FOUNDATION
of the National Lipid Association

What is Familial Hypercholesterolemia?

Familial Hypercholesterolemia, or FH, is a genetic condition where people have very high levels of a type of cholesterol in their blood called low-density lipoprotein cholesterol (LDL-C), which is sometimes called the "bad" cholesterol. People who have this condition are at higher risk of early heart disease (heart attack or stroke) if their high cholesterol is not treated. FH is caused by changes in a gene that lowers the body's ability to remove the LDL-C from the blood, which makes the levels of LDL-C in the blood very high. Cholesterol builds up in the walls of arteries forming hard structures called plaques. Over time, these plaques can block the arteries and cause heart attacks or strokes.

FH is usually passed from parent to child, and in most cases, a parent with FH has a 50% chance of passing the gene that causes FH to their child. If a person is diagnosed with FH, their parents, siblings, and children should all have their cholesterol checked.

FH is more common than many people realize. Worldwide, about 1 in 300 people have FH. FH is usually a "silent disease", meaning people don't feel different or unwell. Most people (about 90%) with FH do not even know they have the condition.

Criteria for Diagnosis of FH in Children and Adolescents:

FH can be diagnosed by measuring blood cholesterol levels and asking about heart disease in relatives, or it can be diagnosed through genetic testing.

While there are some differences in guidelines, The following criteria can be used to diagnose FH in children, adolescents, and young adults (less than 20 years old):

1. The person has:

    a. LDL-C ≥ 160 mg/dL on at least two cholesterol panels after diet and after other causes of high LDL-C have been looked for and family history of early heart disease (heart attack, stroke, coronary stent, coronary artery bypass graft, or peripheral vascular disease) in a parent, grandparent, aunt, or uncle (≤ 55 years old for male relatives and ≤ 65 years old for female relatives), or one close relative with FH.

2. Genetic testing shows the person has a pathogenic or likely pathogenic mutation associated with FH.

What Does a Diagnosis of FH Mean for My Child?

Children with FH have high blood levels of LDL-C that will raise their risk for a heart attack or a stroke if they are not properly treated. For many people, high cholesterol can be the result of a lifestyle that includes a diet high in saturated or trans-fat, not getting enough exercise, having an unhealthy weight, or having another medical condition like a low thyroid level or diabetes. However, children with FH can be a healthy weight, have a healthy diet, get plenty of exercise, and still have high LDL-C.

For all people with FH, a healthy lifestyle is very important but most people with FH will also need medications to lower their cholesterol level. The sooner that one's cholesterol levels are brought down, the lower their risk of having a heart attack or stroke becomes. Children can be tested for FH with a blood cholesterol test as young as 2 years old.

Usually, FH specialists recommend that a child with FH start a cholesterol-lowering medication sometime between 8 and 10 years old. You should expect that your child will need some sort of cholesterol-lowering medication for their entire life. If people stop the medication, their cholesterol levels go back up again.

It can be very scary to think that your child needs to take medication to prevent an early heart attack, but it can also be an important way for your child and your family to take control of your health. Important healthy life skills like remembering to take medication as prescribed, getting regular activity, and eating healthy foods are easier to learn when people are young and are best learned by example!

Children with FH can go to school, play sports, and lead normal lives. FH does not affect their ability to have a child when they are older, although they should talk to their doctor about their cholesterol-lowering medications prior to becoming pregnant.

Treatment Options for Children with FH:

Guidelines recommend that children with a diagnosis of FH start taking medication to lower their LDL-C starting sometime between 8 and 10 years of age. The first choice in most cases is a type of medication called a statin. Occasionally, other medications are needed, either as an alternative first choice or as a second medication when a statin does not lower LDL-C enough on its own, but most children with FH take a statin as their only cholesterol-lowering medication. Listed below are some of the medication options to treat pediatric FH:

Statins: Statins are medications that lower cholesterol and have been widely used across the world for many years. Examples of statins include simvastatin, rosuvastatin, atorvastatin, pitavastatin, and pravastatin. By preventing the storage and production of cholesterol in the liver, statins reduce the number of cholesterol particles in the blood that can otherwise build up and lead to heart attacks and strokes. All statins are FDA approved for use in children, some as young as 8 years old, others at age 10 and older. Statins are pills that are taken by mouth, once daily, either with or without food. Statins can usually be taken with other medications. Some people can experience muscle aches with statins; however, they are usually well tolerated, and muscle aches are very rare in children. If this occurs, please talk to your Healthcare Team to decide if any new aches are related to the statin medications or related to activities like playing or exercising. These medications have been found to lower LDL-C by about 20% to more than 50% depending on the dose.

Ezetimibe: Ezetimibe may be used in addition to a statin or on its own based on the individual child's needs and tolerance to other medications. Ezetimibe is a commonly prescribed medication that is well-tolerated. Ezetimibe works by modifying how much cholesterol is absorbed from food in the gut to the bloodstream. Ezetimibe is FDA-approved for use in children 10 years of age or older. Ezetimibe is a pill that can be taken once daily, with or without food. Ezetimibe has few side effects but may include

abdominal pain, flatulence, or diarrhea. These medications have been found to lower LDL-C by an additional 20% beyond statin therapy.

Bile acid sequestrants: Bile acid sequestrants are used less commonly; however, they may serve as a beneficial addition to a child's regimen to further lower cholesterol. Examples of these medications include cholestyramine and colesevelam. Bile acids are natural chemicals in the body that break down cholesterol from food in the gut to absorb cholesterol in the blood. Bile acid sequestrants are medications that bind with these substances in the gut to help prevent the absorption of cholesterol from food. This medication is commonly a powder that can be measured at the dose provided by your Healthcare Team and mixed into juice, water, or semi-solid food with a high liquid content, like applesauce. It is also available in pill form although the pills are large, and several are needed per dose. Given that these medications stay in the gut and block absorption to the bloodstream, it is advised that these medications be taken one hour before or four to six hours after other medications to ensure that the doses of other medications are properly absorbed. These medications are not absorbed and stay in the gut, which can lead to some side effects such as upset stomach, constipation, or heartburn. Typical LDL-C reduction is about 20%. The effect is additive with statins.

PCSK9 inhibitors: PCSK-9 inhibitors are medications typically used in addition to statin therapy but may be used on their own based on the child's needs. One of the PCSK-9 inhibitors, evolocumab, is approved by the FDA for use in children 10 years or older. These medications are an injection that can be administered into an area of fat tissue, such as the abdomen, at home by a family member and given to a child every 2 weeks or every 4 weeks depending on the dose prescribed by the Healthcare Team. PCSK-9 inhibitors are generally well tolerated but can cause irritation, redness, or itchiness when injected. These medications have been found to lower LDL-C by about 45% to 60% beyond statin therapy.

For all of these medications, it is important to talk to your Healthcare Team prior to starting any new medications or supplements to ensure that they are safe to take with the prescribed medications. Following the start of new medications, dose adjustments, or discontinuation of certain cholesterol-lowering medications, your Healthcare Team will request repeat laboratory tests to check the impact of the medication on cholesterol levels, which can serve as a marker for risk of heart disease. Additional monitoring tests, such as liver tests, may be needed on a less frequent basis. As always, if you have any concerns with medications, please discuss them with members of your Healthcare Team.

Lifestyle Recommendations for Children with FH:

Lifestyle recommendations for children with FH are very similar to lifestyle recommendations for all people. Eating a wide variety of foods with plenty of fruits and vegetables, lean proteins (chicken, turkey, tofu, and shrimp are a few examples), and whole grains are key to keeping LDL-C levels as low as possible and may be able to help minimize the amount of medication someone needs.

Reducing the amount of saturated fat, cholesterol, and trans-fat in the diet can also help lower LDL-C. Cholesterol and saturated fats are from animal sources, like full-fat dairy, pork, and beef, and are also present in processed foods or fried foods. Coconut oil and palm oil should also be limited as they are high in saturated fat. Hydrogenated oils are the main source of trans fat in the diet. Some foods naturally contain small amounts, but most are added by manufacturers to processed foods. Try to avoid

eating hydrogenated oils whenever possible. (You can read the ingredient list on the food label to find "hydrogenated" or "partially hydrogenated"). Some common sources of hydrogenated oils include:

1. Commercially baked goods like cakes, cookies, and pies
2. Refrigerated dough, like for ready-to-bake biscuits or rolls
3. Shortening and stick margarine
4. Some types of microwave popcorn
5. Some types of hot chocolate mix
6. Non-dairy coffee creamer

More heart-healthy sources of fat are fats called mono-unsaturated or poly-unsaturated fats. Common sources include canola, soybean, corn, olive, peanut, and avocado oils.

Regular physical activity is also very important! Encourage your child to try different activities to find something they like. Ideally, they will want to continue an active lifestyle on their own.

Finding a Pediatric FH Specialist in Your Area:

Pediatric lipidology, or the treatment of high cholesterol in children, is a small but growing field in medicine. Some pediatric FH specialists are pediatric cardiologists, some are pediatric endocrinologists, some are pediatricians, and some are adult lipidologists with an interest in caring for children with high cholesterol.

It can be challenging to find a pediatric FH specialist. Your child's primary care provider may know the pediatric FH specialists in your area. On the website for your health care system, review providers in pediatric cardiology and pediatric endocrinology and look for key interests like "lipid clinic", "cholesterol", or "preventive cardiology", or search those terms under medical conditions the system treats. We recommend that if you are interested in additional patient educational materials you visit The Family Heart Foundation at www.familyheart.org.