UNMASKING THE GENETICS OF EARLY HEART DISEASE

Catching familial hypercholesterolemia early can save lives

By HEATHER STRINGER

Katherine Wilemon was 15 when she discovered that she was living with extremely high cholesterol levels in her blood. At the time, she and her doctors had no idea how seriously this would put her life at risk as she grew up.

Katherine had gone to the family doctor because she was suffering from pain in her Achilles tendons, and he ordered a series of tests to identify the problem. The lipid panel revealed a low-density lipoprotein (LDL) level of 385 milligrams per deciliter (mg/dL); anything above 190 is considered "very high" in adults. She had large amounts of LDL, or "bad" cholesterol, in her blood. No one realized that her pain was the result of crystallized cholesterol buildup in her tendons—the symptom of a serious genetic disorder.

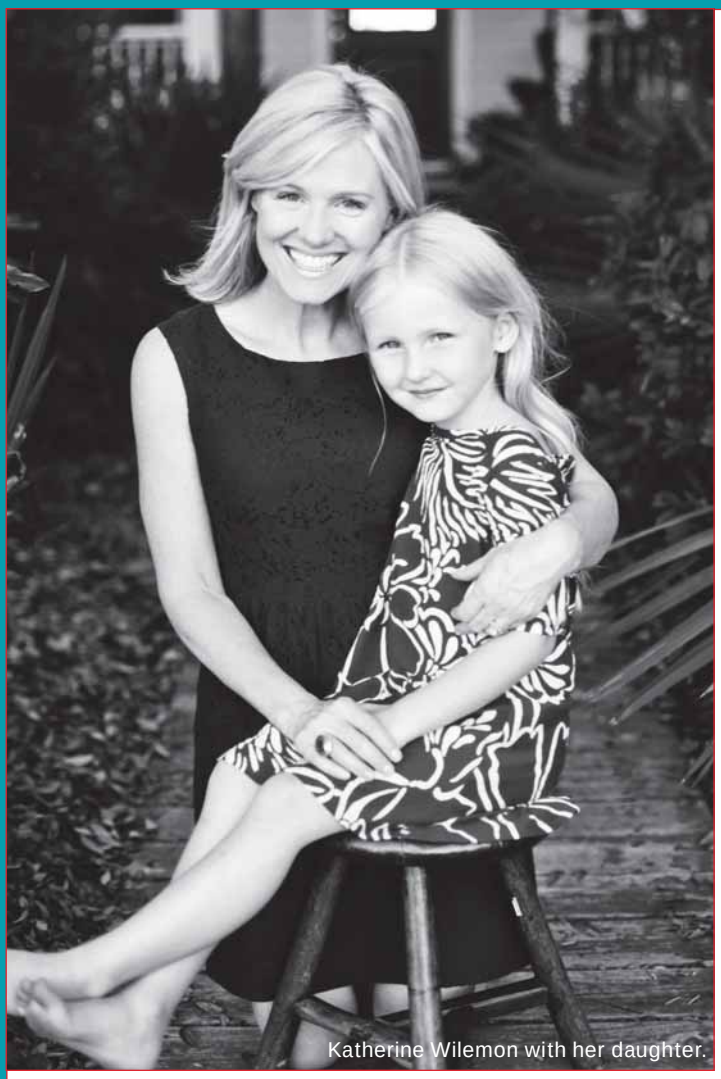
She started taking medication intermittently to lower the LDL, but her levels remained elevated. At the age of 39, Katherine, who lives in San Marino, California, was gardening when she started feeling pain in her chest and radiating down her right arm. "When the paramedics arrived, I told them about my high cholesterol and that I was concerned about a heart attack," she says. "But they said there was no way it could be a heart attack because I was a young woman."

But the paramedics were wrong. Katherine *had* suffered a heart attack. She learned that the main artery to her heart was completely blocked, and she underwent surgery to insert a stent, a small tube that could support the inner wall of the artery. In the ensuing months, she lived in fear of a second heart attack that would end her life. Finally, at the age of 41, she was referred to a lipidologist, who diagnosed her with *familial hypercholesterolemia (FH)*, an inherited disorder that leads to aggressive and premature cardiovascular disease.

"The lipidologist was the one who explained what FH was and told me I needed to have my two-year-old daughter tested because she had a 50 percent chance of inheriting the condition," says Katherine, who founded the FH Foundation in 2011 to raise awareness, promote research, and support people with FH.

Although exercise and a healthy diet can decrease LDL to target levels in many people, this is not the case for the estimated 1 million people in the United States who have FH. Most cholesterol circulating in the body is produced by the liver and used to make natural hormones, steroids, and cell membranes, but people with FH are unable to break down the natural supply of cholesterol that is not used by the body. Starting in the womb, they are exposed to high levels of LDL and are at risk of having a heart attack or stroke decades earlier than most people.

Statins and other drugs can reduce LDL to safer levels in many people with FH, but in cases like Katherine's these medications alone are not enough. Now new drugs are making it possible for people like her to finally attain safer levels.



Katherine Wilemon with her daughter.

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"The most important thing to understand is that FH is genetic and passed in families, so if you find one person, you need to screen others in the family," says Josh Knowles, MD, an attending physician at the Stanford Center for Inherited Cardiovascular Disease and the chief medical adviser of the FH Foundation. "Ninety percent of people with FH are undiagnosed, but if you find it early enough, you can prevent all the downstream problems like premature heart attack."

WHAT TO WATCH FOR

A variety of genetic mutations cause FH, and Katherine was born with a more severe mutation that causes severely elevated levels of LDL to circulate in her blood. The American Heart Association recommends FH screening for people with LDL levels greater than 190 mg/dL and a first-degree relative with premature heart disease. For children LDL levels greater than 160 mg/dL warrant screening for FH. In 2014 the American Academy of Pediatrics started recommending universal lipid screening for children between the ages of nine and 11, as well as screening for FH at age two for children with a known family history of the condition.

Genetic tests are increasingly available to diagnose FH but are not required, Dr. Knowles explains. Cholesterol deposits near the joints, known as *xanthomas*, and yellowish deposits of cholesterol around the eyes are also warning signs, but these findings are not seen in everyone.

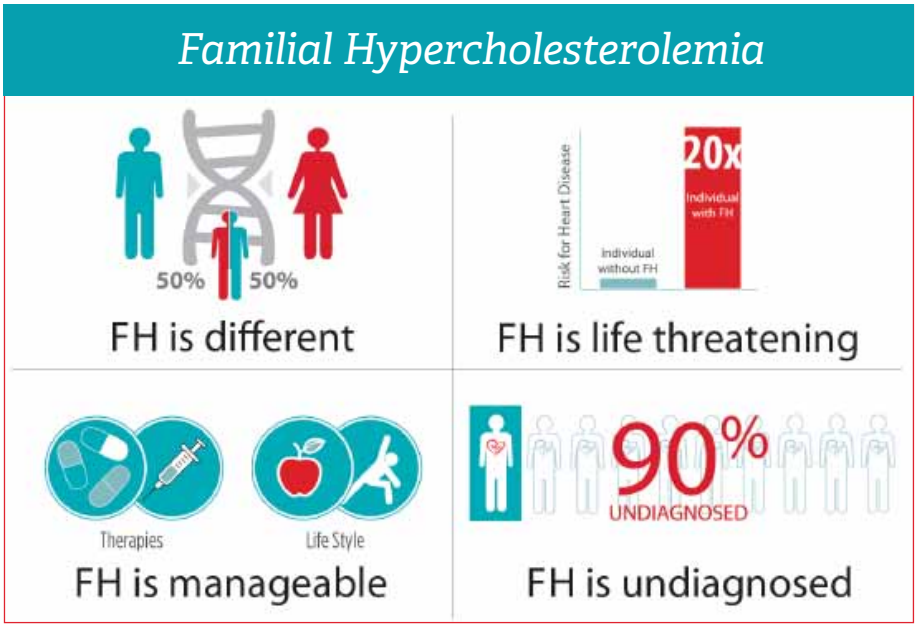
Katherine has *heterozygous FH*, an inherited genetic mutation from one parent, and about one in 250 people worldwide have this form of the disorder. About one in 160,000 people inherit the mutation from both parents, which is called *homozygous FH*, a more serious form of the condition that can lead to heart disease in early childhood and the teenage years.

STRATEGIES FOR LOWERING LDL

The first line of treatment is a *statin*, says Dr. Knowles, which "tricks the liver into producing more LDL receptors to help the liver get rid of LDL in the blood." These drugs typically reduce the LDL level by 50 percent. A statin alone is all that's required for many patients with FH, but a substantial percentage require more than one medication to lower LDL to target levels of less than 100 mg/dL, Dr. Knowles says.

The second line of treatment is typically the cholesterol-lowering drug *ezetimibe*, which prevents the absorption of cholesterol in the gut. This type of medication reduces LDL levels by about 15 percent, Dr. Knowles says.

The newest type of drugs, known as *PCSK9 inhibitors*, were approved in 2015. Used in combination with the other medications, they prevent the body from degrading



Source: the FH Foundation

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Josh Knowles, MD

the receptors that are necessary for breaking down LDL. These drugs can reduce LDL levels by an additional 50 percent and are typically injected under the skin once every two to four weeks. For Katherine this new type of drug cut her LDL level from 170 to 60 mg/dL.

"I used to live in fear that I wouldn't get to see my children graduate from high school or get married," she says. "Now that my LDLs are so much lower, I feel more hope. I'm doing everything scientifically possible in addition to exercising and eating a low-fat diet."

Within the past few years, new medications have also been approved for people with homozygous FH. This is particularly good news for this patient population because typically they have had to resort to LDL apheresis, which involves cleansing the blood with a machine every other week or sometimes more frequently.

Women with FH who are interested in becoming pregnant should talk to their physician about whether it is safe to pursue this option.

RAISING AWARENESS

Although Katherine is grateful that the newly approved medications for FH have lowered her LDL significantly, she acknowledges that she was exposed to high levels of bad cholesterol for four decades before she began taking the needed medications. After she was diagnosed, Katherine began talking to physicians about her condition and realized that many doctors were unaware of FH.

"These were cardiologists who had been doing catheterizations and heart bypass surgeries on people in their twenties, thirties, and forties, and they were shocked when they realized that they had been missing this diagnosis," she says.

Source: the FH Foundation

HOW TO LEARN MORE

The FH Foundation
thefhfoundation.org

Foundation of the National Lipid Association
lipidfoundation.org

American Academy of Pediatrics
aap.org; cholesterol screening recommendation for children

FH was originally thought to be somewhat rare, occurring in only one in 500 people, but studies conducted in the Netherlands and Denmark in the past few years revealed that the prevalence was twice as common,[1] says Anne Goldberg, MD, a professor at the Washington University School of Medicine in St. Louis, Missouri.

Through the FH Foundation, Katherine hopes to raise awareness and increase the chances that people with FH will be identified as early in life as possible—and perhaps never need more than statins. The foundation created the first national registry of patients with FH in an effort to collect research data on diagnoses, individuals' experiences, disease patterns, and trends and gaps in care.

FH also has lacked an official code in the International Classification of Diseases, which makes it difficult for health providers to record and identify the condition and classify it for insurance reimbursement. The foundation, along with the National Lipid Association, applied to the National Center for Health Statistics for a diagnosis code, and their efforts were rewarded. The new codes for FH were approved in the spring of 2016 and went into effect the following October.

For physicians like Dr. Goldberg, there are signs that awareness among patients is growing. "I've seen a lot of families with FH, and people whose parents and grandparents had heart disease at a young age," she says. "But we're seeing more people who start treatment and do not experience early heart disease. Now more than ever there is a lot more hope for people who are born with FH." ✿

References
1. Goldberg AC, Gidding SS. Knowing the Prevalence of Familial Hypercholesterolemia Matters. Circulation. 2016;133(11):1054-57. doi: 10.1161/CIRCULATIONAHA.116.021673.

Source: the FH Foundation

PATIENTS RISING: ACCESS MATTERS

If you pay for health insurance coverage, your healthcare needs and medications should be covered by your insurance provider. Right? That's the concept of insurance most of us have when we sign on for coverage. But what if the industry we look to for care was instead conspiring against us?

Increasingly, this seems to be the case, as insurance providers enact policies that come between patients and the therapies prescribed by their doctors.

Specifically, insurance providers have enacted "step therapy" policies, also known as "fail-first" policies, to contain prescription costs. These policies require another medication or treatment before they will approve the use of the medication the doctor believes is right for the patient. Step therapy interferes with the doctor-patient relationship and requires a one-size-fits-all treatment approach.

There is a better way: Put patients first. It's not only the right moral choice, it would have the added tangible benefit of driving scientific innovation and making the drug delivery system more sustainable through creativity instead of cutting. Finally, it would target the soft bigotry that looks at patients as a commoditized drain on public resources, rather than a community of human beings we know how to help.

Cardio patients around the country are working hard to raise awareness of this issue, fighting back through Mended Hearts, Power of the Patient Voice, to help enact step therapy laws in 12 states and counting.

FH patients in America might not number in the millions, but, like so many other people facing a health issues, each one represents a patient at the crossroads, waiting to learn their fate: will they be discovered, diagnosed, and treated with medicine that is at the ready? Or, will they be designated too expensive to treat and too costly to save?

As patients and advocates, will you choose to help?

To stay informed on policy issues for patients, sign up at PatientsRising.org. To join Mended Hearts Power of the Patient Voice visit MendedHearts.org/get-involved. The collective patient voice must lead the conversation.