First genetic mutation linked to heart failure in pregnant women

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Researchers at the Intermountain Medical Center Heart Institute in Salt Lake City have identified the first genetic mutation ever associated with a mysterious and potentially devastating form of heart disease that affects women in the final weeks of pregnancy or the first few months after delivery.

The disease, peripartum cardiomyopathy (PPCM), weakens a woman's heart so that it no longer pumps blood efficiently. The disease is relatively rare, affecting about one in 3,000 to 4,000 previously healthy American women. Most PPCM patients are treated with medicine, but about 10 percent require a heart transplant or mechanical heart-assist device to survive. The cause of PPCM has been unknown.

"This is an important breakthrough," said Benjamin Horne, PhD, director of cardiovascular and genetic epidemiology at Intermountain Medical Center and lead researcher for the study, which has just been published in the online edition of *Circulation:* Cardiovascular Genetics and will soon appear in the print edition of the journal.

"Until now, no one has identified a genetic link to the disease. This gives us and other researchers a roadmap that tells us where to look in the human genome for more information about the disease," said Dr. Horne. "Someday this may lead to early testing during pregnancy that can identify women who are at risk for peripartum cardiomyopathy. We may be able to reduce or even prevent some of the complications of this disease."

The research team gathered DNA samples at Intermountain Medical Center from 41 women in their 20s and 30s who had suffered from PPCM. They also took samples from 49 women who were over age 75 and had never experienced cardiac problems. The samples were sent for testing to a lab in Iceland, which used a special credit-card size device covered with 550,000 tiny dots of protein that, when mixed with human DNA, can isolate genetic mutations.

"The initial testing was a fishing expedition," said Dr. Horne. "We didn't know what genes or mutations in the human genome lead to PPCM, so we were just going to test anything out there and see what popped up," he said.

To the group's surprise, the testing found that about two-thirds of the women with PPCM shared a genetic mutation on chromosome 12. So they performed a second round of testing in a different set of patients - again, one group of women with PPCM and a control group of older women who had never experienced heart problems. This time, a second control group of younger women was also evaluated. The results of the second round mirrored the first. So they did it again with a third healthy group of women.

In the end, all three sets of tests confirmed their first finding: Women with PPCM in the study were about two-and-a-half times more likely than healthy women to carry the genetic mutation. In the world of medicine and genetics, that's a significant finding, said Dr. Horne.

"It turns out that the mutation on chromosome 12 is located near a gene that is a good candidate for pregnancy-related cardiomyopathy," said Dr. Horne. "That gene has been shown to be involved in regulating blood pressure and muscle contraction in the uterus and the heart."

The research group from Intermountain Medical Center is already

moving forward with new studies that aim to build on this discovery and help women who develop this devastating condition.

Provided by Intermountain Medical Center