

Announcer: 00:02 Welcome. You're listening to a series of four familial hypercholesterolemia podcasts, brought to you by the American Heart Association, and the FH Foundation. This is series is focused on educating patients, caregivers, and healthcare providers on ways to improve awareness, detection of FH, and management of high cholesterol.

Cat Davis Ahmed: 00:25 Hi everyone. My name is Cat Davis Ahmed, and I'm the Vice President for Policy and Outreach for the FH Foundation. I myself, have familial hypercholesterolemia. Our first podcast is all about, what is familial hypercholesterolemia, or FH? I'm happy to be talking with Dr. Josh Knowles, Attending Physician at the Stanford Center for Inherited Cardiovascular Disease, where he treats patients with FH. He is also the Chief Mission Advisor for the FH Foundation.

Hi Dr. Knowles. Thanks for joining us for this discussion on, what is FH?

Dr. Knowles: 01:00 Thanks so much Cat, for having me on. Thanks to the American Heart Association and the FH Foundation. Feel free to call me Josh if you want.

Cat Davis Ahmed: 01:10 All right. Thanks Josh. Let's start with the basics. What is familial hypercholesterolemia?

Dr. Knowles: 01:18 That's kind of a mouthful, isn't it? Familial hypercholesterolemia, and we often call it FH, but another way to think about it is, family high cholesterol. FH is a condition. It's a genetic condition. It's passed in families. If you got it, you inherited it from your mom or your dad. It results in very high LDL cholesterol levels from birth. Overtime, that LDL cholesterol is toxic to blood vessels, especially those that feed the heart. It puts people at very high risk of early onset heart disease, heart attacks, strokes, and procedures like stenting or bypass surgery. FH is caused by genetic mutations that control the body's ability to recycle LDL cholesterol. LDL cholesterol has been in the news a lot lately. Some people think that it is not as deadly as it is, but high LDL levels are toxic to blood vessels over time, and really need to be lowered extensively in FH patients.

Cat Davis Ahmed: 02:31 Thank you. A lot of people have high cholesterol and they may be wondering why they've never heard of FH. How common is FH?

Dr. Knowles: 02:44 That's something that we've learned a lot about over the last few years. When I was in medical school, not that long ago, we

used to say FH affected 1 in 500 individuals. But we now know through very large modern genetic studies and other studies, that FH is much more common than we once thought, about 1 in 220. It affects all races and ethnic groups. It's present in all countries that have been surveyed so far. That means that there's at least 1,300,000 individuals in the United States with FH. Unfortunately, many individuals with FH do not know they have it. They do not know that they're walking around with a risk of early onset heart disease. Maybe as few as 10% actually have been diagnosed properly. There are many reasons for that, but the biggest reason is that people are not looking for it.

Cat Davis Ahmed: 03:36 I'm so glad we have this opportunity to talk about FH, and hopefully there may be people who are listening who can recognize themselves and their families in this broadcast, quite frankly, and then look into it. If it sounds familiar, how would somebody go about finding out if they have FH? How is FH diagnosed?

Dr. Knowles: 03:59 That's really the critical question, and unlike many conditions for which individuals might have symptoms, high cholesterol doesn't necessary cause any symptoms until a bad event like a heart attack occurs. But we should really be looking for FH because it can be diagnosed relatively straight forwardly. The first thing is looking at the cholesterol levels. In an adult if the LDL cholesterol is over 190, or if a child, if the LDL cholesterol's over 160, we should have a high degree of suspicion for FH. If there's a family history of early onset heart disease, if your mother or your father, or your sister or your brother had a heart attack before age 60 for men, or 50 for women, they should really strongly consider FH as being involved. Really, a few years ago the American Heart Association endorsed those kind of criteria as when we should really be suspicious for FH.

Cat Davis Ahmed: 05:04 How about genetic testing? I know there's a lot of information in the news about genetic testing. FH is a genetic disorder. What's the role of genetic testing for FH?

Dr. Knowles: 05:15 That is also something that's really emerging as being extremely important. In many countries around the world, FH genetic testing has been standard of care for many years, and it's been shown to be highly efficacious in increasing the ability to find individuals with FH, making sure they are motivated to take the right therapies, and then especially screening other potentially affected family members. In the US, until recently and even currently, FH genetic testing is not as commonly done as it maybe should be. There's many reasons for that. It has been relatively expensive and people haven't known how to order

the tests. But just a few weeks ago the FH Foundation helped convene and publish a paper from the FH experts around the world that endorsed the use of genetic testing, offering genetic testing to all individuals suspected of having FH.

The reason that genetic testing can be so useful is that it can confirm a diagnosis, and the genetic testing can also offer prognostic information, that is, if you have a mutation you might be more severely affected. It can potentially affect the way individuals view their condition. They might be more likely to take a medication when they know it's not their fault. The final reason is that it really improves our ability to do family based screening. One of the key messages that we like to convey is we never find an individual with FH, we only find families with FH. We need to be looking within families to find unaffected individuals before something bad happens.

Cat Davis Ahmed: 07:02 That's great. But, it's true though, as you said though, that most people are diagnosed without genetic testing, and while it may be helpful, at the moment it's not required for diagnosis. Is that correct?

Dr. Knowles: 07:14 Oh, absolutely. This was an emerging field. Many lipidologists, cardiologists, physicians don't know how to order genetic testing. They're scared about interpreting the results. Some individuals don't want genetic testing, and it's not necessary for a diagnosis, but it can in certain circumstances be very useful. We encourage all people to talk to their healthcare provider about whether that would be something that's useful for them.

Cat Davis Ahmed: 07:44 At the FH Foundation we also want to be sure that people hopefully have the opportunity to talk to a genetic counselor and understand the considerations that they might have before they go ahead and have the genetic testing done. For example, does it go into your medical record, and all of those things? Just things to be educated about before you order the test.

One thing I hear, because I talk to people with FH all the time, I have FH myself, I think as you mentioned a little earlier, people question whether cholesterol really matters. Since FH is a disorder of high LDL cholesterol, I wanted to ask, why should we worry about high cholesterol? Is it really the risk factor, or is there something else? I want people to understand, what is the role of cholesterol in the development of heart disease?

Dr. Knowles: 08:43 That's something that we deal with every day in clinic. I think in some ways a little understanding of the development of atherosclerosis. Atherosclerosis is the deposition of plaque in

the arteries, especially those that feed the heart. A little understanding of how that process works might be useful here. Atherosclerosis is a condition that affects all of us. It progresses in the same way, but at different rates. It can be viewed as a response to injury. Things like diabetes, or high blood pressure, or smoking can all damage the blood vessel wall and trigger this atherosclerotic response. But one of the most potent stimuli for atherosclerosis is high LDL cholesterol. LDL cholesterol can get inside the blood vessel wall, and trigger an inflammatory response. That can lead to plaques in the arteries that get larger and larger over time, and sometimes can rupture and cause heart attacks.

One of the key messages for individuals with FH is, they've been born with a predisposition to extremely high LDL levels. Those LDL levels can trigger that atherosclerotic response early in life. They can progress more rapidly than in other situations. FH individuals are often affected 20 or 30 years prior to their other individuals that don't have FH, and can be very severely affected in their 40s and 50s with heart disease.

- Cat Davis Ahmed: 10:19 That's certainly something that I worry about, and inspires me to take my medication every morning. Can you talk to us why then, if high cholesterol is a risk factor for everybody, why distinguish FH? Why does FH diagnosis matter?
- Dr. Knowles: 10:40 Again, I think it's really important for people to understand this. LDL cholesterol can be conceptualized, can be thought of as a waste product. We all need a little bit of cholesterol, but not very much. The body takes the little bit of cholesterol it needs from the blood, and sends the rest back for recycling. LDL is really a waste product. Individuals with FH are exposed to extremely high levels of that LDL cholesterol really starting early in childhood, age two, three. The burden that their blood vessels are exposed to is really high. The reason that it's important to make this distinction is that because individual with FH are at such high risk, they need to be treated aggressively. We need to combat that extra burden that they've been exposed to by lowering the LDL level substantially, to basically make up for lost time.
- Cat Davis Ahmed: 11:45 All right. Because the levels are so high, do you have to treat it differently than you would with other people with high cholesterol? Does it get treated-
- Dr. Knowles: 12:01 We know a lot about this. The FH Foundation several years ago, started the National Patient Registry. Individuals with FH were kind enough to allow us to look at some of their data from their

medical records, and look at their cholesterol and look at how severely they're affected. What we learned from that is that many individuals with FH are affected by heart disease at a very early age, that are not diagnosed until very late, often after they've had a heart attack or stroke. We know from other data, that the good news about FH is that you identify it early enough and treat it aggressively enough, that you can prevent almost all the downstream consequences. One of the major goals of the FH Foundation has is to try to prevent every individual with FH from becoming a patient with FH. The way we do that is by lowering the LDL cholesterol, maybe even more aggressively than we would do for other people. In most individuals, treatment with a single drug like a statin might be enough, but in a substantial proportion of FH patients, more than one cholesterol lowering medication is needed. In our registry, about 40% or 50% of FH individuals required a second medication to lower cholesterol. About 20 required three medications. It's harder to treat, but more importantly to treat aggressively.

Cat Davis Ahmed: 13:27 That's very helpful, and I know we have a future podcast that will go more in depth. I think that's great to let people know that there is combination therapy available if somebody needs that. What do we do then, if you find out that you have FH, and you're diagnosed with FH, and again, you're managing it yourself, then what do you? Because if it's genetic ... I think to my own family, the importance of understanding that FH is different from other causes of high cholesterol is that it might affect my children.

Dr. Knowles: 14:13 Yeah. I think what you're getting at is, what do we do once we know that there's somebody in a family that has FH? What do we do for the individual, and what do we do with the family? I think the first thing to know here is that you should not do it alone, that there is a community out there of FH individuals like Cat. You're one of the prime examples of somebody who's trying to spread the word, and be a support, both figuratively and literally for other individuals. You can learn from other folks with FH, how they've dealt with their condition, their struggles with getting medications approved, or their struggles of convincing family members that this is important, or even convincing their healthcare providers that this is important.

The first thing is get connected, and the FH Foundation is a great way of do that. The second thing is that you should find a healthcare provider that you're comfortable with, that takes this diagnosis seriously, that is educated and is willing to get more educated about FH. There's a list of FH specialists that can

be found online. It's surprising that even many experienced healthcare providers and cardiologists are not as up to date on FH care as they should be, so find a lipid specialist, or a cardiologist, or an endocrinologist or a healthcare provider that is really willing to go the extra mile.

Of course the other thing that you need to do is take care of yourself. That means, if you're into a very healthy diet and lifestyle, exercising every day, 45 minutes or an hour, not smoking, making sure you control your blood pressure and your weight and your other risk factors. And then most importantly, control your cholesterol. One of the key messages for FH is that diet and exercise, while important are never enough by themselves. It's only with the use of medications that we can lower cholesterol effectively in these individuals with a genetic predisposition. Taking your medications regularly, getting your LDL cholesterol down, usually down certainly to a LDL less than 100 mg/dL. Many of us treat it to a LDL less than 70, is really important.

Then the final thing that I always say is that again, we never find an individual with FH. We only find family members with FH. A diagnosis of FH in the family should prompt you to get connected to your other relatives. All first degree relatives need to be screened, mother, father, brothers, sisters, children all need to be tested for FH, and that can usually done with a lipid panel or genetic testing is available. That can also help.

That's sort of a long answer, but I think an important answer.

Cat Davis Ahmed: 17:06

Perfect. I think it's a great answer. When I get the chance to talk to people with FH, especially when they're newly diagnosed and worrying about themselves and their children, I often say, you can only do what you know to do. A diagnosis actually can really give you the tools that you need to address this risk factor that most people with FH, we know that heart disease runs in the family. Once we've got the FH diagnosis, we know what to do about it, and to try to prevent heart disease in ourselves and in our children and our grandchildren, and generations to come. I think it's a really hopeful message, as hard as it can be to have FH. Along those lines, what would you say Josh [crosstalk 00:17:55] Yeah, sorry.

Dr. Knowles: 17:56

No. I was just going to say, on that note, I think that word hopeful is a really important one. I remember cutting a video. We had a little illustrated video about being hopeful when you have FH. I think that's really a key message, that even if one individual in a family is affected profoundly by FH, maybe

they've had a heart attack, or if they've had bypass surgery, that knowledge can be so empowering to the rest of the family, and really with early intervention and treatment, all those other family members can be spared the downstream problems. It's a critical ... We should be hopeful for FH.

There's lots of very effective therapies. Unlike some conditions where we can't do anything, for FH we can do everything. We can make people live just as long, and just as healthy as individuals that are not affected. This is why FH, I think about FH as being the epitome of personalized medicine. It's a genetic condition for which there's very effective therapies available. It's extremely important that we keep our eyes open. There's this expression that I love. The eyes cannot see what the mind does not know. The first thing to do is get educated.

- Cat Davis Ahmed: 19:08 I'm so glad we had the chance to do that today. I'm grateful for the American Heart Association because they're working together with the FH Foundation to get the word out about FH. That was certainly a lot of information. Thank you so much Josh, for your time today, and for all you do.
- Dr. Knowles: 19:29 Oh, thank you Cat. Thanks to the FH Foundation and the American Heart Association, and keep up the good work.
- Cat Davis Ahmed: 19:35 In case you missed any of what we've discussed on this podcast, you can visit the FH Foundation at the FHFoundation.org, and the American Heart Association at www.Heart.org/cholesterol. Thanks so much.
- Announcer: 19:56 Views expressed in this podcast do not necessarily reflect the official policy or position of the American Heart Association and American Stroke Association. For transcripts of this podcast and more information about cholesterol, please visit Heart.org/cholesterol, or engage with us via social media using the [#understandcholesterol](https://twitter.com/understandcholesterol).