

High Density Lipoprotein (HDL)

High-density lipoprotein is one of the five major fat and protein particles (lipoproteins) whose role it is to enable blood fats (lipids), such as cholesterol and triglycerides, to be transported within the water-based bloodstream. Commonly referred to as the “good” cholesterol, as we will see HDL appears to be rather like the curate’s egg – “good in parts”!

HDL is the smallest and densest of the lipoproteins, containing the highest proportion of protein to cholesterol. In a normal healthy individual, HDL carries about a quarter of the total amount of cholesterol in the blood, whereas most of the remainder is carried in LDL (low density lipoprotein) “bad cholesterol” particles. The framework of LDL is a single protein called apolipoprotein B (Apo B), whereas HDL contains many proteins, the most important being apolipoprotein A1 (Apo A1).

HDL is important for the synthesis of steroid hormones but it is better known for its protective role against cardiovascular disease. A low HDL is thought to speed up the rate at which arteries furr up. HDL has three main benefits:

- HDL removes excess cholesterol from the tissues and arteries, and returns it back to the liver for recycling and removal from the body. This is known as “reverse cholesterol transport”.
- HDL also helps protect the artery walls against LDL cholesterol (an anti-inflammatory effect).
- HDL has a positive anti-oxidant effect, which helps protect blood cells and important chemical messengers in the blood from being broken down.

Together these effects prevent arteries from furring up. Atherosclerosis is the term used to describe this process. It happens over many years and is caused by initial damage to the artery wall followed by fatty substances getting into the artery wall and causing fatty deposits known as plaques. Over time these fatty deposits can cause severe enough narrowings to reduce the flow of blood, or they can break up, causing sudden clots and blockages, resulting in heart attacks and strokes.

What causes low HDL?

Women usually have higher HDL and levels above 1.2mmol/L are considered healthy. In men, HDL levels above 1mmol/L are considered healthy. Males also tend to have smaller sized HDL particles compared to females.

Young boys and girls have similar HDL levels but after puberty HDL levels decrease in males, and remain lower than those in females for all subsequent age groups.

In most people who have a low HDL the problem stems from lifestyle factors such as smoking, abdominal obesity (apple shaped obesity) and diabetes in which levels of an ordinary blood fat (triglycerides) are high. In some cases the low HDL and high triglycerides are part of an inherited condition with a genetic cause (one of several familial dyslipidaemias including Familial Combined Hyperlipidaemia (FCH)) but the problem can be made worse by smoking, having abdominal obesity or diabetes. Genetic conditions that can cause a low HDL (but normal triglyceride level) include Tangier disease and ApoA1 deficiency.

In cigarette smoke a toxic chemical called Acrolein appears to interfere with the normal functioning of HDL by changing the structure of its protein ApoA1. This damage may actually play a part in speeding up atherosclerosis, because of the reduced ability for HDL to remove cholesterol from the artery wall. Simply stopping smoking can increase HDL levels by up to 10%.

Insulin resistance: When the body contains too much stored fat, this interferes with the ability of insulin to regulate the blood sugar. This problem, known as insulin resistance can result in the metabolic syndrome leading to fatty liver, elevated blood pressure and type 2 diabetes. It also leads to characteristic changes in the pattern of fats in the blood (lipid profile) often referred to as “dyslipidaemia”. Typically there is a pattern of high triglycerides and low HDL levels with normal or slightly high LDL. The LDL particles also tend to be smaller and more toxic to artery linings.

Familial Combined Hyperlipidaemia (FCH): FCH is a fairly common condition in the UK believed to affect around 1 in every 100 of our population. Similar to diabetes people with

FCH usually have high triglycerides and low HDL but much higher LDL. This pattern of abnormal blood fats in FCH is also influenced by diet and lifestyle.

Tangier disease is a very rare condition which causes complete absence or extreme deficiency of HDL levels and LDL cholesterol levels are also usually reduced.

Medicines can sometimes reduce HDL levels too. These include beta blockers, thiazide diuretics, androgens, progestogens and anabolic steroids.

How can I increase my low HDL?

The good news is that there are several things you can do to increase your HDL. It can take about 12 weeks from when you start making these changes to seeing the difference in your blood results. There are 4 things you can do.

1. Adopt a healthy diet

HEART UK recommends a Mediterranean diet approach. To start with try eating fewer foods that contain saturated fat and eat more foods that are rich in unsaturated fats. If you are overweight remember to use only in small amounts as all fats are a concentrated source of calories.

Where to find saturated fat: fatty meat and meat products like sausages, dairy fats like full cream milk, cheese, yoghurt and cream. Spreading and cooking fats like butter, hard margarine, ghee, lard and coconut oil. Foods containing any of these as ingredients such as cakes, biscuits, pies, puddings and pasties.

Where to find unsaturated fats: cooking and spreading fats such as olive, rapeseed, sunflower and nut oils, soft spreads made from these oils, oily salad dressings, nuts, seeds, oily fish and avocado.

It is also sensible to:

- eat a more plant based diet that is rich in whole grains, fruits and vegetables, pulses, nuts and seeds and to have several meat free meals each week.
- have more soluble fibre such as that found in oats and barley, pulses and some fruits and vegetables as this can help improve overall cholesterol levels.
- pick oily fish such as salmon, herring, mackerel and sardines at least once and up to 4 times a week. Oily fish contain omega-3 fats that can raise HDL and lower LDL and triglyceride levels.
- avoid trans fatty acids which come largely from the industrial processing of foods. Partially hydrogenated vegetable oils on the ingredient labels of biscuit, crisp, cake wrappers is a clue that they are present. Watch out too for deep fried and takeaway foods and some foods cooked at high temperatures. Not only do trans fats increase LDL and triglyceride levels, they also reduce HDL levels. However in recent years, most food manufacturers have removed trans fats from their products.
- if you are frying at home its best never to re-use any oil and never heat it to the point when it starts to smoke.

2. Be more active

Any exercise, such as walking, jogging, swimming or cycling that raises your heart rate for 20 to 30 minutes at a time is beneficial. Ideally you should be active for at least 30 minutes on five or more days of the week. This is a very effective way to increase your HDL. Recent evidence suggests that the duration of exercise, rather than the intensity, is the more important factor in raising HDL cholesterol but both have been shown to have positive benefits. Regular aerobic exercise (exercise which raises your heart rate and gets you out of breath) can increase HDL cholesterol by about 5 % within 2 months, improve your LDL levels and also lower triglycerides.

3. Reduce your waist circumference

Storing excess fat around your waistline (apple shaped obesity) can cause your LDL cholesterol and triglycerides to increase and reduce your HDL. This is because excess calories start to be stored in and around the organs such as your liver and pancreas. Any fat stored in the liver can damage it. Because the liver plays a central part in controlling the amount of fat in your blood, this can result in abnormal levels of LDL, triglycerides and HDL. Fatty liver can result from eating too much or by drinking too much alcohol.

By losing inches around your waistline you can help increase your HDL levels, even if the scales do not show any weight loss. Gaining excess weight or inches around your waistline can lead to unhealthy patterns of cholesterol and increase the risk of diabetes and metabolic syndrome.

4. Stop smoking

If you are a smoker then stopping smoking could be key to increasing your HDL.

Smoking is a very common cause of low HDL. Not only this, it can also damage the fragile lining of artery walls making it easier for fat to get trapped inside. Smoking also makes LDL cholesterol more "sticky" and increases the chances of it getting trapped inside the damaged artery wall. Smoking also increases the heart rate and reduces the oxygen carrying capacity of the blood. Smoking is responsible for about one fifth of all heart disease deaths.

Treatments to raise low HDL levels:

Most drugs have only a limited effect on HDL cholesterol levels. Statins and fibrates help reduce LDL cholesterol and triglycerides very effectively but only have a small effects on HDL levels.

Tredaptive, a preparation of Nicotinic Acid (or niacin, a form of vitamin B3 not available to buy) was highly effective at raising HDL, between 10-30%, but this has been withdrawn from prescription due to the results of the HPS Thrive study which showed a significant increase in the risk of non-fatal serious side effects.

Potential new medicines are currently being tested in clinical trials. These include CETP inhibitors, which lower the activity of the cholesterol ester transfer protein in the blood, which in turn reduces the amount of LDL cholesterol and increases the amount of HDL.

Are higher HDL levels more protective?

Most health professionals are taught that the higher the HDL the more protection it offers. However some specialist doctors are beginning to question this. Even so it is still not entirely clear at what level the protection from HDL is lost or reduced, and indeed this protection may depend on properties of HDL particles that are very difficult to measure.

High HDL levels can be due to excessive alcohol intake, exercise and medicines such as the oral contraceptive pill or oestrogen replacement therapy. Your doctor should consider this in the first instance. They may also ask questions about your family to determine whether HDL-cholesterol is high due to an inherited cause. A family history of longevity is reassuring whereas a history of early cardiovascular disease may prompt a referral to a specialist. Only they can decide if the high level of HDL is relevant and decide whether other family members should be tested. Some people with a Japanese ancestry have been found to have high HDL levels due to a genetic deficiency of the protein, the cholesterol ester transfer protein (CETP).

Very high levels of HDL have been reported to speed up the development of atherosclerosis in some cases, but the mechanism for this effect is not clear. Recent research findings have suggested that the more HDL there is, the greater the chance that it may malfunction. This could mean that HDL does not do its normal job of clearing fatty deposits (plaques), it actually makes the plaques more unstable by causing further inflammation in the arteries.

According to HEART UK experts the protective effect of HDL appears to reach its maximum when levels are roughly 1.5mmol/L. Beyond this, higher levels of HDL may not provide additional protection and current research is suggesting that levels in excess of 2.3mmol/L may behave more like LDL cholesterol, raising the risk of developing cardiovascular disease and heart problems, particularly in women who are going through, or are post menopause.

How is HDL cholesterol affected by the menopause?

Doctors have suggested that the benefits of having a high HDL are reduced during the menopause as a result of changes in hormone levels. The University of Pittsburgh Graduate School of Public Health carried out a study in 2015 to show how the quality of HDL is affected during the menopause. They studied 225 women in their mid and late 40s using a series of scans to measure the level of plaque build-up in their arteries over nine years. All women were free of cardiovascular disease when they had their first scan. They found the following:

- the normal fall in oestrogen associated with the menopause changed the quality of HDL and its function
- increases in HDL cholesterol during the menopause were actually associated with a greater plaque build-up, independent of other factors such as body weight and levels of LDL cholesterol

They concluded that the quality of HDL may be altered during the menopausal transition period, making it less effective in providing the normal heart health benefits.

Recent research has also suggested that HDL particles change their makeup in other circumstances such as acute infection or chronic conditions linked to inflammation such as rheumatoid arthritis. More work is needed to understand this. Other findings have suggested that high HDL levels may be harmful to kidney dialysis patients by worsening inflammation and tissue damage.

What is the treatment for people with high HDL?

If you have a family history of early heart disease and your HDL is very high (above 3 mmol/L) and there is no obvious cause then ideally you should be referred to a lipid clinic for further investigations. If both total and HDL cholesterol are high (total cholesterol over 7.5 mmol/L with HDL cholesterol over 2.5 mmol/L in women) then treatment decisions are better guided by the levels of bad cholesterol (LDL and/or non-HDL-cholesterol) than by the Total/HDL-cholesterol ratio which may be misleading in these circumstances.

As yet it is not clear whether people with isolated very high HDL cholesterol will benefit from medicines such as statins or any new drugs in development. More research is needed to fully evaluate HDL function and to help develop strategies to prevent and treat heart disease.

In the meantime health professionals should encourage anyone with a high HDL to adopt a healthy diet and lifestyle and manage any other risk factors they might have. This is especially important in women prior to, during and following the menopause.