Quest Diagnostics™

The benefit of **knowing**

Genetic testing for familial hypercholesterolemia (FH)

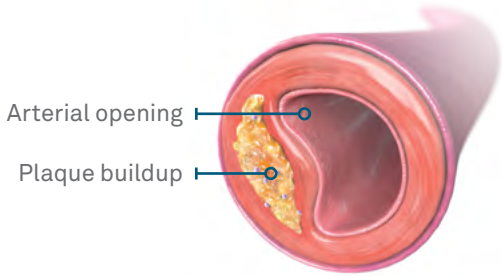
A patient support guide

Does high cholesterol **run in your family**?

In some families, high cholesterol is caused by **familial hypercholesterolemia**, called FH for short. In FH, genetic changes cause high cholesterol levels and affect the way the body processes cholesterol. These genetic changes are called mutations.

As many as 1 in 300 to 500 people have FH, but most have not been diagnosed. It is important to know whether your high cholesterol is caused by FH so your doctor knows how to treat your high cholesterol. Proper treatment can greatly lower the chance of early **coronary artery disease (CAD)**. Knowing if you have FH also helps you know whether your family is at risk. Review this guide with your healthcare provider to learn if genetic testing is right for you.

High cholesterol can lead to plaque buildup that can clog arteries.



How can genetic testing for FH help?

A blood test can help you find out whether you have a mutation that causes FH. It can also help you learn more about what is causing your high cholesterol levels. If the test detects a mutation that causes FH, you have treatment options, which could lower your risk for CAD. Getting tested can also provide important information to your family.

Who should be tested?

Talk with your provider about testing if any of the below are true about you or someone in your family:

- Has untreated **low-density lipoprotien (LDL-C)** levels ≥190 mg/dL (≥160 mg/dL with treatment) or levels ≥160 mg/dL in an untreated child
- Has early CAD or other cardiovascular disease
- Has **xanthomas** or **corneal arcus**
- Has a mutation that causes FH

Any one of these could be a reason to think about genetic testing for FH.

Some words in this guide are highlighted, **like this**. You will find the definitions on page 7, **Important terms to know**.

What will the results tell me?

These tests can tell if you have a mutation(s) that is causing your high cholesterol or the high cholesterol that runs in your family.

Remember, if you find a genetic cause for your high cholesterol, it can help your doctor treat you more appropriately and lower your risk for CAD.

If testing finds a mutation that causes FH, what does this mean for my family members?

We share some of our genes in common with our relatives. If someone in the family has a mutation that causes FH, other family members may have the same mutation. This would mean an increased risk for high cholesterol leading to CAD.

The most common form of FH is called **heterozygous FH**, or HeFH for short. This means you inherited a mutation that causes FH from either your father or your mother. If you have HeFH, your brothers, your sisters, and your children each have a 50% chance of having the same mutation. Other relatives are also at risk. It is important to share your test results with your family.

Relative	Relative's chance of having the same mutation that causes FH
Identical twin	100%
Parent, sibling, child, fraternal twin	50%
Grandparent, uncle, aunt, niece, nephew	25%
First cousin	12.5%

There is a less common form of FH called **homozygous FH**, or HoFH for short. This means that you inherited a mutation that causes FH from both your mother and your father. If you have HoFH, your relatives may be at risk for either HeFH or HoFH. They should discuss this further with their doctors.

The genetic testing process

The first step is to talk with your healthcare provider or genetic counselor about your personal and/or family history of high cholesterol or CAD. This will help you figure out if testing is right for you.

Does insurance cover the cost of genetic testing?

It depends on your insurance company. Your insurance may cover some or all of the cost. Call Quest Genomics Client Services at 1.866.GENE.INFO (1.866.436.3463) and ask to speak to our Prior Authorization team to get help.

How long will it take for my results to come back?

Your doctor will get the results in around 14 to 21 days.

Could I lose my health insurance based on my test results?

Most likely not. There is a federal law called the Genetic Information Nondiscrimination Act (GINA). You can visit http://ginahelp.org for more information.

Making sense of your test results

Your healthcare provider or genetic counselor will explain what your test results mean. There are three possible results:

Negative

The test did not find a mutation that causes FH.

- If your family has a known FH-related mutation and your cholesterol is normal, then you are not at risk for FH.
- If your family does not have a known FH-related mutation, then your risk for high cholesterol may still be increased. In some cases, testing other genes or other relatives may be recommended.
- If you have a clinical diagnosis of FH, your negative genetic test does not change your diagnosis. You may have a form of FH caused by rare genetic changes, some of which may not yet be known.

Positive

The test found a mutation that causes FH. You may see mutation referred to as a pathogenic or likely pathogenic **variant** on your report.

Individuals with FH have high levels of LDL cholesterol (LDL-C). This may increase the risk for early CAD and heart attack. Individuals with FH may have either HeFH or HoFH.

You and your healthcare provider will talk about ways to lower your risk, such as medications and lifestyle changes.

Variant of unknown clinical significance

It is not uncommon to find changes in genes with an unknown effect. We call these "**variants of unknown clinical significance (VUS)**." Over time, we may learn more. Check with your healthcare provider each year for updates about VUS.

Important terms to know

Corneal arcus: A white ring around the colored part of the eye, caused by cholesterol buildup.

Coronary artery disease (CAD): A disease in which plaque made of cholesterol builds up inside the coronary arteries. This can lead to a heart attack.

Familial hypercholesterolemia (FH): A genetic condition where cholesterol is not properly removed from the blood. People with FH have especially high cholesterol levels.

Heterozygous FH (HeFH): People with HeFH have one mutation in one of the genes that causes FH.

Homozygous FH (HoFH): People with HoFH have two mutations in one of the genes that causes FH or one mutation in two genes that cause FH. HoFH is less common and tends to be more severe than HeFH.

Low-density lipoprotein (LDL-C): A term for cholesterol.

Variant: A permanent change in DNA. Variants can be helpful, neutral, or harmful.

Variant of Unknown Clinical Significance (VUS): A DNA change with an unknown effect. It could be a normal change, or it could be harmful.

Xanthoma: A soft nodule on the skin made of cholesterol buildup.

Feel good about genetic testing. The more you know, the more you can do to enjoy better health.

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