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## Genetic factors and cholesterol

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### Summary

- Familial hypercholesterolaemia is an inherited condition characterised by higher than normal levels of blood cholesterol.
  - Familial hypercholesterolaemia causes up to 10 per cent of early onset coronary artery disease – heart disease that occurs before the age of 55 years.
  - The cause is a mutated gene.
  - Treatment includes dietary modifications, regular exercise, avoiding smoking, and the use of cholesterol-lowering drugs.
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Cholesterol is an essential component of cell membranes and is needed for many bodily functions, such as the production of hormones. It is produced when foods containing oil and fat are digested. It is also produced in the liver.

Cholesterol in the blood is found in two types of particles. The cholesterol in low density lipoproteins (LDL) is known as the 'bad' cholesterol because it contributes to heart disease by 'sticking' to and narrowing the arteries supplying the heart. High density lipoprotein (HDL) cholesterol is known as the 'good' cholesterol because it keeps LDL levels in check.

Familial hypercholesterolaemia is an inherited condition characterised by higher than normal levels of LDL blood cholesterol. Familial hypercholesterolaemia causes up to 10 per cent of early onset coronary artery disease – heart disease that occurs before the age of 55 years.

The cause is a mutation in a gene. About one in every 300 Australians is thought to be affected. Other names for familial hypercholesterolaemia include familial hyperlipidaemia, hypercholesterolaemic xanthomatosis and low density lipoprotein receptor mutation.

### Symptoms of familial hypercholesterolaemia

High blood cholesterol can be asymptomatic, which means the person may not even realise they have it. Some of the signs and symptoms of familial hypercholesterolaemia can include:

- family history of the disorder
- family history of heart attacks at an early age
- high LDL cholesterol levels that resist treatment in one or both parents
- cholesterol deposits on the knees, elbows and buttocks (xanthomas)
- high blood cholesterol levels
- chest pain caused by narrowed coronary arteries (angina)
- heart attack early in life.

### Genetics of familial hypercholesterolaemia

Cholesterol is delivered to cells via the bloodstream. Normally, the tiny particles of LDL cholesterol attach to 'receptor' sites on the targeted cells and are then absorbed. A gene on chromosome 19, called the LDLR gene, controls the production of these receptors. Most familial hypercholesterolaemia is due to a mutation of the LDLR gene that changes the way the receptors develop, either in number or structure. This means that LDL cholesterol is not well absorbed into cells, and remains circulating in the blood.

High blood cholesterol is a risk factor in coronary artery disease, because it sticks to the artery walls, produces fatty plaques and narrows the diameter of the arteries (atherosclerosis). Less commonly, familial

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hypercholesterolemia is caused by a mutation on other genes, such as APOB or PCSK9.

### **Pattern of inheritance for familial hypercholesterolaemia**

Familial hypercholesterolaemia is an autosomal dominant disorder. In the great majority of cases, the gene is inherited from just one parent. Very rarely, it is inherited from both.

#### **One parent**

If one parent has one mutated gene and one normal gene in the pair, each child of this parent has a 50 per cent chance of inheriting the mutated gene. The risk of developing early coronary artery disease depends on the gender of the child and includes:

- Around 50 per cent of males who inherit the genetic mutation from this parent will develop coronary artery disease before the age of 50 years.
- All of the affected male children of this parent will develop heart disease by the age of 70 years.
- About 85 per cent of affected male children of this parent will have a heart attack before the age of 60 years.
- Around 12 per cent of females who inherit the genetic mutation from this parent will develop coronary artery disease before the age of 50 years, and 74 per cent by the age of 70 years.

#### **Two parents**

If both parents carry the mutated gene, each child has a 25 per cent chance of inheriting both the genes containing mutations. In this case, the child will develop a severe form of coronary artery disease very early in life, perhaps while still in childhood. This form of familial hypercholesterolaemia is resistant to treatment.

Despite medical intervention, the risk of heart attack remains high. Symptoms can include patches of excess cholesterol collecting in the skin, particularly at the elbows, knees and buttocks.

### **Diagnosis of familial hypercholesterolaemia**

Familial hypercholesterolaemia is diagnosed using a number of tests including:

- physical examination
- blood tests
- heart tests, such as the stress test
- genetic tests.

### **Treatment for familial hypercholesterolaemia**

There is no cure for familial hypercholesterolaemia. Treatment aims to reduce the person's risk of coronary artery disease and heart attack, and may include:

- **Dietary changes** – recommended dietary changes include reduced intake of saturated fats and cholesterol-rich foods, and increased intake of fibre. Modifying the diet is usually the first line of treatment. After three months, test results will show whether more aggressive treatment is needed.
- **Plant sterols and stanols** – these substances are structurally similar to cholesterol, but aren't absorbed by the cells. Studies show that increasing the intake of plant sterols and stanols can substantially reduce blood cholesterol. Sources include corn, rice, vegetable oils and nuts.
- **Exercise** – regular exercise has been shown to reduce blood cholesterol levels. Any exercise program should be supervised by your doctor.
- **Weight loss** – obesity is a risk factor. Maintaining a healthy weight for your height can reduce your risk of coronary artery disease and heart attack.
- **Avoid smoking** – cigarette smoke encourages cholesterol to 'stick' to artery walls. Quitting can significantly reduce your risk of heart attack.
- **Medication** – very few people with familial hypercholesterolaemia will be able to reduce their cholesterol levels by diet and lifestyle changes alone. Most will need special cholesterol-lowering drugs.

### **Where to get help**

- Your **GP (doctor)**

- **Victorian Clinical Genetics Services (VCGS)**, Royal Children's Hospital Tel. **(03) 8341 6201**
- **Dietitians Association of Australia** Tel. **1800 812 942**
- **Genetic Support Network Victoria** Tel. **(03) 8341 6315**
- **Heart Foundation** Tel. **(03) 9329 8511**

**This page has been produced in consultation with and approved by:**

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