



# Unlocking the Mysteries of Women's Heart Disease

Since 1984, heart disease, America's number one killer, has claimed more women than men. Three million women in the U.S. suffer from a distinctive form of heart disease that traditional tests developed for men don't detect. Dr. C. Noel Bairey Merz is heading a landmark study that looks deep into the hearts of women and offers hope that lives can be saved and improved.

BY ROBIN HEFFLER

It happened the first time during the summer of 2004. Denise Weiss, then 42 and otherwise healthy, was hiking with her husband in the mountains near their Idyllwild vacation home when she experienced severe chest pains. The next day, the pain came back, only worse; she was nauseous and broke out in a cold sweat. Weiss drove herself straight to the emergency room, where she had an EKG test; according to the test, her heart was functioning normally.

She experienced 10 more harrowing episodes over the course of a year, and eventually saw a cardiologist who ordered an angiogram—the imaging technique long considered the gold standard for detecting coronary artery disease, or heart disease, and in which dyes are injected into the arteries. Oddly enough, Denise Weiss's angiogram showed no blockage of her major arteries. She was given medication for the symptoms, but no explanation for what she was experiencing.

Then one day she received notice of a study that was being conducted on women under 55 who had had an angiogram within the previous year. This led Weiss to Dr. C. Noel Bairey Merz.

## A DISEASE UNDER THE RADAR

An internationally recognized cardiologist and researcher, Dr. Bairey Merz has been overseeing and engaging in research into women's heart disease since 1998. She is the medical director of Cedars-Sinai's Women's Health Program, medical director of the Preventive and Rehabilitative Cardiac Center, and holder of the Women's Guild Chair in Women's Health.

Cardiologist C. Noel Bairey Merz, M.D., medical director of Cedars-Sinai's Women's Health Program, and Louise Thomson, M.D. a nuclear physician and cardiac imaging specialist, use cardiac MRI to study and diagnose heart disease in women.



---

Through the WISE study, Bairey Merz and other researchers have found that two-thirds of women exhibiting chest pain appear to be healthy on an angiogram, but actually do have heart disease.

---

Dr. Bairey Merz also chairs the Women's Ischemic Syndrome Evaluation (WISE) study, a landmark National Institutes of Health study of nearly 1,000 women across the country, the largest study to date on women's heart disease.

Through the WISE study, Bairey Merz and other researchers have found that two-thirds of women exhibiting chest pain appear to be healthy on an angiogram, like Denise Weiss, but actually do have heart disease. They are suffering from a condition known as coronary microvascular dysfunction. In women with the condition, the heart doesn't receive enough blood for strenuous activities because the small arteries of the heart—which are not seen on an angiogram—don't open sufficiently or properly.

Some 12 million people in the United States have heart disease, half of them women. It is estimated that about two to three million women in the U.S. may suffer from coronary microvascular dysfunction and are not being diagnosed by conventional detection methods.

### TWO HEARTS BEAT AS TWO

Under Dr. Bairey Merz's leadership, the WISE study has been striving to make up for lost time and attention by investigating the causes, detection, and treatments of the number one killer of women.

"Heart disease kills 500,000 women each year, more than all the cancers combined," says Bairey Merz, noting that the figure tops the number of men who die annually from the disease. "Not much research has been done on this until the last 10 years."

Women with coronary microvascular dysfunction outnumber men. They are also at risk for heart attacks, stroke, and death at a rate that is two and one half times higher than unafflicted women. Women not only develop heart disease in a different way than men, they also often exhibit different warning signs. Severe fatigue, not chest pain, is the most common symptom for women, followed by shortness of breath, making this silent disease sometimes difficult to recognize and diagnose.

Besides bringing to light coronary microvascular dysfunction and the shortcomings of traditional testing methods, the WISE study has shown that 80 percent of women with the disease do have plaque buildup in their major arteries. The buildup is just not visible because it is spread diffusely in the vessel walls. The study also shows that there are genetic determinants in the area of the nerves that control arterial constriction. A further study is examining gender- versus nongender-linked differences.

### NEW TESTING TECHNOLOGIES

Along with increased awareness of this serious health risk, several new and powerful testing methods are helping researchers to better diagnose heart disease in women. One of the most promising is a cardiac MRI, which produces an image that can show poor blood supply to the inside layer of the heart muscle. Another advanced approach uses an angiogram that looks not only at how open the vessels are, but also at how they relax in response to medication. The test is called provocative coronary angiography, and it has become the preferred means for diagnosing this condition.

Another new testing method allows investigators to see diffuse plaque buildup in major arteries through a miniature ultrasound probe that is inserted into the coronary arteries using a catheter. "For women with unusual chest pain presentations," says Dr. Louise Thomson, a cardiac imaging specialist with the Cedars-Sinai Medical Imaging Group, "this is a ray of hope." Dr. Thomson conducts cardiac imaging tests for the WISE study. "This technology," she says, "may allow for a diagnosis to be made. That translates into more appropriate treatment and management of their symptoms, and possibly a better long-term prognosis with a reduction in the chance of heart attacks, hospitalization, and death."

Along with the WISE study, Bairey Merz and other Cedars-Sinai investigators are deeply engaged in related research and clinical studies to unlock the mysteries of women's heart disease.

One study seeks to determine if a non-invasive test called peripheral arterial tonometry (PAT), which measures blood flow in the fingertips, can measure small-vessel function as effectively as other more invasive procedures. Another looks at whether women with low estrogen levels are at greater risk for coronary artery disease. Both studies are supported by the Women's Guild at Cedars-Sinai.

Bairey Merz has been examining a wide range of topics related to heart disease in both men and women for two decades. Her previous studies have looked at mental stress as a cause of heart dysfunction, and at transcendental meditation as a way to lower blood pressure or curb a tendency toward diabetes. One of her current studies examines whether acupuncture can be used as an effective treatment for heart disease.

She proudly notes that she is able to have her hand in so many projects thanks to a committed and highly skilled research team. That team includes longtime research coordinator Maura Paul-Labrador, M.P.H., who assists in trial design, management, and data analyses. "I have been working with Dr. Bairey Merz for 15 years," says Paul-Labrador, who is completing a doctoral degree in epidemiology. "It is fascinating work and very rewarding to participate in research that may lead to better treatments and improved health for us all."





Maura Paul-Labrador, M.P.H., prepares Denise Weiss for peripheral arterial tonometry (PAT) testing.

### THE WOMEN'S HEART CENTER

There are immediate beneficiaries of this scientific quest: the women who are taking advantage of the newly launched Women's Heart Center at Cedars-Sinai, which aims to be a center of excellence for women's heart health. The program offers two services: a comprehensive assessment for those who may be at risk for heart disease based on their medical and family history, and testing and consultation for women who have symptoms or have already been diagnosed.



The Red Dress Pin is the national symbol for women and heart disease awareness.

Dr. Bairey Merz acknowledges that the WISE study is a particularly demanding undertaking. "We have done a tremendous amount of work in eight years," she says. "Soon we will seek funding for a third phase of the study to focus more intensely on clinical treatment. We hope to answer questions about the clinical significance of this work. How should physicians alter their care? What should women know and be asking their doctors about? And what additional research is needed?"

Among those waiting for answers is Denise Weiss. She has had fewer chest-pain episodes in recent months, is on blood pressure and cholesterol medication, and practices healthier eating and exercise routines. As an active participant in the clinical trials designed by Dr. Bairey Merz and her team, she understands that medicine still needs to learn a lot more about her condition to effectively treat her. 🦋

## THE WOMEN'S HEALTH RESEARCH REGISTRY: WOMEN'S GIFT TO WOMEN

**IN THE PAST, WOMEN WERE OFTEN EXCLUDED FROM MEDICAL RESEARCH STUDIES.**

But scientists are becoming increasingly aware that medical treatments often work differently in women than in men. However, successful research requires a sufficient number of subjects, and federal privacy laws have made it difficult to reach out to new research participants.

Supported by a grant from the Women's Guild, two Cedars-Sinai physicians and prolific researchers, cardiologist Dr. C. Noel Bairey Merz and gynecologist-

oncologist Dr. Beth Karlan, started the Women's

Health Research Registry. Created in 2004, the

registry helps investigators enroll women in

clinical research; some studies

are carried out with healthy

participants, and others

enroll only those with a

specific medical condition

that may be helped by the

treatment they receive. Now

with an online component, more

than 700 women have signed up for

the registry, according to Karen Nosakowski, registry coordinator. The goal is to have 10,000 women participating within five years.

Unlike other registries, no particular health status is required. Potential participants are only asked to be willing to get involved as the need arises. The Cedars-Sinai registry is also distinctive in not restricting research subjects to local residents. Although most are from Southern California, women from all over the United States and Canada have signed up.

"We are now at a point where there are enough people enrolled in the registry that we will be able to contact them about a study," says Dr. Bairey Merz.

*For more information, visit [www.cedars-sinai.edu/whrr](http://www.cedars-sinai.edu/whrr) or call (310) 423-9224.*

