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Why do only some people with hereditary heart disease experience symptoms?

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As many as 500,000 people in the United States have a heritable and potentially fatal heart disease called hypertrophic cardiomyopathy.

The disease can cause irregular heartbeats, heart valve problems, heart failure and, in rare cases, sudden cardiac death in young people. But some people who carry gene mutations that cause hypertrophic cardiomyopathy never experience symptoms.

A new study helps explain why. For the first time, researchers have found that, in addition to gene mutations, environmental stress plays a key role in development of the disease.

The study, led by senior author Sakthivel Sadayappan, PhD, MBA, of Loyola University Chicago Stritch School of Medicine, is published in the *Journal of Molecular and Cellular Cardiology*.

In hypertrophic cardiomyopathy, the heart muscle becomes abnormally thick, making it harder for the heart to pump blood. The disease can cause irregular heartbeats such as atrial fibrillation; obstructed blood flow that can cause shortness of breath, chest pain, dizziness and fainting spells; problems with the mitral valve; an enlarged ventricle (pumping chamber) that reduces the heart's ability to pump blood; heart failure; and sudden cardiac death. It's the leading cause of heart-related sudden death in people under age 30, including many athletes. For example, Boston Celtics basketball star Reggie Lewis died at age 27 after collapsing during a practice session.

More than 1,400 gene mutations have been linked to hypertrophic cardiomyopathy. An individual will have a 50 percent chance of inheriting the condition if one parent has the disease. About 1 in 500 people has hypertrophic cardiomyopathy, but the risk is much higher among people from India and other south Asian countries.

Dr. Sadayappan's study involved mice that carried mutations that cause hypertrophic cardiomyopathy. To study the effect of environmental stress, researchers performed a procedure that mimics high blood pressure. This environmental stress significantly increased three measures of hypertrophic cardiomyopathy: The hearts became heavier, the pumping ability decreased and there were lower levels of a protein that is critical for the normal functioning of the heart. The protein is called cardiac myosin binding protein-C, or cMyBP-C.

The findings suggest that carriers of hypertrophic cardiomyopathy mutations who do not yet have symptoms may be at greater risk of developing cardiomyopathy from a variety of environmental stressors, such as high blood pressure, diabetes and alcohol use. This is due to the compounding effects of stress and insufficient levels of cMyBP-C, Dr. Sadayappan and colleagues wrote.

In an accompanying editorial, Jennifer Strande, MD, PhD of the Medical College of Wisconsin, wrote that the findings were unexpected. The findings lead to the "provocative suggestion" that stress plays a role in the disease process and may help explain why only some of the carriers of gene mutations get the disease.

"Stress may be a new modifier of the disease process and it is definitely worth another look,"Dr. Strande wrote. Dr. Strande earned her MD and PhD degrees from Loyola.

Provided by Loyola University Health System