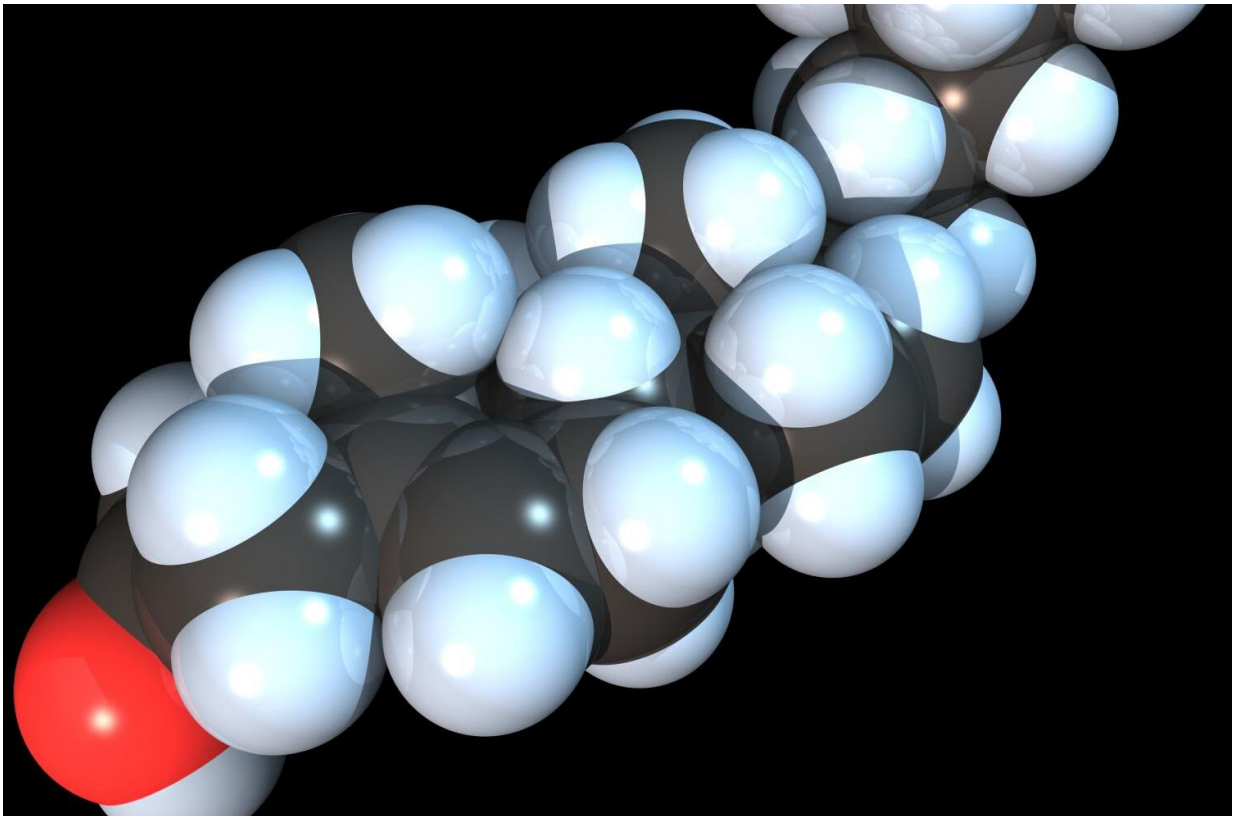


Researchers show cholesterol type can affect your heart attack risk

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Space-filling model of the Cholesterol molecule. Credit: RedAndr/Wikipedia

Vascular plaque. It starts with inflammation. Perhaps your blood pressure has been a little too high for a little too long, putting strain on your blood vessels.

Small particles—lipoproteins containing cholesterol—attach themselves to the artery wall and are then attacked by immune cells. A lump of fat and dead cells builds up under a thin, protective membrane.

This lump remains invisible to the naked eye, until one day the lump completely blocks the vein. Or until it suddenly bursts. Oxygen is unable to reach the heart, resulting in a heart attack.

"The type of plaque you have is also important. Some people have vulnerable or unstable plaque. There is usually a large volume of these types of plaque, narrowing the arteries. As the plaque grows, it affects blood flow.

"In addition, plaque usually has a [high fat content](#), and is surrounded by a thin membrane or capsule that can easily burst. It is like a huge pimple," says Elisabeth Kleivhaug Vesterbekkmo, senior consultant at the Clinic of Cardiology at St. Olavs Hospital.

This process is called atherosclerosis, which means hardening of the arteries. Among other things, this is caused by cholesterol, which isn't an issue for most of us until we reach a certain age, but by then it may be too late.

Different types of cholesterol

The number of people who die from cardiovascular disease has decreased significantly in Norway over the past 40 years. Yet more than 10,000 people experience acute heart attacks each year.

"The question is: could any of these have been avoided? We know that over 55% of these heart attacks have what we call metabolic drivers. We are talking especially about high LDL cholesterol as well as elevated blood sugar and high blood pressure," says Vesterbekkmo.

The scientists agree that there is a direct causal relationship between LDL cholesterol and atherosclerosis. The more LDL cholesterol there is in circulation in the body, the higher the risk of inflammation and build-up of plaque.

"Everyone is in agreement about this. There is an overwhelming amount of data confirming it. The lower the LDL, the better the situation."

However, there are also other cholesterol-containing particles that raise the risk of cardiovascular disease—substances that are not routinely measured. One example is VLDL cholesterol, a type of fatty substance that has a high triglyceride content.

"VLDL cholesterol has been shown to increase plaque formation," says Vesterbekkmo.

Another important fatty substance in the blood is lipoprotein(a), commonly called Lp(a). This substance consists of an LDL particle that has a special protein called apolipoprotein A bound to it. High levels of Lp(a) increase the risk of cardiovascular disease. Approximately 5% of the population have significantly elevated levels of this risk factor, which is hereditary.

"If there is a significant history of [cardiovascular disease](#) within the family, patients should be checked for an elevated level of Lp(a)," Vesterbekkmo explains.

Bad guys in the blood

Some people have a heart attack without having elevated levels of LDL cholesterol in their blood.

"This means that we have to look for other causes," says Vesterbekkmo.

One common factor for all pathogenic cholesterol-containing particles is that they have a small "additional protein" attached to them, called Apo-B.

"Apo-B is a real bad guy. We can measure Apo-B level in the blood, which tells us how many Apo-B particles are circulating and that might reach the walls of your [blood vessels](#). This gives us important additional information," says Vesterbekkmo.

In other words, a person can have what appears to be a perfectly acceptable cholesterol level, when only LDL cholesterol, HDL cholesterol, and the total cholesterol in the blood are measured. This is the standard cholesterol test that you get at your GP. At the same time, people can have elevated levels of other lipoproteins that increase the cardiovascular risk, without being aware of it.

"Cholesterol levels increase with age. This is why you should keep an eye on developments as you get older. For example, if you have significantly elevated levels of Lp(a), you can quickly reach a level where preventive medication is recommended," says Vesterbekkmo.

Searching for new markers

Julie Caroline Sæther has recently completed a Ph.D. on biomarkers that can detect fatty plaque and the risk of future heart attacks. She has been searching for new markers that can be detected through a simple blood test.

"Some patients who are hospitalized with a heart attack do not have the common, classic risk factors. They might not even have had any symptoms prior to the heart attack," says Sæther.

For these patients, a [heart attack](#) is like a bolt from the blue. The cause

may lie in the type of atherosclerosis the unsuspecting patient has. As Vesterbekkmo puts it: Some types of plaque are more unstable than others.

"Lipid-rich plaque, i.e., plaque with a high fat content, is more prone to ruptures. The membrane covering the plaque is thinner and bursts more easily," says Sæther.

If a rupture occurs, the contents enter the bloodstream. This can quickly turn into a clot that completely blocks the blood vessel, leading to an emergency situation. Quick treatment is then crucial to minimize damage to the heart muscle and reduce the risk of further complications.

MicroRNA, Lp(a) and small HDL particles

Sæther, Vesterbekkmo and their colleagues are now trying to find markers in the blood that reveal the presence of fatty and unstable plaque that increases the risk of acute events.

"We have used advanced imaging techniques inside the coronary arteries of patients known to have pathogenic plaque in order to determine the fat content in the plaque. In addition, we have measured microRNA and various lipids in the blood to see if we could find markers that indicate the fat content of the plaque," says Sæther.

The scientists found one microRNA as well as two lipid particles, which other research has also shown to be associated with atherosclerosis.

"We found that patients with fatty plaque, i.e., plaque with a high fat content, had higher levels of a microRNA called miR133b. These patients also had higher levels of Lp(a) and free cholesterol in the smallest HDL particles. However, more research must be conducted before we can say with certainty that our findings are true. We need to

carry out larger studies with more patients," says Sæther.

All the patients in the study were on statins, which are cholesterol-lowering medications.

"This probably erased some potential findings, but we know that both HDL and Lp(a) are not significantly affected by statins," says Sæther.

At the same time, research on miR133 and lipid subgroups is divergent. According to Sæther, there is still a lot of lab work that needs to be done.

"Although we now have adequate methods to measure microRNA, the analyses are costly and time-consuming. By contrast, the methods used to measure subgroups of lipids have become so good that using them in clinical practice may be possible if it is seen that they provide important information about risk," says Sæther.

Checking family history is important

At the Clinic of Cardiology at St. Olavs Hospital, Vesterbekkmø is focused on the early detection of potential future heart patients as a preventative measure.

"Our aim is to slow down the atherosclerosis process at an early stage. If we identify young people with high cholesterol and start treatment early, we can prevent disease to a large extent," she said.

If you come from a family where either parent has had heart problems early on in life, i.e., before the age of 55 for fathers, or before the age of 65 for mothers, you may have a hereditary predisposition to the disease. Having middle-aged cousins, aunts and uncles who had to have arteries unblocked may be a further sign of hereditary predisposition.

"This may be a sign that you may have an elevated risk, which you can actually do something about, but you need to know your lipid profile. In addition, you must take other more traditional risk factors into consideration," Vesterbekkmo says.

Familial hypercholesterolemia (FH) is one of the most common inherited conditions in the population. Approximately 1 in 200–300 Norwegians have this genetic defect, many without knowing it.

Vesterbekkmo thinks doctors should start with the simplest things: asking the patient if there is a history of heart disease or strokes caused by atherosclerosis in the family.

"If you combine family history with cholesterol measurements, you quickly get an important overview of risk. However, traditional risk factors must also be taken into account."

After the fact

Once atherosclerosis is established, the plaque and the disease remain, even if the patient has received treatment with a stent, known as angioplasty. Therefore, Vesterbekkmo emphasizes that good medication adherence and lifestyle changes are important.

"Medications such as statins and other modern medicines can reduce and stabilize plaque to some extent, but lifestyle changes and regular exercise are also important. Our research group has conducted studies showing that regular exercise not only has a positive effect in relation to risk factors, but also affects the plaque directly," says Vesterbekkmo.

Exercise makes the [plaque](#) more stable, reduces the fat content and has a beneficial effect on the lipid profile, but it does not change the "bad" cholesterol.

"We cannot outrun our LDL level. The only way to reduce the level of bad cholesterol is through effective medicines, especially for people with significantly elevated levels. And the sooner, the better," says Vesterbekkmo.

Provided by Norwegian University of Science and Technology

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