and exercise adjustment are not sufficient to normalise glucose levels; consider switching to a PI-sparing regimen if taking a PI. Increase dietary fibre, reduce alcohol.
Diabetes	As above

Risk factors	How the risk can be reduced?
Lack of exercise	Start gradually and aim for 30 minutes of non-stop activity 2-3 times a week
Overweight	Diet and exercise to reduce fat
Cocaine or amphetamine use	Avoid use; these stimulants substantially increase your risk of heart attack or stroke in the hours immediately after use.

Vascular disease (e.g. heart attack, stroke) develops, in part, because cholesterol begins to stick to the walls of blood vessels, including those in the heart. Gradually, deposits called plaques build up – these can rupture and cause

blood clots, or may narrow the arteries, causing increased blood pressure and eventually, blockage of the artery. This process takes many years and it is unclear if short-term increases in lipid levels on combination therapy will lead

to an increased risk of these problems in later life. Your lipid levels should be tested regularly once you start combination therapy, and should be tested before you start treatment to get a baseline for comparison. They should be tested first thing in the morning before breakfast to get the most accurate measure: this will show the absolute minimum level.

Triglyceride levels may also need to be tested after a meal, because they rise very high within an hour or so of eating. Very high levels of the triglycerides may cause pancreatitis, a life-threatening illness.

HIV itself causes high triglyceride levels in advanced disease. Low levels of HDL cholesterol are also a result of HIV infection.

Changes in glucose levels

Changes in the way your body handles sugar (its glucose metabolism) can also occur on protease inhibitor treatment or with substantial body shape changes. The most severe change is the development of diabetes, a serious disorder. This has happened in around 1-4% of people in studies, but less serious changes in sugar levels and sugar metabolism also occur. These changes can cause tiredness, excessive thirst, frequent urination and poor concentration.

34 Treatment for metabolic changes

Treatment for lipid changes usually starts with non-drug options: diet and exercise.

Reducing the amount of fat you eat, and particularly saturated fats, is normal advice for someone with high lipid levels and a risk of heart disease. However, it's not so simple for many people taking anti-HIV treatment.

When thinking about diet changes, bear in mind that protease inhibitors (apart from amprenavir and indinavir) need to be taken with some fatty food in order to be absorbed properly. You may also be underweight because of past illnesses, or because your treatment is failing to control viral load, or because of lipodystrophy.

Instead, it may be best to focus on making changes to the kinds of fat you eat. Saturated fats are the ones that cause most problems for the heart and your blood vessels. They are:

- Animal fats (the fat on or within meat or poultry, lard in pastry, food fried in lard).
- Coconut milk and coconut cream (used in African, Caribbean, Thai and other Asian food).
- Ghee (used to make curries).
- Palm oil (used a lot in African & Caribbean food and in some margarines).

- Dairy fats – butter, cheese, cream, ice cream, full fat milk, cakes.
- Cocoa fat (chocolate, cakes, biscuits).

If you have high lipid levels, try to cut down the amount of these fats you eat and save them for special occasions.

Omega-3 fatty acids

These are special polyunsaturated fats found in oily fish and certain seeds. They help reduce lipid levels, thin the blood to help reduce the risk of thrombosis, and also improve the flexibility of blood vessels. There is strong evidence that eating more oily fish prevents further development of heart disease.

Fruits and vegetables

Fruits and vegetables are a good source of antioxidant vitamins such as Vitamin A and Vitamin C. Eating more fruits and vegetables will help prevent the cholesterol in the blood from oxidising, and furring up the arteries. Taking megadoses of some vitamins has not been shown to reduce the risk of heart disease.

Foods which are claimed to lower cholesterol

Margarines claimed to lower cholesterol may have a modest effect by blocking the absorption of dietary cholesterol. They tend to be very expensive, however.

Eating tips

- You should eat fish such as salmon, fresh tuna, pilchards, red snapper, swordfish, sardines, kippers and mackerel three times each week. Those who don't eat fish can get Omega-3 oils from linseeds and from flaxseeds.
- Replace red meats, sausages and burgers with, for example, lean chicken, turkey, tofu, and other meat substitutes.
- Cut down on full-fat dairy products, but make sure you are still getting enough fat to absorb protease inhibitors. Try lower fat cheeses, and low fat yoghurt instead of cream.

- Try to eat at least five portions of fruit or vegetables each day - this will provide anti-oxidant vitamins, along with other helpful chemicals found in plants (but not in vitamin supplements).
- You get the maximum benefit when you eat lots of different coloured fruits and vegetables – you don't just need to eat greens.

If you are trying to gain weight:

- Eat frequently – have three snacks and three meals each day.
- Eat starchy foods such as potatoes, pasta, bread, oatmeal porridge, rice, maize porridge.

- Eat more monounsaturates and polyunsaturates:
- Olive oil, olive oil spreads
- Vegetable oil (especially those made out of rapeseed oil)
- Peanut butter
- Avocados
- Groundnut oil
- Sunflower oil
- Soya oil

Remember: always consult a dietitian for personalised dietary advice.

Alcohol

Anything you eat or drink that provides energy in the form of sugar will be converted into triglycerides. Reducing the amount of sugar and alcohol you eat and drink will help reduce triglyceride levels.

A glass or two of wine or beer each day can increase your levels of good HDL cholesterol.

On the negative side, larger amounts of alcohol will damage the heart muscles, increase blood pressure and add to weight gain if you drink more than one to two units per day. All of these effects further increase the risk of heart disease in people with high lipid levels. A high

intake of alcohol will increase the risk of high triglyceride levels.

Exercise

See pages 15 to 20 for information about aerobic exercise, which is recommended as a way of reducing the risk of heart disease.

The contraceptive pill

There is some evidence that the contraceptive pill increases risk of heart disease in women with high lipid levels. If you are currently using the pill, you should talk to your HIV consultant about your contraceptive needs, and ask whether using the pill will increase your risk of heart disease.

Switching treatment

Lipid levels may be improved by switching from a protease inhibitor to an NNRTI regimen. This may be an important reason for switching treatment if you have very high lipid levels and/or a high risk of heart disease due to other factors such as age, weight, prior heart condition or family history, and particularly if you have both.

However, switching treatment may not be enough to reduce lipids to normal levels if you have very high levels. This strategy may only be suitable for people with plenty of treatment options, such as those on first-line therapy.

Smoking damages the walls of your blood vessels, increases blood pressure and reduces the amount of oxygen being carried in the blood. If your cholesterol levels are also high, this means that your heart must work even harder to pump blood, and you run more risk of narrowing arteries and blood clots, leading to heart attacks and strokes.

If you have any risk factors for heart disease:

- The single most important thing you can do to reduce your risk of heart disease if you are about to start antiretroviral therapy is to stop smoking.

The benefit of reducing the number of cigarettes you smoke is very small compared with stopping altogether, but may help to make it easier to give up altogether in the future. Reducing to low tar cigarettes is of no benefit. Heart disease is caused by the nicotine, carbon monoxide and other ingredients in cigarette smoke, not tar.

Your GP can prescribe a variety of things to help you stop smoking, and your HIV clinic may also be able to help. Some people find nicotine replacement therapy (patches or gum) helpful. However, the drug most commonly used to help stop smoking, *Zyban*, may interact with protease

inhibitors or NNRTIs. *Zyban* should not be taken with ritonavir, or by people with a history of seizures, or existing heart disease.

Drugs that lower lipids (fats) in the blood, and are used to treat heart disease and hardening of the arteries, may be prescribed for people with HIV who have high lipid levels.

These drugs are used to treat high lipids or coronary heart disease in people who have not responded to dietary changes.

Three classes of drugs may be prescribed to people with HIV.

Statins

Statins are lipid lowering drugs which have been used successfully to lower lipid levels in people on HIV therapy. The statins are less effective than the fibrates in reducing triglycerides, but are

effective at reducing LDL cholesterol, and have been shown to reduce cholesterol levels by around 20% in people with HIV.

The drug used most often is pravastatin. This is because some protease inhibitors may cause substantial and potentially dangerous increases in blood levels of statins other than pravastatin, increasing the risk of muscle damage.

The main side-effect of statins is inflammation of the muscles. A person taking a statin is advised to report muscle weakness, tenderness or pain to their doctor promptly. The risk of muscle pain and weakness is increased if a

statin is taken with certain other drugs such as fibrates (see below), cyclosporin or nicotinic acid. Kidney and liver function should be closely monitored if these drugs are taken with a statin.

Fibrates

Fibrates are active against elevated triglycerides but they also tend to lower LDL cholesterol and raise HDL cholesterol.

Fibrates include: clofibrate, bezafibrate, ciprofibrate, fenofibrate and gemfibrozil.

These drugs should not be used in people with kidney, gall stone or liver problems, and should not be taken by

pregnant women. Side-effects are infrequent but may include: nausea, stomach pain, rash, impotence, dizziness, fatigue and muscle pain.

The fibrates are less likely to interact with protease inhibitors than statins.

Gemfibrozil has been tested in people with HIV, and produced modest triglyceride reductions without significant side-effects.

Fish oils

A fish oil preparation that is rich in omega-3 marine triglycerides can reduce elevated triglycerides but may raise HDL cholesterol levels. It is considered a

relatively weak treatment and a large dosage would be needed to reduce the very high triglycerides associated with protease inhibitor therapy, adding between three and ten capsules to the number of pills you would need to take each day.

Drugs to normalise or control glucose and insulin

You may hear more about these drugs in the future; their use is still highly experimental in HIV infection.

Metformin	Keeps glucose levels down without stimulating insulin production. Also lowers cholesterol and triglyceride levels and may cause modest weight loss. Diarrhoea and nausea are common side-effects.
Sulphonylureas (glyburide, glipizide, gliclazide)	Stimulate insulin production so that blood glucose can be controlled.
Glitazones or TZDs	A new group of drugs that reduce the amount of insulin you need to control your blood sugar. Still experimental in HIV, and may interact with antiretrovirals. May also reduce central fat and increase sub-cutaneous fat.

- Lipodystrophy refers to changes in body fat and the metabolism of fat and sugar seen in people with HIV, mainly in people taking protease inhibitors and nucleoside analogues (NRTIs) together.
- d4T and to a lesser extent AZT have been associated with fat loss.
- Changing from d4T or AZT to abacavir or tenofovir can lead to a very slow improvement in fat loss. Exercise has been shown to improve central fat and metabolic problems.
- Facial fat loss may be improved by injections of a substance called poly lactic acid. This is available on the NHS at some, but not all clinics.
- Cholesterol, triglyceride and glucose levels may rise after you start combination therapy. If you have existing heart disease, or several risk factors for heart disease, your doctor may suggest treatment to reduce these levels.
- The significance of metabolic changes in people without major risk factors for heart disease is still unknown.

aerobic exercise Exercise that increases heart rate and use of oxygen.

central fat Fat around the organs, not under the skin.

cholesterol A waxy substance, mostly made by the body.

glucose Sugar.

HDL The less harmful, or 'good' cholesterol; protects against heart disease.

LDL 'Bad' cholesterol; high levels increase risk of heart disease.

lipids General term for fats in the blood.

lipodystrophy A disturbance in the body's distribution and handling of fats.

NRTIs Nucleoside analogue drugs (AZT, ddI, d4t, ddC, 3TC, abacavir, and FTC).

peripheral fat Fat on the limbs and face, also called subcutaneous fat.

triglyceride The basic building blocks from which fats are formed.

Notes

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