Familial Hypercholesterolemia Fact Sheet

Overview
Familial hypercholesterolemia (FH) is an inherited condition that causes high levels of low density lipoprotein cholesterol (LDL-C or 'bad' cholesterol) and cardiovascular disease (e.g., heart attacks or strokes) at an early age. People who have FH have high levels of LDL-C because they cannot remove bad cholesterol from the blood stream properly, via the liver. Cholesterol is a fat-like substance that is found in the cells of the body and is also found in some foods. The body needs some cholesterol to work properly and uses cholesterol to make hormones, vitamin D and substances that help with food digestion. However, if too much cholesterol is present in the blood stream, it builds up in the walls of the arteries, a condition known as atherosclerosis, and increases the risk of cardiovascular disease.1

Causes/Risk Factors
Patients can have either one of two types of FH, heterozygous or homozygous FH. Both types of FH are inherited in families in an autosomal dominant manner. This means that a parent who carries an altered gene that causes the condition has a 50 percent chance to pass on that altered gene to each of his or her children.1

Heterozygous FH (HeFH) is the more common type of FH and occurs in approximately one in 200 to 500 people.1,2,3 Individuals with HeFH have one altered copy of a cholesterol regulating gene. In general, individuals with HeFH have LDL cholesterol levels twice as high as normal (e.g.,190-350 mg/dL).1,4

Homozygous FH (HoFH) is the rare form of FH. It occurs in approximately one in a million individuals.5 An individual with HoFH has two altered copies of a cholesterol regulating gene (one from each parent). Homozygous FH, which is a much more severe form of hypercholesterolemia, can cause a four-fold increase in LDL-C levels (e.g., 400-1,000 mg/dL).1,4

Familial hypercholesterolemia is found in all populations and ethnic groups. However, some groups, including the Afrikaner, French Canadians and Lebanese Christians have high rates of specific mutations that make FH particularly common. In these populations, FH can be more common than in the general population.5,6

Diagnosis
Because FH is associated with a high risk for premature cardiovascular disease (e.g., heart attacks and strokes), health professionals need to be alert to the signs found during a physical examination (e.g., fatty skin deposits, cholesterol deposits in the eyelids or corneal arcus) and to the laboratory values suggestive of FH.1 If the first-degree relatives of a patient with FH are screened, other gene carriers can be identified and treated.1 Individuals with HeFH or HoFH are characterized by significantly elevated LDL-C, as determined by a lipid panel blood test, usually to levels well above 190 and up to 1000 mg/dL.3,4,7 Other tests that may be done include studies of cells called fibroblasts to see how the body absorbs LDL-C.7

FAST FACTS
• The worldwide prevalence of HeFH is estimated to be approximately 1 in 200 to 500 people.2,3
• Familial hypercholesterolemia is caused by a gene mutation located on chromosome number 191
• Men with HeFH can have heart attacks or strokes in their 40's to 50's; 85 percent have a heart attack by age 601
• Women with HeFH can have heart attacks or strokes in their 50's and 60's1
• Homozygous FH can lead to heart attack, stroke, and death as early as age 301
Family History:
- A strong family history of familial hypercholesterolemia or early heart attacks
- High levels of LDL in either or both parents

Signs/Symptoms
Signs and symptoms that may occur include:1,7
- Fatty skin deposits known as xanthomas over the elbows, knees, tendons and cholesterol deposits (corneal arcus) around the cornea of the eye
- Cholesterol deposits in the eyelids (xanthelasmas)
- Chest pain (angina) or other signs of coronary artery disease; may be present at young age

Blood tests may show:7,8
- High levels of total cholesterol (greater than 300 mg/dL in adults and greater than 250 mg/dL in children)
- High LDL levels (greater than 190 mg/dL in adults and greater than 160 mg/dL in children)
- Normal triglyceride levels

Treatment
The goal of treatment is to reduce the level of LDL-C in order to reduce the risk of cardiovascular disease.1 Early detection and aggressive management to lower the LDL-C level helps prevent or slow the progression of atherosclerosis.6

Lifestyle Changes: For patients with HeFH, diet and exercise, which includes weight loss and reducing total fat intake to less than 30 percent of the total calories, can be tried before drug therapy is initiated. If lifestyle changes do not change a patient's cholesterol levels, their physician would typically recommend lipid-lowering medication.1

Therapies/Medications: There are several types of drugs available to help lower LDL-C and triglycerides, and raise HDL (‘good’) cholesterol.7 The most commonly used and effective drugs for treating high LDL-C are called statins9; however, while they are effective in reducing LDL-C levels and the risk of heart disease, many patients continue to have cardiovascular events.9 Other cholesterol-lowering medicines include ezetimibe, bile acid-sequestering resins, fibrates and nicotinic acid.7 Individuals who inherit only one copy of the defective gene, HeFH, may respond well to statin drugs combined with ezetimibe and dietary changes. Patients with two altered copies of a cholesterol regulating gene, HoFH, tend to be less responsive to these interventions. In addition, since their LDL-C is so high, they typically require other treatments, like LDL apheresis, which involves the removal of LDL in a method similar to dialysis, when it is available, or microsomal triglyceride transfer protein inhibitors and antisense oligonucleotides.2,7

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References