West Midlands Familial Hypercholesterolaemia Service

Information sheet for patients with polygenic hypercholesterolaemia

Familial Hypercholesterolaemia (FH)

You have been found to have high levels of cholesterol in your blood and possibly also a family history of early heart disease. This led to your doctor suspecting that you may have a genetic condition called familial hypercholesterolaemia (FH). Your clinic assessment excluded other conditions and dietary causes so a blood sample was sent for a genetic test to look for a change in the DNA sequence in one of four different genes. These particular genes tell your liver to make proteins that are important in clearing cholesterol from the blood. Changes in the DNA sequence of these genes can result in the proteins being unable to remove the cholesterol from the blood. These are called gene alterations. The type of FH where we find an alteration in one of these genes is called monogenic FH.

Your test result was negative, meaning we did not find an FH-causing gene alteration.

What does a negative test result mean?

Research in the UK has shown that an FH-causing gene alteration cannot be found in around 60–70% of patients who are suspected to have FH. So you are not alone in not receiving a clear answer as to why you have high cholesterol. There are several possible explanations:

- It could be that you don't have FH, and your high cholesterol is mainly due to environmental factors. Cholesterol levels are affected by eating foods high in saturated fats and cholesterol, like high-fat dairy products, fried food or fatty meat. This cause of high cholesterol can be helped by adopting a healthy diet and lifestyle, and your general practice nurse can give you advice on this

- It could be that you do have FH, but you have a gene alteration in a completely new gene that is not included in the current test. Again we think this is unlikely, but if you have given us consent, we will keep your DNA stored and test it again if a new FH gene is discovered

- The most likely explanation is that you have what we call "polygenic" hypercholesterolaemia. Research shows that, in at least 80% of patients with high cholesterol and no FH-causing gene alteration, the likely cause is they have inherited an above average number of common variations in genes that can cause raised cholesterol. Each of these has only a small cholesterol-raising effect, but when several occur in combination, together these can raise an individual's cholesterol levels to those often seen in monogenic FH

You have been tested for these common cholesterol-raising DNA sequence changes and the results show that you have polygenic hypercholesterolaemia.

How does this affect my treatment?

You have high cholesterol and it's important that this is reduced by taking cholesterol-lowering medication such as statins. This treatment will reduce your future risk of developing heart disease. Patients with polygenic hypercholesterolaemia usually respond well to standard statins and see a good reduction in cholesterol levels. Your GP may manage this condition, or you may also be referred to a specialist lipid clinic for advice.

What does this mean for my family?

If we had found a gene alteration causing FH in your DNA, we could have tested your relatives to see if any of them had also inherited the same gene alteration. On average, about 50% of your close relatives would also have the gene alteration. Since we didn't find a gene alteration, there is no DNA test we can offer your relatives. Some of them may also have polygenic hypercholesterolaemia, but research has shown that about 70% will have normal cholesterol levels. However we would still advise them to ask their GP for a cholesterol test.

Any questions or concerns?

If you have any questions or concerns about this information, please contact the FH team on **0121 371 8179**.

Further Information regarding cholesterol and polygenic hypercholesterolaemia can be found on the following websites:
www.bhf.org.uk
www.heartuk.org.uk

How did we do? ☺ 😐 ☹

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