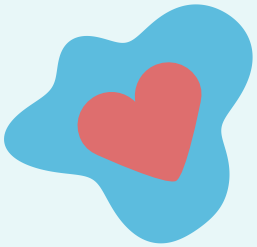
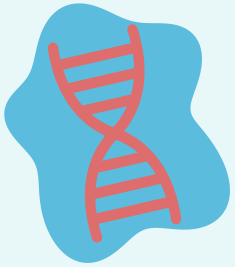
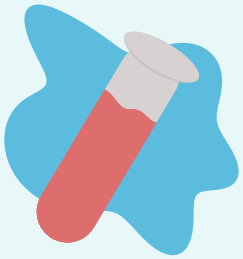
Genetic Support Foundation

A Provider's Guide to

Familial Hypercholesterolemia

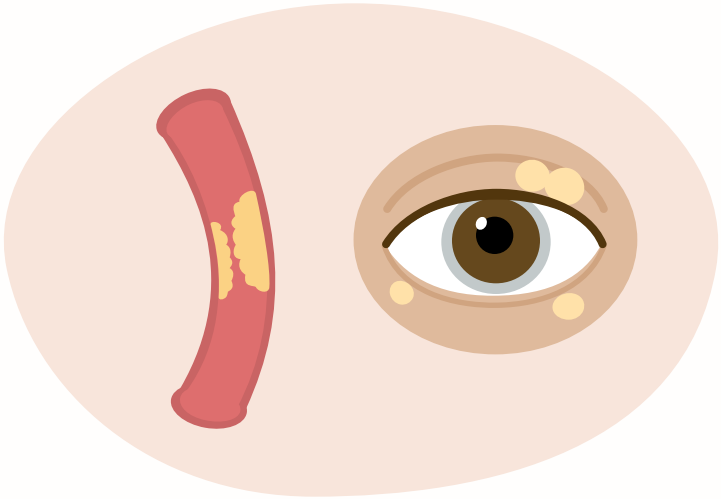






What is Familial Hypercholesterolemia?

- Familial Hypercholesterolemia (FH) is an inherited condition that causes **build-up of cholesterol** in the body.
- Without treatment, cholesterol accumulation in coronary arteries and valves can lead to **heart disease**, **heart attacks**, and **strokes**.
  - Untreated, males with FH have a 50% risk of a coronary event by age 50.
  - Untreated, females with FH have a 30% risk of a coronary event by age 60.



- Other symptoms of FH include:
  - **Xanthomas**: cholesterol deposits in the tendons
  - **Xanthelasmas**: cholesterol deposits around the eyelids
  - **Corneal arcus**: opaque rings formed by cholesterol deposits around the corneas

How is FH diagnosed?

- FH is a common and treatable condition, making universal FH screening crucial.

1 in 250 people **have FH**, but fewer than

1 in 10 people with FH **have a diagnosis**.

- **Cholesterol levels** are an important component of establishing a diagnosis of FH.

Lipid Screening

The American Academy of Pediatrics (AAP) recommends that **all children receive lipid screening between ages 9-11 and again between ages 17-21**.

FH should be suspected in individuals with extreme hypercholesterolemia:

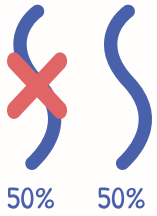
Children	LDL-C: >130 mg/dL, or Total cholesterol: >230 mg/dL
Adults	LDL-C: >190 mg/dL, or Total cholesterol: >310 mg/dL

- **Genetic testing** can confirm a clinical diagnosis. It can also identify FH before the onset of symptoms, which can then allow for early preventative treatment.

What are the genetic implications of FH?

Inheritance

- FH is caused by **mutations** in one of several genes that play critical roles in regulating cholesterol levels (*LDLR, APOB, LDLRAP1,* or *PCSK9*). However, about 20-40% of people with FH will not have a mutation in one of these genes.
- FH is **most often** inherited in an **autosomal dominant** pattern. This means that parents, siblings, and children of a person with FH each have a 50% chance of having FH. Screening family members of people with FH is therefore especially important.



- However, when FH is caused by mutations in the *LDLRAP1* gene, it is inherited in an **autosomal recessive** pattern. While siblings of a person with *LDLRAP1*-associated FH each have a 25% chance of having FH, other family members are not at as high of a risk.

Genetic Testing

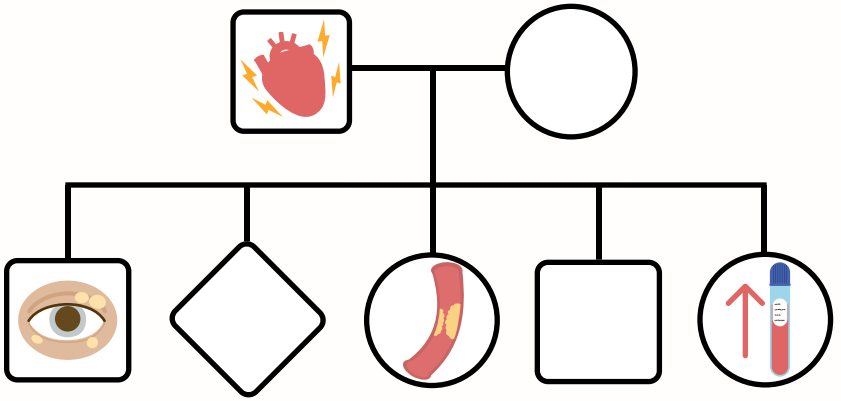
While FH can be diagnosed without genetic testing, a **molecular diagnosis can provide additional value**, such as:

- Confirmation of a clinical diagnosis
- Identification of a more severe, homozygous form of FH
- Clarification of the inheritance pattern and therefore recurrence risks for family members
- Early diagnosis of FH in family members, which can then allow for early preventative treatment

Personal and Family History

FH should be suspected in an individual with a personal or family history of any of the following:

- **Extreme hypercholesterolemia** (see "*Lipid Screening*," p.2).
- **Premature coronary artery disease** (CAD) such as myocardial infarction, obstructive CAD, or other cardiovascular disease. "Premature" typically means before age 55 in males and age 65 in females.
- Physical exam findings of **xanthomas**, **xanthelasmas**, or **corneal arcus**.



Genetic Counseling

You can refer a patient with suspected FH to a **certified genetic counselor** with Genetic Support Foundation. The genetic counselor will meet with your patient to discuss FH genetics, recurrence risks, and genetic testing.

Just fax the relevant medical records and insurance information to **844.813.3892**. We will then contact the patient to schedule an appointment.

How is FH treated/managed?

Medication and Monitoring

- People with FH have an impaired ability to remove cholesterol from the body, making **cholesterol-lowering medications** necessary to reduce the risk of heart disease.
- Treatment typically involves a **statin** drug. Other cholesterol-lowering medications are also often required to lower LDL-cholesterol to healthy levels.

Statin Therapy

Children	Statin therapy may be required by age 8-10, especially when LDL-C levels are ≥190 mg/dL Refer to lipid specialist if LDL-C remains ≥130 mg/dL
Adults	Statin therapy to reduce LDL-C levels by ≥50% or to <100 mg/dL Refer to lipid specialist if LDL-C levels cannot be reduced by ≥50% or to <100 mg/dL

- Lipid levels, including TC, LDL-C, HDL-C, triglycerides, and lipoprotein(a), should be **regularly monitored** in people with FH **starting at the age of 2.**

Preventative medication, monitoring, and lifestyle changes can significantly reduce the risk of health issues in people with FH. **Early detection** is therefore integral to caring for patients with FH.

Lifestyle

It is important that people with FH maintain a **healthy lifestyle alongside taking their medication**.

People with FH should:

- Avoid **risk factors** for cardiovascular and coronary artery disease, such as smoking, obesity, diabetes, and high blood pressure.
- Engage in regular **physical exercise**.
- Eat a **heart-healthy diet** that is low in saturated/trans fats and sodium, and high in fiber, fruits, and vegetables.