



What you should know about
cholesterol



The innovative **Swiss** pharmaceutical company

mepha



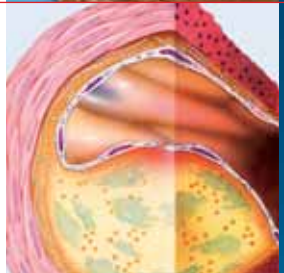
Cholesterol is an essential substance for life but too much can be dangerous



Cholesterol is taken up in greases from animals and produced from the body itself



Cholesterol can be divided in "good" and "bad" cholesterol



Cholesterol can be lowered if it is too high to avoid heart attacks and strokes



Important

- Cholesterol is important for life but too much can be dangerous. The right balance is important to stay healthy.
- The body cells need cholesterol to build different hormones, vitamin D, cell membranes and for the digestion of greases.
- The body produces enough cholesterol by itself, mainly in the liver and the intestine. Additional cholesterol is taken up with the diet.
- Cholesterol is a lipid that needs to be transported through the blood with transporters, so-called lipoproteins like LDL and HDL.
- LDL is called the "bad" cholesterol. If too much LDL cholesterol is circulating in the blood, it can accumulate in the blood vessel walls where it forms cholesterol depots. This is the initial step for a disease called "atherosclerosis". If these depots rupture, a thrombus can form and – by closing the lumen of the vessel – can cause a heart attack or a stroke.
- HDL is called the "good" cholesterol because it can collect excess cholesterol from the blood stream and transport it to the liver where it is degraded and secreted into the intestine.
- The imbalance of good and bad cholesterol is called dyslipidemia and should be treated with lifestyle changes and/or with a drug therapy.
- Dyslipidemia is an important risk factor for cardiovascular disease like heart attack and stroke. It is especially dangerous in combination with other risk factors like
 - Smoking
 - Hypertension (high blood pressure)
 - Diabetes
 - Obesity
 - Sedentarity

Elimination of these risk factors can reduce the risk for cardiovascular disease and improve the personal well-being.

What is cholesterol?

Cholesterol is a lipid that is essential for life and is present in literally every cell of a human body. Too much cholesterol in the blood however is a serious risk factor for cardiovascular diseases like heart attack and stroke. A person does not feel when the levels of cholesterol are elevated.

What other lipids are important?

Triglycerides are the classical oils and fats. They consist of three fatty acids and a glycerine molecule. Fatty acids can be divided into saturated and unsaturated ones depending on their chemical properties. Unsaturated fats are easier to metabolise than saturated ones and should therefore be preferred for a healthy diet. The concentration of unsaturated fats is higher in plant oils and in fish while in fat from other animals saturated fats dominate.

Phospholipids like lecithin are special triglycerides that consist of a water-loving and a lipid-loving part. They are therefore often found at the boundaries between lipids and water and play an important role in cell membranes.

Because cholesterol is a lipid while blood consists mostly of water, cholesterol needs a carrier to be transported through the blood.



Where does cholesterol come from?

Cholesterol is produced in our body and also taken up with food. The human body can produce all the cholesterol it needs and does not require additional cholesterol from the diet.

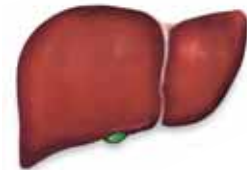
Every day 1–2 g of cholesterol are newly synthesised predominantly in the liver and the intestine. Additionally up to approximately 0.2–0.8 g are taken up with the diet.

A human body contains approximately 150 g of cholesterol. Most of it is used in cell membranes. Only approximately 5% of the cholesterol is circulating in the blood.

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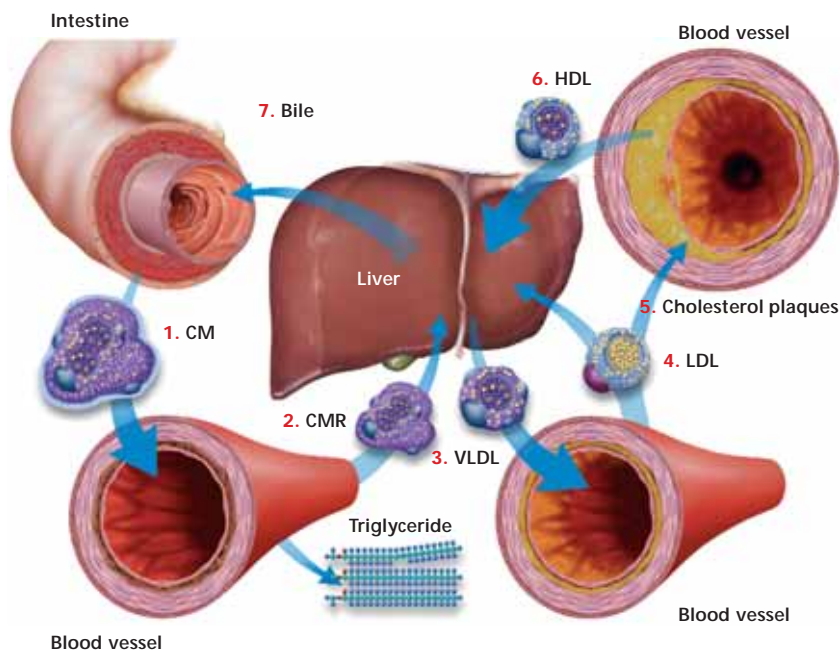




How is cholesterol transported?

Cholesterol is transported by the blood into the body. Because cholesterol is a lipid while blood consists mostly of water, cholesterol needs a carrier to be transported through the blood. The body uses different transporters for different tasks. These transporters consist of cholesterol, other lipids (triglycerides and phospholipids) and proteins.

The transport of lipids through the body



- 1. Chylomicrons (CM)** transport lipids from the intestine into the body. They deliver mainly triglycerides to the body cells.
- Deprived of triglycerides they are called **chylomicron remnants (CMR)** which are taken up by the liver where they are disassembled.
- Very low density lipoproteins (VLDL)** transport lipids from the liver into the body. Again triglycerides are the main content.
- Deprivation of triglycerides starts a transformation first into intermediate density lipoproteins (IDL) and then further into **low density lipoproteins (LDL)** which are again taken up by the liver where it is disassembled.
- Low density lipoproteins can also enter the blood vessel walls and accumulate there to cause cholesterol plaques. This is why LDL is called the bad cholesterol.
- High density lipoproteins (HDL)** transport mainly cholesterol and phospholipids from the body (and from plaques) back to the liver. This is why HDL is called the good cholesterol.
- Excess cholesterol is secreted with the bile into the intestine where it helps to digest lipids.



Why do we need cholesterol?

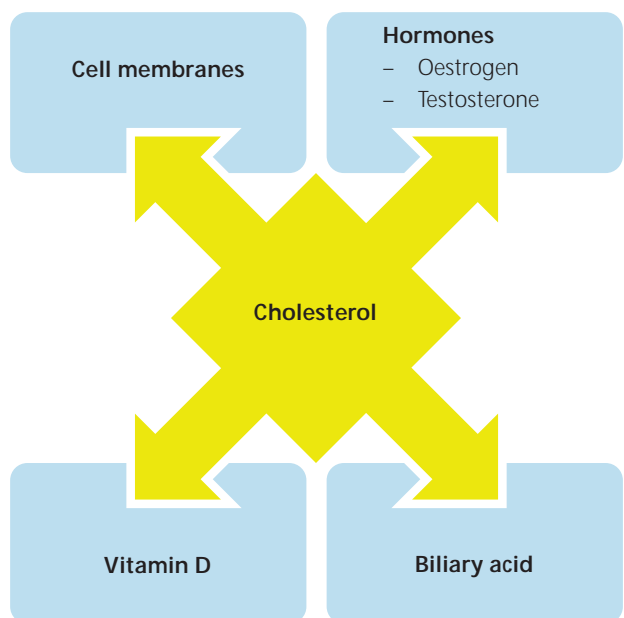
The word cholesterol is derived from the Greek word "chol" that means bile. Biliary acid is generated from cholesterol. Together they are secreted into the intestine to facilitate the digestion of lipids.

The body is excreting 2 g of cholesterol every day through the bile into the intestine. Roughly 1.6 g however are reabsorbed in the upper part of the intestine. Together with biliary acid, that is generated from cholesterol, it facilitates the absorption of other lipids mainly triglycerides.

Cholesterol is also the basic substance for the synthesis of all steroid hormones in the body like testosterone or oestrogen that regulate a variety of body functions.

Vitamin D is generated from cholesterol and plays an important role in the formation of bones.

Most cholesterol however is located in cell membranes.



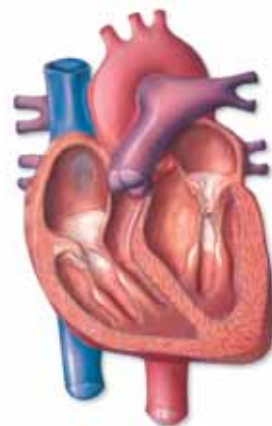
Why is cholesterol dangerous?

If the concentration of LDL cholesterol in the blood is high, the liver is not able to absorb it fast enough. When LDL circles too long in the blood, it can be oxidised (a chemical reaction with oxygen). Oxidised LDL is less likely to be recognised by the LDL receptors in the liver and therefore continues to circulate in the blood.

Another receptor called scavenger receptor begins then to play an important role. This scavenger receptor however does not only exist in the liver. White blood cells that are called macrophages use them too to eliminate unwanted material from the blood.

When macrophages contain high concentrations of cholesterol, they are called sponge cells that will die and form cholesterol plaques in the artery walls. Such cholesterol plaques are the initial step of atherosclerosis. Since the plaque usually starts to grow to the outside of the blood vessel, the blood flow is barely compromised. This is why atherosclerosis often does not cause any symptoms at this early stage of the disease. At a later stage of atherosclerosis the plaque also grows into the lumen of the blood vessel and disturbs normal blood flow.

When a plaque ruptures, the blood starts to clot and builds a thrombus to close the injured blood vessel wall. This can cause an acute event when the thrombus blocks the blood vessel or when the thrombus is swept away in the blood stream and blocks another blood vessel. Depending on the location where the blood flow is blocked it causes a stroke (brain), myocardial infarction or heart attack (heart).



Heart attack
A blocked artery can cause an infarct.



The good and the bad cholesterol

LDL cholesterol is called the **bad** cholesterol because high LDL-levels can cause cholesterol plaque in the blood vessel walls.

HDL cholesterol is called the **good** cholesterol because it is able to extract cholesterol from the blood and transport it back to the liver.

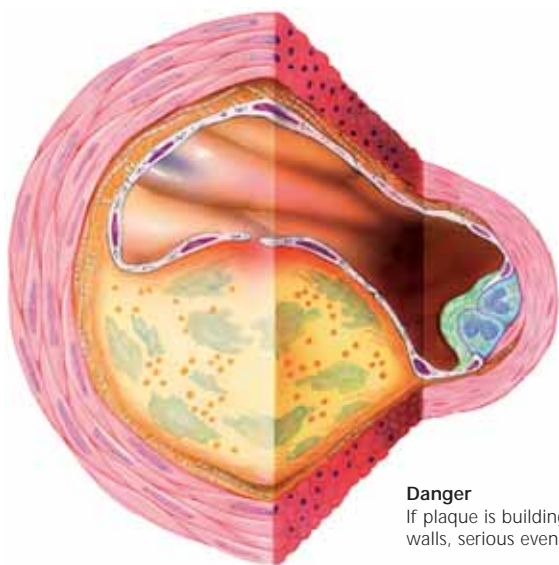
High LDL and low HDL concentrations are dangerous. This is why specialists call this misbalance dyslipidemia.

Often the total cholesterol in the blood is measured. This is easier than measuring LDL and HDL which can only be done under fasting conditions. High total cholesterol often indicates that the LDL is also elevated. In case of elevated total cholesterol it makes therefore sense to measure also the LDL and HDL values to get a better picture of the risk.

Remember

- **LDL** should be **Low**
- **HDL** should be **High**

Triglycerides can also be elevated. They indicate elevated levels of VLDL or CM.



Danger
If plaque is building up in the vessel walls, serious events can result.

Who is at risk?

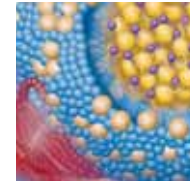
Elevated cholesterol does not cause symptoms. Atherosclerosis often begins more than ten years before the first clinical manifestations occur. For roughly half of the patients the first symptom of elevated cholesterol is an acute event like a heart attack or a stroke. The treatment of these events has greatly improved over the last decades. Nevertheless many of them are still fatal or cause a major reduction in the quality of life of the affected patients. It is therefore important to diagnose high cholesterol, as early as possible to prevent events rather than trying to cure them afterwards.

The higher the cholesterol levels are or the greater the misbalance between good HDL cholesterol and bad LDL cholesterol the bigger is the risk for developing atherosclerosis.

For every 0.8 mmol/l (30 mg/dl) of LDL the risk for a cardiovascular event increases 30%.

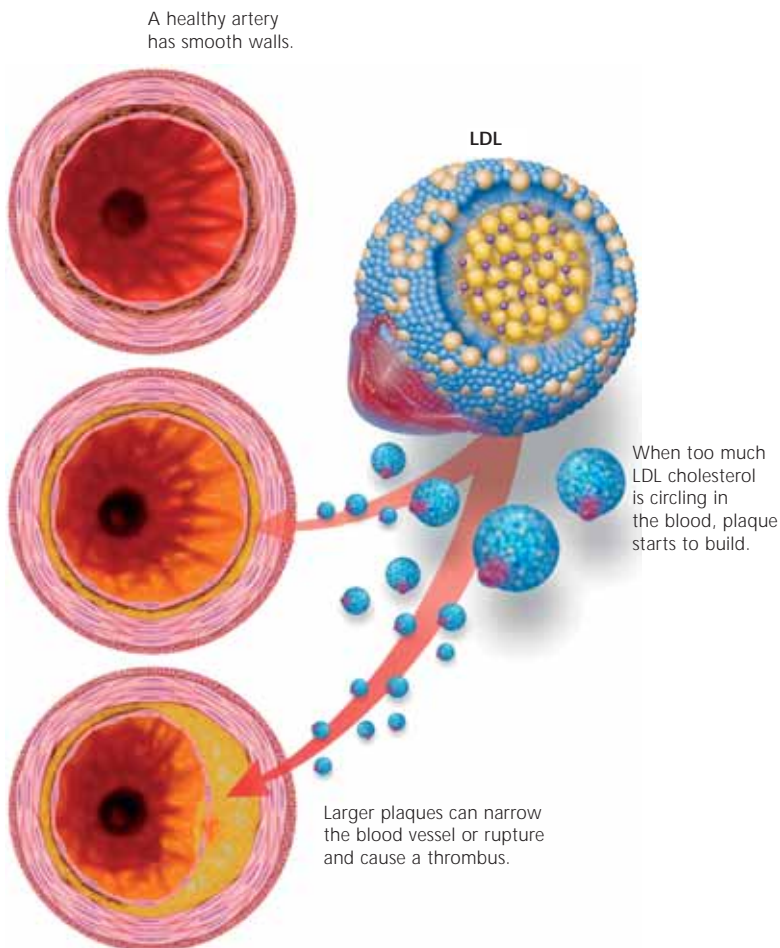
High cholesterol is especially dangerous if other risk factors for cardiovascular disease are present. The risk of different risk factors is not only added, it is almost multiplied. Therefore having several risk factors can be dangerous even when each risk factor is only slightly elevated.

Some risk factors cannot be altered like the age, sex or family history of cardiovascular disease. Other risk factors like smoking, obesity, sedentarity, hypertension or diabetes can be changed either by lifestyle variations or with a drug therapy.



Risk factors for atherosclerosis

- Cardiovascular event in the past
- Age (men > 50 years, women > 60 years)
- Family history of cardiovascular disease
- Smoking
- Obesity
- Sedentarity
- Diabetes
- Hypertension (high blood pressure)
- Dyslipidemia (high cholesterol)



What are normal values?

A newborn child has an LDL cholesterol of 1 mmol/l (40 mg/dl). This increases as the need for cholesterol decreases when the body stops growing. There is no normal value for LDL cholesterol as the risk increases the higher it is and decreases with lower values. The reference values were set arbitrarily reflecting the scientific evidence and take into account the overall risk of a person.

The overall risk is influenced by the risk factors. For a person without other risk factors much higher values of cholesterol can be tolerated than for a patient who has an increased risk due to other risk factors. The cholesterol values that make a drug therapy advisable depend on the overall risk as do the target values for the therapy.

Two different units are used to measure blood lipids (mmol/l and mg/dl). The conversion of these units is different for cholesterol and triglycerides.

Since there is no absolute value as of which cholesterol is dangerous, different organisations (NCEP-ATP3, 3JE/ESC, IAS, AGLA) have created different guidelines based on clinical trials and also on the absolute risk of the respective population to best reflect the needs of their country or region. It is almost impossible to combine them into generally applicable recommendations. Therefore the below given recommendations should be regarded a generalisation to give a global perspective. Your physician can inform you about your local guidelines.



What are normal values?

	LDL cholesterol level at which a drug therapy should be considered	LDL cholesterol level at which therapeutic life-style changes are advised	LDL goal
High risk (patients with cardiovascular disease, diabetes or a 10-year risk for cardiovascular disease of > 20%)	≥ 2.6 mmol/l (≥ 100 mg/dl)	≥ 2.6 mmol/l (≥ 100 mg/dl)	< 2.6 mmol/l (< 100 mg/dl) In some cases < 1.8 mmol/l (< 70 mg/dl) might be advisable.
Moderate to high risk with 2 or more risk factors and a 10-year risk of > 10%	≥ 3.4 mmol/l (≥ 130 mg/dl)	≥ 3.4 mmol/l (≥ 130 mg/dl)	< 3.4 mmol/l (< 130 mg/dl)
Moderate risk with 2 or more risk factors and a 10-year risk < 10%	≥ 4.1 mmol/l (≥ 160 mg/dl)	≥ 3.4 mmol/l (≥ 130 mg/dl)	< 3.4 mmol/l (< 130 mg/dl)
Low risk with 0 or 1 risk factor and a 10-year risk of < 10%	≥ 4.9 mmol/l (≥ 190 mg/dl)	≥ 4.1 mmol/l (≥ 160 mg/dl)	< 4.1 mmol/l (< 160 mg/dl)

If the total cholesterol is > 4.9 mmol/l (190 mg/dl), it is helpful to measure the LDL, HDL and triglyceride levels to get a better estimate of the risk.

HDL cholesterol < 1.0 mmol/l (40 mg/dl) has to be seen as an additional risk factor.

Triglycerides > 2.0 mmol/l (180 mg/dl) are an independent risk factor.

What can be done against high cholesterol?



Weight loss, a healthy diet and exercise can reduce cholesterol levels, eliminate additional risk factors and increase the quality of life. If this is not enough, a drug therapy can further reduce blood lipids.

■ A healthy diet can reduce the cholesterol levels

It is important to note that not only the cholesterol contents of the diet has an impact on the cholesterol level in the blood. Since the body can upregulate the cholesterol production when the amount of cholesterol in the diet is reduced, avoiding cholesterol alone often has a limited impact on the blood cholesterol values. For the production of cholesterol in the liver the amount of saturated fats in the diet plays an important role and can impact the cholesterol level in the blood. Some aliments with high levels of cholesterol like eggs also contain healthy fats like phospholipids and should therefore not be condemned only based on their cholesterol contents. However, one egg already contains the suggested amount of cholesterol per day in a healthy diet.

■ Functional food

Plant sterols and certain fibres can reduce the absorption of cholesterol in the intestine. Different products that are enriched with these substances are available and have been shown to reduce cholesterol. There is no proof, so far, that functional food can actually reduce cardiovascular events.

■ The recipe for a healthy diet

When changing a diet it is important that the changes are sustainable. Diets that restrict what to eat are often only followed for a limited time. The risk of returning to the old unhealthy lifestyle is high.

A good diet is fun because healthy food is very tasty and easy because it only requires following a few principles:

- Try to eat aliments that are rich in fibre like oatmeal, potatoes, legumes, vegetables and fruits. They can help to reduce your cholesterol level.
- Reduce the consumption of saturated fats that occur predominantly in animal fats like butter, milk products and meat but also in plant fats like coconuts or chocolate.
- Prefer fat-sparing preparations like boiling, steaming or grilling and choose if possible oils like olive oil, rape oil, sunflower oil.
- Consume food with a high content of cholesterol like eggs, shell fish and innards with moderation.
- Watch out for hidden fat and cholesterol in sausages, bakery and processed food.

Eat with moderation, especially fats and cholesterol, and drink enough water and juices.



What can be done against high cholesterol?



■ Regular exercise should become a habit

The human body adapted over centuries to a life where getting enough food was a challenge and required intensive physical activity. Today in most countries getting enough food is not an issue and work is often done in a sitting position.

Physical activity does not only require energy and helps to burn the calories that we often consume in excess of our needs, it also increases our performance and it can help to increase the HDL cholesterol.

It does not matter if you prefer jogging, swimming, hiking or riding a bicycle. These and other endurance sports are ideal because body fat is burnt effectively. New studies have shown that power sports like weight lifting are also beneficial. It does not matter what you do as long as you practice regularly and at least for 20 minutes at a time.

■ Start slow

Do not overdo the fitness training. Start slow and you will see that you can increase the intensity rapidly. Watch your pulse. Especially if you want to burn fat, your pulse should not be too high. Burning fat requires energy to mobilise these reserves. If the exercise intensity is too high, the body will burn carbohydrates and proteins instead of fat.

As long as you can still talk normally while working out your pulse is OK. This is an easy way to adapt the intensity. If you want to control your pulse while exercising more accurately, many tools like watches or belts are available.

Talk to your physician if you want to start exercising, especially if you have heart problems. He can consult you on safe ways to do so.

■ Reduce other risk factors

Smoking is an important risk factor for cardiovascular disease and cancer. Smoking can double the risk for having a heart attack or a stroke. Smoking increases free radicals and therefore promotes the oxidation of LDL cholesterol making it more likely to be deposited in the blood vessel walls. Smoking narrows the blood vessels and increases the blood pressure, another risk factor. Smoking also decreases the HDL cholesterol levels. Smoking cessation can therefore be seen as the most important lifestyle change to reduce the risk for cardiovascular disease.

Obesity often causes increased cholesterol and triglyceride levels. The increased body fat especially around the waist line can also increase the likeliness of plaques in the blood vessels to rupture through chemical processes. A small reduction in body weight can already have a measurable impact on the cholesterol and triglyceride levels in the blood. The reduction of the body weight should be done in a sustainable way. Many diets require drastic changes and are only maintained for a limited time. The body adapts quickly to the decreased supply with energy and starts to work in a more economic fashion. When returning to the old habits the lost weight is therefore regained very quickly. This is called the yo-yo effect. Rather use small changes of your diet that can be maintained for the rest of the life. Diets can even be a health risk because the supply of your body with essential vitamins or mineral salts is not guaranteed. Consult your physician or a dietician when you consider losing weight. He can offer you professional assistance and help you to find a healthy way of doing so.



Drug therapy

Different drug classes are available to reduce blood lipids: **statins, fibrates, nicotinic acid, absorption blockers and resins. They all have specific advantages and disadvantages.**

■ Statins

To reduce cholesterol statins are the most effective, widest studied and most used class of drugs. Statins reduce the production of cholesterol in the liver. Depending on the statin and the strength used cholesterol can be reduced 20 to 60%. In large clinical trial with many thousand patients statins were shown to reduce heart attacks, strokes and cardiovascular deaths significantly.

■ Fibrates

Are not very effective reducing cholesterol but act strong against elevated triglycerides.

■ Nicotinic acid

Are an older class of drugs with limited clinical evidence to reduce clinical events. They have more side effects and are not as effective as statins in reducing cholesterol. They are nowadays mostly used in small dosages in combination with a statin in severe cases.

■ Absorption blockers

Are mostly used in combination with a statin in severe cases since they reduce the cholesterol by a different way.

■ Resins

Are only used in severe cases as a combination or if other drugs are not tolerated since they are relatively expensive and are not as well tolerated as the alternatives.

All these drugs require a prescription. Your physician will initiate the therapy if you require drugs to lower your cholesterol and advise you about their utilisation.



Your physician:

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