Familial Hypercholesterolemia

Other Names: Hyperlipoproteinemia, Type II; Hyper-Low-Density-Lipoproteinemia; Hypercholesterolemic Xanthomatosis, Familial LDL Receptor Disorder

Familial hypercholesterolemia is an inherited condition characterized by high levels of LDL cholesterol in the blood. It is most often caused by mutations in the LDLR gene which makes the protein called low-density lipoprotein receptor.

Characteristics of Familial Hypercholesterolemia

Familial hypercholesterolemia (FH) is a common genetic condition characterized by high levels of LDL (low density lipoprotein; bad cholesterol) cholesterol and total cholesterol. This excess cholesterol can build up in the arteries and can cause heart attacks at an early age. Individuals with FH can develop cardiovascular disease, specifically coronary artery disease, in their 30s-40s, and sometimes as young as 20s. Coronary artery disease can have symptoms of chest pain or tightness with exertion or heart attack. Individuals with FH often develop cholesterol deposits that look like solid waxy-appearing bumps on the skin or tissues that connect muscle to bones. The bumps are common on the backs of the hands, fingers, elbows, knees and heels. Individuals with FH may also develop cholesterol deposits around the outer layer of the eye (cornea) and cholesterol deposits on the eyelids. All of these symptoms are due to the buildup of cholesterol.

Diagnosis/Testing

Most individuals with FH have a change or mutation in a gene called LDLR. This gene makes the low-density lipoprotein receptor protein. This protein is needed to remove extra LDL from the blood. Mutations in the LDLR gene either reduce the amount of protein made or do not allow the protein to function properly. This leads to a buildup of cholesterol. Less commonly, mutations can occur in the APOB, PCSK9 or the LDLRAP1 genes.

Management/Surveillance

Preventive management is extremely important for individuals with FH and often includes physical, lifestyle and nutritional changes as well as cholesterol-lowering medications. This includes exercising regularly, not smoking, and eating a healthy diet. Most individuals with FH who follow treatment correctly do not get cardiovascular disease.

Mode of inheritance

FH is almost always inherited in an autosomal dominant pattern. This means inheriting one LDLR mutation is enough for an individual to be affected and show signs of FH. The mutation can be inherited from an affected parent or it can occur brand new (de novo) in an affected child, although the overwhelming majority of cases are inherited.

Risk to family members

The risk to family members depends on whether or not the individual with FH has a parent affected with FH. If a parent also has FH, the risk of having a child with FH is 50% with each pregnancy. If a parent does not have FH, the risk of other siblings being affected is very low.
Special considerations
None

Resources
The FH Foundation
http://www.thefhfoundation.org/
Genetics Home Reference: Hypercholesterolemia
NHGRI: Learning About Familial Hypercholesterolemia
http://www.genome.gov/25520184

References

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Created by: Jennifer Boomsma, CGC
Edited by: Seema Jamal, MSc, LCGC