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Blood Fats Explained



HEART UK
THE CHOLESTEROL CHARITY

Lowering Cholesterol, Saving Lives

www.heartuk.org.uk

Blood fats and genetic conditions explained

In this booklet, you can read about blood fats and how they can affect your heart and blood vessels. It's for anyone affected by a blood fat condition.

We cover the different blood fats and what can affect them, including genetic conditions. We also cover the changes you can make to your lifestyle and the treatments available to manage raised blood fats and genetic conditions.

- What are blood fats?
- What is cardiovascular disease (CVD)?
- The heart
- Checking your blood fats levels
- What can affect your blood fats?
- Lipid clinics
- Genetic conditions explained
- Diet and lifestyle
- Medicines and other treatments

What are blood fats?

Blood fats, also known as lipids, are fats that are carried around the body in the blood. Cholesterol and triglycerides are both blood fats, and they have essential roles in the body.

Cholesterol is used to:

- build cell walls
- make steroid hormones and vitamin D which keep your bones, teeth and muscles healthy
- make bile acids which are released into the gut to help digest food.

Some of our cholesterol comes from the food we eat, but most (around 80%) is made by the liver.

Triglycerides are used for energy. They can be used straight away or stored for later. We get some triglycerides from food but, like cholesterol, most are made by the liver.

We all need some cholesterol and triglycerides in our bodies, but too much in the blood can lead to health problems that affect the heart and blood vessels. These problems are known collectively as cardiovascular disease, or CVD (see page 5).

What are lipoproteins?

Cholesterol and triglycerides can't travel loosely in the blood so they're carried in tiny round parcels called lipoproteins. 'Lipo' means fat and 'proteins' simply means proteins.

There are different lipoproteins which vary in size and how much cholesterol, triglycerides and protein they carry. Smaller ones are more dense – they carry more protein and are lower in fat. Larger ones are less dense – they are higher in fat and lower in protein.

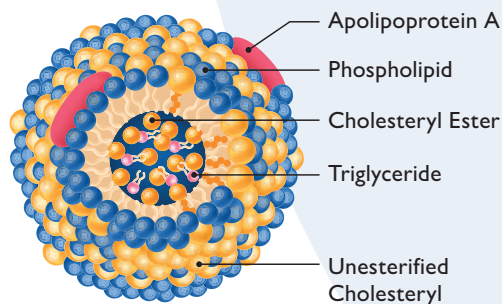
- **Chylomicrons** are the largest lipoprotein. They contain a large proportion of fat – they are about 80-90% triglycerides and about 7% cholesterol. After a meal, triglycerides and some cholesterol are packaged into chylomicrons and enter the blood through the intestines. They are carried in the blood to tissues throughout the body so the triglycerides can be used for energy or stored for later. Once the triglycerides have been released, the chylomicron becomes a 'chylomicron remnant' which is removed from the blood by the liver.
- **Very low-density lipoproteins (VLDL)** mainly carry triglycerides made by the liver to tissues to be used for energy, or to fat (adipose) tissue to be stored for later. VLDL contains roughly 60% triglycerides and 15% cholesterol.



- **Intermediate density lipoprotein (IDL)** are half way between VLDL and LDL. They are the 'VLDL remnant' after some of the fats have been released. They are quickly converted into LDL cholesterol in the liver, so they are only present in the blood for a short time.
- **Low density lipoproteins (LDL)** are made in the liver and carry cholesterol from the liver to cells around the body. They contain most of the cholesterol in the blood (70%). LDL contains about 50% cholesterol and 10% triglycerides. Too much LDL cholesterol in the blood can lead to a build-up of cholesterol in the artery walls, causing problems such as heart disease and stroke. This is why it's sometimes called "bad cholesterol".
- **High density lipoprotein (HDL)** carries excess cholesterol away from cells and artery walls back to the liver to be broken down and recycled. This is why it's sometimes called "good" cholesterol or the "protective particle". It also has anti-inflammatory and antioxidant-effects, which also help to protect against disease. It's mainly made of protein so it's very dense, which is why it's called 'high density'. It's made up of about 5% triglycerides, 15% cholesterol and protein.

What are the proteins in lipoproteins (apolipoproteins)?

- The proteins in lipoproteins are called **apolipoproteins**, and there are different types. These can be helpful to know about for people with certain genetic conditions (see page 14). **Apolipoprotein B-100, or ApoB**, is the key structural protein for most lipoproteins Apart from HDL.
- **Apolipoprotein A1, or ApoA1**, is the main protein in HDL, which does not contain ApoB.
- **Apolipoprotein B48, or ApoB48**, is a shorter form of ApoB. It is released by the gut and is important in the structure of chylomicrons.
- **Apolipoprotein (a), Apo (a) or "little a"** is different to ApoA1, above. It is very sticky which means it can readily attach itself to blood vessel walls. It is added to an LDL-like particle to form a lipoprotein known as lipoprotein (a) (see page 15).
- **Apolipoprotein (E)** allows the liver to remove chylomicron remnants from the blood, and there are different types ie. E2, E3 and E4 (see page 15).

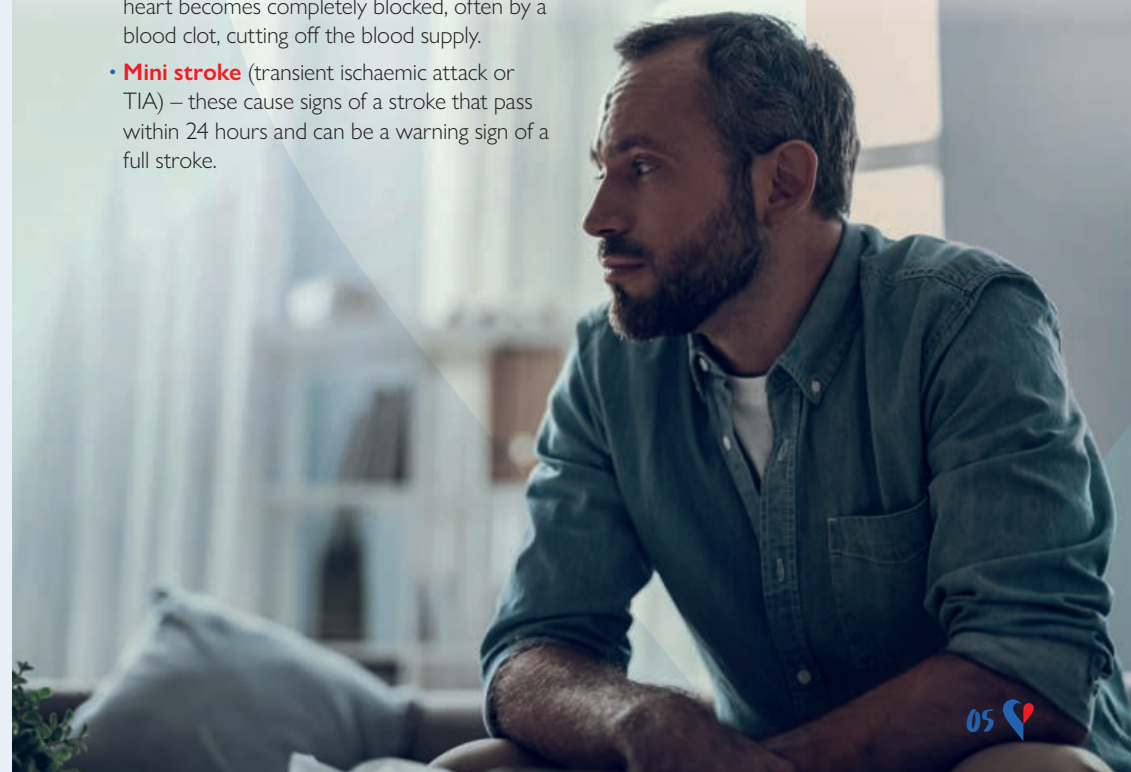


The HDL Lipoprotein

What is cardiovascular disease (CVD)?

Cardiovascular disease (CVD) is the medical name for diseases of the heart and blood vessels. These include:

- **Coronary heart disease (CHD)** – this is the most common type of heart disease. It's where the arteries have become clogged up and stiff and blood can't flow easily.
- **Angina** – chest pain caused by narrowed arteries which mean the heart can't get enough blood.
- **Acute coronary syndrome** – a collective term which includes unstable angina and heart attacks.
- **Heart attack** (also known as myocardial infarction) – when an artery leading to the heart becomes completely blocked, often by a blood clot, cutting off the blood supply.
- **Mini stroke** (transient ischaemic attack or TIA) – these cause signs of a stroke that pass within 24 hours and can be a warning sign of a full stroke.
- **Stroke** – when an artery in or leading to the brain becomes blocked, cutting off the blood supply.
- **Peripheral arterial disease (PAD)** – when arteries leading to the legs and feet become blocked or narrowed, so not enough blood can reach them.
- **Vascular dementia** – where problems with the blood supply to the brain cause problems with memory, thinking and talking.



What raises your risk of CVD?

A number of things can mean you're more likely to develop CVD. These are known as 'risk factors' and there are two types – things you can change (known as modifiable) and things you can't change (known as non-modifiable). There are also some health conditions that can have an effect. The more risk factors you have, the greater your risk of developing CVD.

Risk factors you can't change (non-modifiable)

- Increasing age – the older you are, the greater your risk.
- Gender – men at all ages have a higher risk of developing CVD than women.
- People in your close family have had CVD at a young age (below the age of 60).
- Ethnic background – people of South Asian or Sub-Saharan African origin have a greater risk.

Things you can change (modifiable)

These are known as 'modifiable risk factors' and include:

- unhealthy levels of blood fats such as cholesterol and triglyceride
- smoking
- alcohol
- high blood pressure
- type 2 diabetes which is not well managed
- being overweight
- not being physical active
- an unhealthy diet, including eating too much saturated fat.

Your health and wellbeing

Some health conditions add to your risk of CVD, including:

- atrial fibrillation (AF) – the most common form of irregular heart beat
- rheumatoid arthritis
- chronic kidney disease (CKD) and a kidney problem called nephrotic syndrome
- mental health issues and stress
- menopause – LDL and HDL cholesterol can rise after the menopause
- growth hormone deficiency.



Having a healthy diet, not smoking, being active and keeping your waistline in check are good for everyone and can help you keep healthy.

Managing your risk of CVD

There are many ways in which you and your healthcare professional (HCP) can manage your risk.

Lower your blood fats. A healthy diet and lifestyle can help you manage your cholesterol and triglycerides (see page 10), but some people will need medications (page 21). There are many other influences on cholesterol and triglycerides – you can read more about these throughout this booklet.

Stop smoking. Toxins in cigarette smoke damage your blood vessels and your heart, raising the risk of blood clots. Smoking also lowers your HDL cholesterol and makes the LDL cholesterol more "sticky", meaning it can "stick" to your artery walls more easily. People who smoke are at higher risk of stroke, heart attack and breathing problems.

Stopping smoking makes a big difference to your health within days, and after one year, your risk of coronary heart disease will be halved.

Lower your blood pressure. Your blood pressure is the pressure your blood puts against your blood vessel walls as it flows around your body. It is measured in millimetres of mercury (mmHg) and is written as two numbers – a top number (systolic) and bottom number (diastolic). High blood pressure damages the blood vessel walls and, if left untreated, raises the risk of CVD. It can also damage organs including the eyes, kidneys and brain.

High blood pressure is usually diagnosed when you have three or more readings above 140/90mmHg, rather than a one-off high reading. The only one way to know your blood pressure is to get a blood pressure check – either at your GP surgery, pharmacy, or using a home monitor. A healthy lifestyle, and sometimes medication, can help bring your blood pressure down to a healthy level.

Manage type 2 diabetes and pre-diabetes. People with type 2 diabetes sometimes have:

- raised triglycerides
- lower HDL cholesterol
- smaller-sized, denser, LDL.

This pattern of blood fats means you have a higher risk of CVD. Your healthcare professional can help you manage diabetes and prediabetes. It can be treated with healthy diet and lifestyle changes including weight loss, and medication.

Lose weight if you need to. Losing just 10% of your body weight can help you to:

- lower your triglycerides
- lower your total cholesterol
- raise your HDL cholesterol
- lower your systolic blood pressure (the top number)
- lower your risk of type 2 diabetes.

If you carry extra weight around your middle (if you're 'apple shape') you are more likely to develop heart and liver disease, as this can lead to fat building up in your organs.



Aim for a healthy body mass index (BMI):

You can work out your BMI using your weight and height to give you an idea of whether you are a healthy weight.

The BMI ranges are: underweight, healthy weight, overweight, obese and severely obese. The healthy range is between 18.5 and 24.9 for most adults.

Some ethnic groups have a higher risk of illness at a lower weight and need to use a lower BMI range, including people from an Asian, Chinese, Middle Eastern, Black African or African-Caribbean family background.

To work out your BMI, visit www.nhs.uk/health-assessment-tools/calculate-your-body-mass-index/

Aim for a healthy waist measurement:

Current guidelines now recommend using the waist to height ratio to find out how much fat is stored around your belly. To work out your waist to height ratio visit <https://www.nhs.uk/health-assessment-tools/calculate-your-waist-to-height-ratio>

Make healthy diet and lifestyle changes

A healthy diet and keeping active can help you manage your cholesterol, weight, blood pressure and risk of diabetes, and in turn your overall risk of CVD (find out more about healthy eating on pages 18-20).

The heart

The heart is a muscle which beats continuously. Its main role is to pump blood around the body.

The left side of the heart pumps blood that's rich in oxygen and nutrients under high pressure to the brain, muscles, organs and cells. The right side of the heart is slightly smaller and pumps blood under lower pressure to the lungs where it collects oxygen and carries it back to the heart.

The heart has its own blood supply which comes from the coronary arteries. These arteries are on the surface of the heart and divide into many smaller arteries to give oxygen and nutrients to the heart muscle.

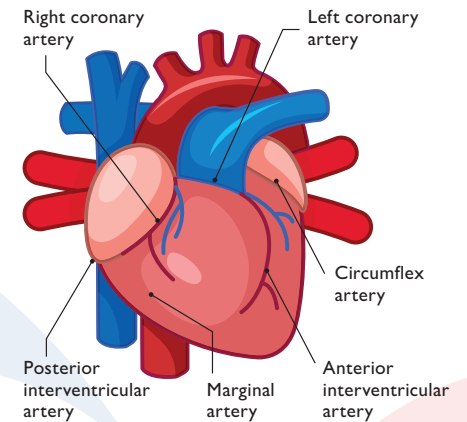
What is atherosclerosis?

If there is too much fat in the blood, it can slowly build up in the artery walls. Over many years, fatty areas known as plaques or atheroma can form. They can become harder with time, making the arteries stiffer and narrower. This process is called atherosclerosis (pronounced ather-o-scler-o-sis).

How does CVD develop?

The process of atherosclerosis can lead to CVD and coronary heart disease (when it affects the coronary arteries). Sometimes arteries can become so narrow that not enough blood can flow through them.

During exercise, the lack of blood flow (and oxygen and nutrients) to the heart can cause symptoms such as chest pain, shortness of breath and dizziness which usually resolve with rest. This is known as stable angina.



The heart and the coronary arteries

When the fatty deposits (atheroma) in the blood vessels become very large, they may burst. The body sees this as a sign of injury and reacts by producing platelets which gather to form a blood clot to repair the injured area. Sometimes, the clot can partly or completely block the coronary artery, stopping the flow of blood to the heart. This is known as acute coronary syndrome (ACS), an umbrella term that includes unstable angina and heart attacks.

A heart attack happens when an artery leading to the heart becomes partially or completely blocked, cutting off the blood supply to part of the heart. It needs to be treated straight away to avoid serious damage to the heart, and cardiac arrest, where the heart stops beating.

Your liver

The liver plays an important role in controlling the amount of fats in the blood, and it's the target of many medicines for lowering blood fats.

The liver makes most of your cholesterol (in a very complicated 37 step process), and most of your triglycerides. It also takes cholesterol out of the blood so it can be broken down. Liver cells have special hooks on them, known as LDL receptors, which remove LDL cholesterol from the blood.

The liver also makes vitamins such as vitamin D, and hormones such as testosterone and oestrogen.

Checking your blood fat levels

Your healthcare professional can check the amount of cholesterol and triglycerides in your blood with a blood test.

This can help give an idea of your heart health and risk of disease. You don't need to fast for a routine test, but in some cases your healthcare professional might ask you to fast for 12-14 hours beforehand.

What is a healthy level of cholesterol and triglycerides?

Cholesterol and triglycerides are both measured in millimoles per litre (mmol/L) in the UK.

For healthy adults, HEART UK specialists recommend that you aim for the following levels, as a general guide:

- **Total cholesterol should be below 5mmol/L**

Total cholesterol is your HDL cholesterol added to non-HDL cholesterol*. It's the total amount of cholesterol in your blood carried by all the different lipoproteins. As it contains both the "good" and "bad" cholesterol, it doesn't give much information about your risk of disease so it shouldn't be looked at on its own. It's important to get the full breakdown into HDL and non-HDL cholesterol.

- **Non-HDL cholesterol should be below 4mmol/L**

*Non-HDL cholesterol is all the "bad" cholesterol added together as it contains LDL cholesterol plus the cholesterol from all the other lipoproteins such as VLDL (see page 3). It does not contain any cholesterol from HDL, which is why it's called non-HDL cholesterol.

- **HDL cholesterol should be above 1mmol/L for men or above 1.2mmol/L for women**

HDL is protective in three main ways: it's an anti-inflammatory, an anti-oxidant and it transports cholesterol back to the liver. Levels up to 1.4mmol/L are thought to be most protective. It is currently unclear whether very high levels offer extra protection.

- **LDL cholesterol should be below 3mmol/L**

LDL cholesterol is not usually measured. It's normally worked out with equations in a laboratory, and may require a fasting blood test. It can also be measured directly by specialists. LDL cholesterol makes up most of the non-HDL cholesterol reading.

- **Total cholesterol:HDL cholesterol ratio**

The total cholesterol to HDL ratio (written as TC:HDL-C ratio) is only required for calculation of cardiovascular risk using QRISK. It should be interpreted with caution as it can be normal due to a higher level of HDL cholesterol, even though someone has higher non-HDL and LDL cholesterol.

- **Non-fasting triglyceride should be below 2.0mmol/L**

This is the measurement of all the triglycerides carried in the lipoproteins – mainly chylomicrons and VLDL. A fasting triglyceride test will be lower because it will only contain the triglycerides carried by the VLDL (not chylomicrons) but the difference is usually small, about 0.3-0.6mmol/L. A fasting triglyceride should be below 1.7mmol/L.

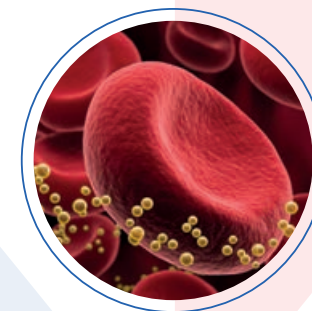
These recommendations are a general guide for healthy adults who:

- don't have CVD or other related health conditions that put you at higher risk of illness
- are not taking cholesterol-lowering medications such as statins
- don't have a family history of early CVD
- are seen as low risk of CVD.

As cholesterol and triglycerides are not the only risk factors for CVD they should not be looked at alone but alongside other risk factors which can contribute to developing CVD

If you don't have CVD, your healthcare professional may carry out a 10 year and Lifetime risk assessment to help to assess your risk. This risk assessment considers all the risk factors that contribute to developing CVD. They are known as modifiable (can be changed) and non modifiable (can't be changed) (see page 6).

If you have CVD, there are specific cholesterol-lowering targets for non-HDL and LDL cholesterol, and the approach is usually "the lower the better".



Checking for lipid conditions

Lipid conditions are usually diagnosed by a combination of:

- Measuring blood fats and other special tests.
- Looking for telltale signs on the body.
- Taking a family history.
- In some cases, doing a genetic test.

What can affect your blood fats?

Many things influence your cholesterol and triglycerides levels. There is a lot of overlap between the things that raise your cholesterol and things that raise your risk of CVD (see page 6). It can be helpful to know about the following.

Secondary (underlying) causes

These include:

- An unhealthy diet and lifestyle, such as a diet high in saturated fats, sugars, fat type diets and restricted diets, for example high fat, low carb diets.
- Medical conditions such as liver and kidney conditions, uncontrolled diabetes, having an undiagnosed, untreated underactive thyroid.
- Medications such as diuretics, beta blockers, steroids and anti-depressants.
- In women, pregnancy and menopause can have an effect.

These are commonly referred to as “secondary” or “underlying” causes. If you have raised cholesterol or triglycerides, your healthcare professional should investigate these first.

If there is no obvious cause for your raised blood fats, and diet and lifestyle changes don't have a significant effect, then the cause could be a genetic condition. It's important for your healthcare professional to consider this possibility.

Genetics

Inherited genetic conditions are passed down through families from parents to children (see page 14). Your healthcare professional should consider these if you have raised blood fats and there is no clear cause, particularly if you have a family history of raised blood fats or early CVD (before the age of 60).

Once all other causes have been ruled out, your healthcare professional may refer you to a specialist at a lipid clinic to find out if you have an inherited genetic condition.



Lipid clinics

Lipid clinics provide specialist help and advice to people with raised blood fats and who may have, or may be at high risk of, developing CVD. They will carry out specialist tests including measuring apolipoprotein levels and genetic tests to help diagnose and manage your condition.

You may be referred to a lipid clinic for several reasons:

- your healthcare professional thinks you may have a blood fat condition that is passed down through families (a genetic condition)
- you have too much cholesterol or triglycerides in your blood
- you are having problems taking a statin or other lipid-lowering medicine or they aren't bringing your blood fats down enough
- you need a specialist screening test such as a genetic test (also known as a DNA test).

There are many different healthcare professionals who work in lipid clinics who are experts in helping people with blood fat conditions. They include lipidologists, chemical pathologists or clinical biochemists, cardiologists, diabetologists and endocrinologists. Their job is to diagnose blood fat conditions, screen close family members, and ensure you get the right treatments.

Lipid specialists work with dietitians, specialist nurses, pharmacists and other healthcare professionals who, along with your own healthcare professional, will help you manage your condition.

An advice and guidance request is a new method of referral in England, where your healthcare professional can contact a specialist at a lipid clinic directly for further support and guidance.

Lipid clinics see people who are referred for specialist help and advice by their own HCP.

Lipid clinic HCPs are experts in treating blood fat conditions.

Genetic conditions explained

A number of inherited genetic conditions can affect your blood fats and your risk of CVD. In this section we look at both inherited high cholesterol and triglyceride conditions, from some of the more common conditions to the rarer ones. In some conditions, both cholesterol and triglycerides will be raised, in others, just one will be affected.

You can read more about all of these at www.heartuk.org.uk/genetic-conditions

Familial hypercholesterolaemia (FH)

FH is an inherited condition that causes very high blood cholesterol. It's caused by a 'change or 'alteration' in a single gene. "Familial" means it runs in families and "hypercholesterolaemia" means high cholesterol in the blood.

FH is a common condition, as many as 1 in 250 people may have it. It raises the risk of early heart disease if it's not diagnosed and treated as early as possible.

With FH, there is a problem removing LDL cholesterol from the blood, so cholesterol levels rise. In adults, your doctor should suspect FH if your total cholesterol levels are above 7.5mmol/L or your LDL-cholesterol levels are above 4.9 mmol/L, with normal triglyceride levels.

Other signs that can help make a diagnosis for FH are:

You have a personal history of early heart disease or you have close relatives with a history of early heart disease or very high LDL cholesterol levels.

Very high cholesterol can sometimes cause physical signs due to the build-up of cholesterol. Not everyone with FH has these and they can also be a sign of other conditions. The signs are:

- swollen tendons (tendon xanthoma)
- a white ring around the coloured part of the eye (corneal arcus)
- fatty deposits in the skin, usually around the eye area (xanthelasmas).

Most people with FH have heterozygous FH, which means there is a problem with a single gene (known as monogenic) which has been inherited from one parent. If you have this type and you have children, each child will have a 1 in 2 (or 50%) chance of inheriting FH.

Genetic testing should be used to confirm the diagnosis and, if an FH causing gene is found, then all close family members should be screened for the same gene (a process known as cascade testing).

Treatment is usually with medication such as statins, ezetimibe, bempedoic acid, and PCSK9 inhibitors given by injection, as well as following a healthy diet and lifestyle.

You can find out more about FH from our booklet "Familial Hypercholesterolaemia".

Polygenic hypercholesterolaemia

Polygenic hypercholesterolaemia is a very common cholesterol condition. It's caused by inheriting a few small gene changes, which can raise LDL-cholesterol. On their own, each small gene change only raises LDL cholesterol by a small amount (+10%), but when there are many, they may have an additive effect. The term "polygenic" means many genes are involved and they can be inherited from both parents.

Sometimes, LDL cholesterol levels can be very high, as in FH (which is caused by a single gene). In this case, the condition is known as "severe" polygenic hypercholesterolaemia.

Now, specialists can test people who have the "severe" type for the genes involved. These are usually people who have been tested for FH but an FH causing gene hasn't be found. This type of testing is known as "next generation sequencing (NGS)", and at least 12 different small gene changes have been found.

Polygenic hypercholesterolaemia is also influenced by getting older, diet and lifestyle, and the menopause in women. Similar to FH, it can raise the risk of developing heart disease when cholesterol levels are high, but the risk is lower than with FH because cholesterol won't be raised from birth. It should still be managed with a healthy diet and lifestyle plus medications such as statins.

High lipoprotein (a), or lipoprotein "little" a

Lipoprotein (a), known as Lp(a), is a large lipoprotein made in the liver (see page 3 for more on lipoproteins). It is very similar to LDL cholesterol but it has a sticky protein attached to it called apolipoprotein (a). This means it can stick to artery walls more easily which may result in narrowing the arteries (atherosclerosis).

A high level of Lp(a) in the blood is a risk factor for developing CVD (see page 5). This is thought to happen in two ways:

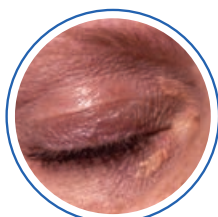
- it speeds up narrowing of the arteries
- it increases blood clot formation.

The amount of Lp(a) in your blood is mainly determined by your genes, specifically, the LPA gene. It is inherited in an 'autosomal co-dependant' way, which means from both parents. Lp(a) is not affected by diet or lifestyle, and the usual medications used to lower blood fats don't have a significant effect.

New medications which work at genetic level are currently being studied in clinical trials and can reduce Lp(a) by about 80-90%. These are known as "gene silencing" or "anti-sense" medications. It's not yet known whether lowering Lp(a) in the blood reduces risk of CVD but results from clinical studies are expected within the next few years. Until then, the specialist advice for those with very high Lp(a) levels is to make sure all other risk factors are well controlled, particularly non-HDL/LDL cholesterol.



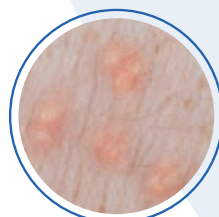
Tendon Xanthoma



Xanthelasma



Corneal Arcus



Eruptive Xanthoma

HEART UK specialists and the Lp(a) Task Force recommends that Lp(a) is measured in nmol/L. They recommend the following thresholds for understanding the risk of CVD:

- 32-90 nmol/L (minor risk of CVD)
- 90-200nmol/L (moderate risk)
- 200-400 nmol/L (high risk)
- more than 400nmol/L (very high risk).

Some people with FH will also have raised Lp(a) levels. If you have FH, your lipid specialist can measure your Lp(a).

Familial hypertriglyceridaemia

Familial hypertriglyceridaemia (also known as Type IV) is a common condition which causes higher than normal levels of triglycerides, usually with a normal cholesterol level. The liver makes too much VLDL (which are high in triglycerides), and too little is removed from the blood, so VLDL and triglyceride levels become raised.

Familial hypertriglyceridaemia is 'autosomally dominant' which means you only need to inherit a copy of the altered gene (or genes) from one parent to have the condition, but it's thought to be "polygenic", meaning a few genes may be involved.

Triglycerides don't usually rise until puberty or early adulthood. Raised triglycerides are usually accompanied by other conditions such as obesity, high blood pressure and high blood glucose. You might also have a lower level of HDL cholesterol.

Familial hypertriglyceridaemia doesn't usually have symptoms but may raise the risk of type 2 diabetes and CVD.

Treatment should include a healthy diet and lifestyle, including cutting down on alcohol and saturated fats. Some people may need medications such as statins and fibrates (see page 21/22).

Familial combined hyperlipidaemia (FCH)

FCH is an inherited condition that affects about 1 in 100 people. It happens when the body makes too much VLDL cholesterol (which is high in triglycerides) and apolipoprotein B (the structural protein, see page 4). People with FCH usually have both raised cholesterol and triglycerides.

FCH is not as well understood as FH, but it is also linked with early CVD. Raised cholesterol and triglyceride levels won't be present in childhood and may not appear until you're in your twenties or thirties. It is most likely to appear earlier in people who are overweight or have an unhealthy diet. The condition is closely linked with type 2 diabetes, raised blood pressure and gout.

People with FCH may also have fatty lumps in the skin (xanthelasma) caused by a build-up of cholesterol, mainly around the eye area, usually on the eyelids.

Some genes have been linked to FCH but genetic testing is not yet available. Specialists can measure apolipoprotein B levels to help make a diagnosis (see page 4). Treatment involves a healthy diet and lifestyle plus taking a medication such as a statin to lower the raised cholesterol. A type of medicine known as a fibrate can also help reduce triglycerides, and if prescribed, should be given alongside a statin.

Type 3 hyperlipidaemia (Type 3)

This condition is also known as "dysbetalipoproteinaemia" or "remnant particle hyperlipidaemia". One in 5,000 to one in 10,000 people are thought to have it. In people with Type 3, both cholesterol and triglyceride levels are high.

Some people with Type 3 have physical signs such as fatty deposits in the creases of the hands, and on the elbows and knees, which can help make a diagnosis. They can also have fatty lumps in the skin (xanthelasma) usually around the eyes, as in FCH, (see page 14).

Type 3 is caused by problems with a protein known as apolipoprotein E (apo E) (see page 4). This protein allows the liver to remove chylomicron remnants, (see page 3) from the blood. When this protein is not working properly, chylomicron remnant levels, and therefore blood fats, are raised. There are different forms of the protein apo E, and genetic testing is available to find out which form is present.

People with type 3 are at very high risk of both heart disease and peripheral arterial disease (PAD), where major arteries supplying the legs, arms and major organs can become narrow, reducing blood flow. Treatment includes medications such as statins and fibrates, alongside a healthy diet and lifestyle.

Rarer genetic conditions

Homozygous FH (HoFH)

This is the rarer form of FH and it is thought that about one in 250,000 people have it. It happens when an FH-causing gene is inherited from both parents, and causes extremely high LDL cholesterol, usually above 11mmol/L in children and above 13mmol/L in adults.

There is more than one type of HoFH. 'Homozygous' means the same gene has been inherited from both parents. There is a form known as 'compound heterozygous FH' which means the genes responsible are not the same. Another form is known as 'digenic' which means a person inherits two completely different gene alterations, one from each parent.

Treatment should be started in childhood. This is usually with lipoprotein apheresis, which is like kidney dialysis and carried out every one to two weeks. Blood is passed through a machine, via a tube, to physically remove the LDL cholesterol from the blood.

Statins are very unlikely to lower LDL cholesterol levels significantly but there are new treatments available which has led to

some people being able to reduce or stop their apheresis. These include evolocumab, lomitapide and evinacumab (see page 24).

Familial chylomicronaemia syndrome (FCS)

FCS is also known as lipoprotein lipase deficiency (LPLD). It's a group of very rare genetic conditions that affect about one in a million people. People with FCS have very high triglyceride levels because they lack lipoprotein lipase, which is the enzyme that clears triglycerides from the blood after a meal.

People with FCS usually have very high triglyceride levels from birth but they may not be diagnosed until they are much older. Signs and symptoms include regular bouts of abdominal pain, fat-filled spots on the skin (eruptive xanthoma) and attacks of acute pancreatitis. In the long term, it can lead to development of type 2 diabetes.

In the past, the main treatment for FCS was following a very low-fat diet as medications such as statins and fibrates were not effective. There have been new developments in treatments for this condition, including Volanesorsen, an injectable treatment used alongside a very low-fat diet (see page 18).

Multifactorial chylomicronaemia syndrome (MCS)

Multifactorial chylomicronaemia (MCS) is a similar condition to FCS but is more common. It's thought to affect one in 600 people. Rather than being caused by a single gene, it's caused by the small effects of many different genes and is influenced by diet and lifestyle.

Triglyceride levels are not as high as in FCS and the condition responds better to diet and lifestyle changes and medications such as statins and fibrates. But, it is linked to a higher risk of CVD. It can sometimes be very difficult to distinguish between MCS and FCS.

Diet and lifestyle

Everyone can benefit from a healthy diet and lifestyle, and they're especially important if you have raised cholesterol and triglycerides.

Be physically active

Being active is a great way to improve your heart health. It can raise your HDL cholesterol, lower your LDL cholesterol and triglycerides, help manage your weight, reduce your waist size, and lower your blood pressure and risk of type 2 diabetes. It can also lift your mood.

Adults should aim for:

- at least 150 minutes of moderate intensity exercise a week – this should get you slightly out of breath
- or 75 minutes of minutes of vigorous intensity activity.

You can spread this out throughout the week. If you haven't exercised for some time, check with your doctor what's suitable for you before you start.

Eat a healthy diet

Like exercise, a healthy diet can help keep your heart healthy and reduce the risk of CVD. It's an important part of your treatment.

• Swap saturated fats for unsaturated fats

Dietary fats fall into two main groups – saturated and unsaturated. Most saturated fat is solid at room temperature and found mainly in foods from animals, such as meat, dairy products, butter, ghee and lard. It is also found in hard margarines, coconut and palm oils and in processed foods such as pies, pastries, cakes and puddings.

Too much saturated fat can raise LDL cholesterol levels. Cutting down on saturated fats and including more unsaturated fats can help lower LDL cholesterol. Unsaturated fats are found in nuts and seeds, oils such as vegetable, olive and nut oils, vegetable spreads made from these oils, oily fish and avocado.

• Eat plenty of fruit and vegetables

Choose a wide variety and don't forget fresh, frozen, canned and dried all count.

• Choose wholegrain foods instead of refined starchy foods

Wholegrains have been linked with a lower risk of heart disease when eaten regularly as part of a healthy diet and lifestyle. They are grains that contain all parts of the grain, and products made from them, such as wholemeal bread, wholegrain breakfast cereals and wholewheat pasta.

• Choose healthy sources of protein

- Include more plant sources of protein such as beans, peas, lentils, nuts, seeds and soya.
- Choose low fat dairy foods instead of full fat varieties.
- Aim for two portions of fish a week, one of which should be oily, for example, salmon, mackerel, sardines and pilchards.
- Avoid processed meat products such as sausages, tinned meat, meat pies and sausage rolls.
- If you eat meat, choose lean meat and watch the quantity.

• Eat fewer processed foods and drinks high in sugar or saturated fat

These include biscuits, cakes, chocolates, pastries, fizzy drinks and cordials.

• Limit high fat takeaways and ready-meals

These can be high in saturated fat as well as salt. It's best to reduce how often you eat these. Better still, cook from scratch more often as you then know exactly what's gone into the meal.



Important...

Five important guidelines for a heart-friendly diet:

1. Swap foods high in saturated fats for those rich in unsaturated fats.
2. Eat more wholegrains, nuts, pulses, vegetables and fruit every day.
3. Choose meat free meals (fish, nuts, pulses, soya, Quorn™) more often
4. Limit food and drinks high in sugar or alcohol.
5. Cook more meals from scratch, and limit takeaway and processed foods high in saturated fat, salt and sugar.

Simple swaps to help you eat well

Small changes can make a big difference. Swapping your usual ingredients for a similar but healthier alternative can help you improve the quality of your diet.

Try swapping this...	...for this
Butter, ghee, lard, coconut oil and palm oil.	Oils made from vegetables and seeds such as olive, rapeseed, and sunflower oil, and fat spreads made from these.
White bread, pasta and rice.	Wholegrain breads, brown pasta and brown rice.
Cornflakes and sugar-coated cereals.	Bran flakes, malted wheats, porridge, oat-based cereals, wheat biscuits and unsweetened muesli.
Sweet and chocolate biscuits, cakes, buns and chocolate.	Oatcakes, rich tea, plain digestives, hot cross buns or currant buns.
Crisps (potato chips).	Unsalted nuts, dried and fresh fruit, and plain unsalted/ unsweetened popcorn.
Pastry, sausage rolls and savoury pies.	Potato topped pies.
Sausages, burgers and fatty meat.	Beans, lentils, peas, nuts, soya, fish, chicken or turkey with skin removed or small quantities of lean meat.
Full fat dairy foods (cheese, milk, yogurts and cream), and coconut yogurts and drinks.	Reduced fat dairy foods and fortified plant-based dairy alternatives, including soya.

Foods that lower cholesterol

As part of a heart-healthy diet, certain foods have been shown to lower cholesterol further if you eat them regularly. These include:

- oats and barley
- nuts (choose unsalted varieties)
- beans including soya foods
- dairy foods fortified with plant sterols and stanols.

Foods fortified with plant sterols and stanols are not suitable during pregnancy or when breastfeeding. Children with an inherited blood fat condition may benefit from these foods but check with your healthcare professional first.

See the HEART UK website for more information on how to lower cholesterol and triglycerides.

Certain foods can raise triglycerides

If you have raised triglycerides, limit these:

- sugar, and foods containing refined, added or “free sugars”
- alcohol – you may need to avoid completely
- Carrying excess weight, especially around the belly, can also raise triglyceride levels. Exercising regularly and losing weight can help lower them.

What about alcohol?

It's best to ask your doctor about drinking alcohol – for some conditions, alcohol is best avoided completely. If they advise it's OK, then stick to within the recommended limits of no more than 14 units spread across the week, with several alcohol-free days in between. If you are pregnant, avoid alcohol completely.

Medicines and other treatments

Diet and lifestyle changes are often not enough on their own to bring blood fats down to a healthy level if you have a genetic condition – although they will help your heart and body stay healthy. Most genetic blood fat conditions need to be treated with one or more of the following medicines.

Statins

Statins are usually the first line of treatment for people with raised cholesterol or triglycerides, who have CVD or are at high risk of CVD. They work by slowing down the production of cholesterol in the liver by blocking an enzyme known as HMG-CoA reductase. The liver then produces more LDL receptors to take cholesterol out of the blood, therefore lowering LDL cholesterol levels (see page 10).

Statins lower triglycerides too and are usually the first line of treatment for those who have conditions such as familial hypertriglyceridaemia, FCH and type 3 hyperlipidaemia.

Statins are very well researched and most people who take them don't have any side effects. Your healthcare professional should carry out blood tests before prescribing a statin to check how well your liver and thyroid are working. They will also check your cholesterol again within two to three months to make sure the statin is working. If you develop any side effects which you think may be due to taking a statin, discuss this with your healthcare professional who will be able to look into this with you.

The most commonly-used statins are atorvastatin and rosuvastatin. They aim to give at least a 40% to 50% reduction in LDL cholesterol, depending on the dose, and are known as high intensity statins.

Ezetimibe

Ezetimibe is a treatment for people who are either unable to take a statin or who are taking a statin but need to lower their cholesterol further. Ezetimibe works in a completely different way to a statin and is known as a “cholesterol absorption inhibitor” which means it works by partially blocking the absorption of cholesterol in the small intestine. This means less cholesterol enters the blood from food and bile, so the liver takes more cholesterol out of the blood. It can reduce LDL cholesterol by about 15-22%.

Adding ezetimibe to a statin is likely to give a greater reduction in LDL cholesterol levels than doubling the dose of the statin (which normally gives an additional 6-7%).



Bempedoic acid

This is a treatment which can be given alongside ezetimibe for people who can't take statins. Bempedoic acid works in a similar way to a statin but is less likely to cause the side effects seen with statins, such as muscle aches. When combined with ezetimibe, it can lower LDL cholesterol by around 38%.

PCSK9 inhibitors

These treatments are given by injection once or twice a month to lower LDL cholesterol. They're known as "monoclonal antibodies". They work by blocking a protein known as PCSK9 which destroys LDL receptors (see page 9). By blocking this protein, more LDL receptors can be made, and more LDL cholesterol is removed from the blood.

There have been few reported side effects. They can reduce LDL cholesterol by up to 60-70% when taken alongside other treatments such as statins and ezetimibe.

Currently, they are only available under specialist prescription, such as via a lipid clinic, and there are strict criteria for prescribing them. This means they are only available for people who are either known to have FH or have been diagnosed with CHD (see page 5).

Inclisiran

This is another treatment given by injection that targets the PCSK9 protein, but in a different way to the monoclonal antibodies. It is known as a "gene silencing" treatment which means it stops the production of the PCSK9 protein at genetic level.

After the first dose, another injection is given after three months, then it is only needed once every six months. It has been shown to lower LDL cholesterol by at least 50% and, so far, there have been few reported side effects.

In England, inclisiran is only licenced for people who have been diagnosed with CVD. In Scotland and Wales, it has been licenced for those with FH or CVD, similar to the monoclonal antibody PCSK9 inhibitors. It should be available in both primary care (such as GP surgeries) and secondary care (in hospital).

Icosapent ethyl

This is a highly purified omega 3 fat made of 95% EPA (eicosapentaenoic acid – the type of fat that's contained in oily fish) and is available in capsule form. It can be prescribed for people who are already known to have CVD, who have well controlled cholesterol levels a fasting triglyceride level of 1.7mmol/L or above, and who are still seen as at risk of CVD.

It is thought to work in several ways: it helps to reduce the amount of triglycerides released from the liver; it helps to stabilise cell membranes; and it has an anti-clotting effect. It can only be prescribed for those who are taking a statin.

Other medications only available under specialist prescription

Fibrates

Fibrates can be prescribed by lipid specialists to lower raised triglycerides, usually when they're above 10mmol/L. If fibrates are taken on their own, they can raise LDL-cholesterol levels, so they should be prescribed alongside a statin. Fibrates can lower triglycerides by 50% and can raise HDL cholesterol by up to 20%. They are useful in mixed cholesterol and triglyceride conditions such as FCH and Type 3 alongside statins. There is weak evidence for their use in CVD reduction and they are not routinely recommended in current guidelines.

Resins (bile acid sequestrants)

These come as a powder, granules or tablets. The powder and granules are taken by mixing them with water, fizzy drinks, fruit juice or yoghurt. They work by binding to bile acids and stopping them from being reabsorbed into the blood – so they are removed from the body. This means the liver takes more cholesterol out of the blood to make more bile acids, therefore lowering LDL cholesterol. Resins are safe for children and pregnant women because they are not absorbed into the body. Since treatments such as statins became available, they are no longer routinely recommended in national guidelines due to lack of evidence for their overall benefit.

Lomitapide

This is a treatment for those with homozygous FH, the rarer form of FH (see page 14). It is known as a microsomal triglyceride transfer protein inhibitor (MTTP inhibitor) which means it blocks the protein that is needed to transport fat from the gut into the blood and around the body. It does not need to rely on working LDL receptors so it can be taken by people who have very few or no working LDL receptors, as seen in homozygous FH.

It is taken by mouth (capsule) along with following a very strict low-fat diet. It can be used with other treatments such as apheresis and PCSK9 inhibitors. Reported side effects include problems with digestion, such as diarrhoea and feeling sick.

Volanesorsen

This is a specialist treatment for the condition FCS which can lower triglycerides. It is known as an antisense oligonucleotide which means it works at a genetic level. It stops the production of a protein known as ApoCIII (which stops enzymes such as lipoprotein lipase working, which raises triglyceride levels) so it allows triglycerides to be broken down. It is given by injection once a week for three months, then once every two weeks.

Evinacumab

This is a new treatment for those with HoFH, known as an ANGPTL3 monoclonal antibody. It has been shown to lower LDL cholesterol independently of LDL receptors. ANGPTL3 is a protein made in the liver which can block enzymes such as lipoprotein lipase, which breaks down fats such as triglycerides. Evinacumab binds to ANGPTL3 and blocks its effect, meaning the enzymes can work again, allowing faster breakdown of fats and reducing circulating levels of triglycerides, HDL and LDL-cholesterol in the blood. It is given as an hourly IV infusion every 4 weeks and is now available for those aged 12 onwards.

Lipoprotein apheresis

This is a treatment that removes the cholesterol and other fats from the blood. It is very similar to kidney dialysis for people who still have very high cholesterol despite medication and a healthy diet, such as those with homozygous FH, high Lp(a) or heterozygous FH with existing CHD.

Blood is passed through a machine which filters out LDL cholesterol, Lp(a) and triglycerides, and returned to the body. It is usually carried out once every one to two weeks in a specialist centre, and can take about two to four hours, although this may vary. The development of new medications such as lomitapide has meant that some adults have been able to either reduce how often they have treatment or stop their treatment completely.

Reporting side effects

Any medication can cause side effects. If you have side effects, let your healthcare professional know. You can also use the yellow card scheme to report side effects and help make medicines safer.

Visit <https://yellowcard.mhra.gov.uk/>

Where can I find out more?

Our range of materials include our Healthy Eating Guide, Understanding Cholesterol and Familial Hypercholesterolaemia booklets. There are web pages on a range of topics on our website including foods that help lower cholesterol, healthy oils and fats and handy tips for eating out.

General enquiries

hello@heartuk.org.uk

Literature orders

literature@heartuk.org.uk

Email or call our Cholesterol Helpline

ask@heartuk.org.uk
0345 450 5988

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