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# WOMEN AND HEART DISEASE

by Margie Patlak

**I**n the spring of her 58th year, Anita Chudnow of Milwaukee, Wis., was working in her garden when a sudden and extreme fatigue overcame her. She went in to lie down and didn't have the energy to get up to make dinner several hours later.

Convinced that something was amiss, her family insisted she see a doctor. He put her through a battery of tests, which revealed that three of Chudnow's heart arteries, called coronaries, were choked with a fat-like deposit called plaque. The plaque had narrowed her arteries, depriving her heart of the oxygen-rich blood it needed to function.

"I couldn't believe it," said Chudnow, recalling her surprise at learning she had coronary heart disease, although she was familiar with the condition because her father had it. "Maybe I thought heart disease was a man's disease because of all those years my father suffered from it. I went with him in the ambulance to the hospital so many times and I never thought the same thing could happen to me," she said.

Unfortunately, Chudnow isn't the only one with that misconception. Although heart disease has been the number one killer of women since shortly after the turn of the century when it overtook infectious diseases, most people aren't aware of how common—and how deadly—the disorder is in women.

"This is a problem," said cardiologist Nanette Wenger, M.D., of Emory University in Atlanta, "because unless women see heart disease as part of their disease profile, they're not going to adhere to heart disease prevention messages early in life

and they're not going to respond to heart disease symptoms later on."

The lack of awareness of heart disease in women was fueled, in part, by the early findings of the landmark Framingham Heart Study. In this study, which began in 1948 and is still ongoing, researchers have scrutinized the habits and health of thousands of middle-aged men and women from Framingham, Mass. After collecting data for a little over a decade, they found that three times more men died from heart disease during this period than women, which led to the conclusion that women were somewhat protected from the condition.

Further analyses of the Framingham data and a study conducted at the Cleveland Clinic revealed, however, that women aren't spared from medical matters of the heart, but rather tend to develop them about 10 to 15 years later in life than men. According to the American Heart Association, 1 in 9 women aged 45 to 64 has some form of heart or blood vessel disease; this ratio soars to 1 in 3 at age 65 and beyond. The approximately 500,000 heart attack deaths that occur annually in this country, in addition, are evenly split between men and women. Each year, nearly twice as many women die from heart disease and stroke than from all forms of cancer combined.

Despite the prevalence and seriousness of heart disease among women, much of what is known and popularized about it is based on research done in men. The studies that have included women suggest, however, that many of the mainstays of diagnosis, treatment and prevention of

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coronary heart disease may not apply to the female gender.

As with other drugs and populations, FDA is responsible for the safety and effectiveness in women of medications for heart disease.

## **Discrepancies in Diagnosis**

One of the telltale signs of heart disease is chest pain or tightness, known as angina, that occurs during physically demanding tasks such as climbing stairs, or under emotional strain. This pain can make a person short of breath. It can radiate to the jaw, neck, shoulders, or inner arms. Angina occurs because narrowed arteries in the heart deprive it of oxygen-rich blood. If a blood clot completely chokes off the blood supply in these arteries in what is known as a heart attack, chest pain usually becomes more severe and lasts longer.

But chest pain may not be as good a diagnostic clue of serious heart disease in women as it is in men. Nearly twice as many men as women with chest pain that may be angina actually have coronary heart disease. This finding is from the National Institute of Health's Coronary Artery Surgery Study. It may stem, in part, from women being more likely than men to have such conditions as heartburn or spasms of the esophagus or heart arteries, which can cause chest pain that resembles angina.

But given the dire consequences of heart disease that goes unrecognized, Wenger said that any woman complaining of chest pain should be taken seriously by her doctor. She and other experts at a 1992 conference convened by the National Heart, Lung, and Blood Institute recommended that doctors carefully evaluate women (and men) with chest pain, based on their symptoms and risk factors for heart disease, such as smoking or high blood pressure. These patients should then have tests to detect abnormalities prompted by narrowed heart arteries or a previously unrecognized heart attack.

But some of these commonly per-

formed tests are less accurate in women than men and have prompted some cardiologists to reject their use in female patients altogether. One standard test is an exercise stress test, during which the patient exercises on a treadmill while the activity of the heart is electrically monitored. But this test falsely predicts heart disease in as many as half the women tested, studies show. In addition, many women cannot exercise long enough for such a test because, at their older age, they have exercise-limiting illnesses, such as arthritis.

Researchers recently developed statistical standards for the treadmill stress test in women that uses a woman's age and risk factors for heart disease to improve accuracy. Wenger is satisfied enough with these modifications to prescribe the treadmill stress test for her female patients, if they can exercise. But other cardiologists still question its accuracy because they think most doctors don't have the information they need to adequately assess a woman's risk factors for heart disease. "I don't do stress treadmill tests in women," said Marianne Legato, M.D., of Columbia University. "They're a waste of \$600."

Legato prefers women to exercise while the heart's activity is monitored by ultrasound in what is known as a stress echocardiogram. Experts agree that this test is accurate in both men and women, as is the thallium exercise stress test, in which blood flow to the heart is imaged during exercise with radioactive tracers injected into a vein. Adjustments must be made for a woman's breast tissue, however, which can obscure the radioactive signals emitted from heart arteries.

Another test, called nuclear ventriculography, uses radioactive tracers to measure how much blood is pumped by the heart with each beat at rest and during exercise. The test is not accurate in women, however, and, according to the American Heart Association, is not recommended as a screening tool for women until standards applicable to them are developed.

None of these tests can effectively and practically screen on a routine basis symp-

tom-free men or women for heart disease. This is unfortunate because women are more likely than men to have "silent" or unrecognized heart attacks.

Part of the reason more women have undetected heart attacks, according to Legato, is because women often have signs of a heart attack that differ from those typical in men. Women are more likely than men to have nausea and pain high up in the abdomen or burning in their chest during a heart attack. "Women ought to be careful of what they're calling 'indigestion'," Legato said.

Other women, such as Chudnow, have atypical angina that includes extreme fatigue on physical exertion rather than chest pain.

## **Deadly Difference**

Whether silent or replete with telltale symptoms, heart attacks or their aftermath tend to be more deadly in women. About one-quarter more women than men die within a year of having a heart attack. This difference may stem from women generally being older than men when they suffer heart attacks. (Their older age makes them more likely to have other illnesses that hamper survival.) Also, women do not respond as well as men to treatments for heart disease usually prescribed during or after a heart attack.

These treatments include coronary angioplasty. In this procedure, a tiny balloon is inserted into blocked heart arteries and their branches, and then inflated to compress the plaque that is obstructing the flow of blood to the heart. A recent study by Sheryl Kelsey, Ph.D., of the University of Pittsburgh found that women were 10 times as likely as men not to survive coronary angioplasty. When women and men of the same age and with the same history of heart disease were compared, women's risk of death during the procedure was still nearly five times higher than men's.

Other studies show that women are twice as likely as men to have heart disease symptoms four years after angioplasty, according to Wenger. She speculates the effectiveness of angioplasty

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in women might be limited by their smaller blood vessel size. Angioplasty cannot be performed on blood vessels that are too small, so doctors may not be able to treat all the blockages in women's heart arteries with the procedure, Wenger said.

An alternative therapy to angioplasty is coronary bypass surgery, in which portions of leg veins or an artery in the chest are removed and attached to the heart to provide alternate routes for blood flow, bypassing blocked arteries. Women are two to three times less likely than men to survive this procedure, according to Wenger, perhaps because women are generally older and sicker than men when they have the surgery. If women do survive the operation, however, their five-year survival rate following heart bypass surgery is the same as for men.

A treatment for heart attacks that appears to be equally effective in men and women is "clot-busting" drugs and biologics such as tissue plasminogen activator and streptokinase, both approved by FDA for this purpose. When one of these is given within hours of a heart attack, it can limit the damage to the heart by quickly dissolving the clots blocking heart arteries. But women are more likely than men to suffer internal bleeding complications, including a hemorrhagic stroke, from these products. Wenger speculates the standard doses, set from testing done mainly in men, are not appropriate for women.

Aspirin and beta-blocker drugs are equally effective in women and men in preventing a second heart attack. But when it comes to other commonly used heart medications, such as those used to dilate blood vessels, "virtually none of these drugs have been studied in women," said Wenger.

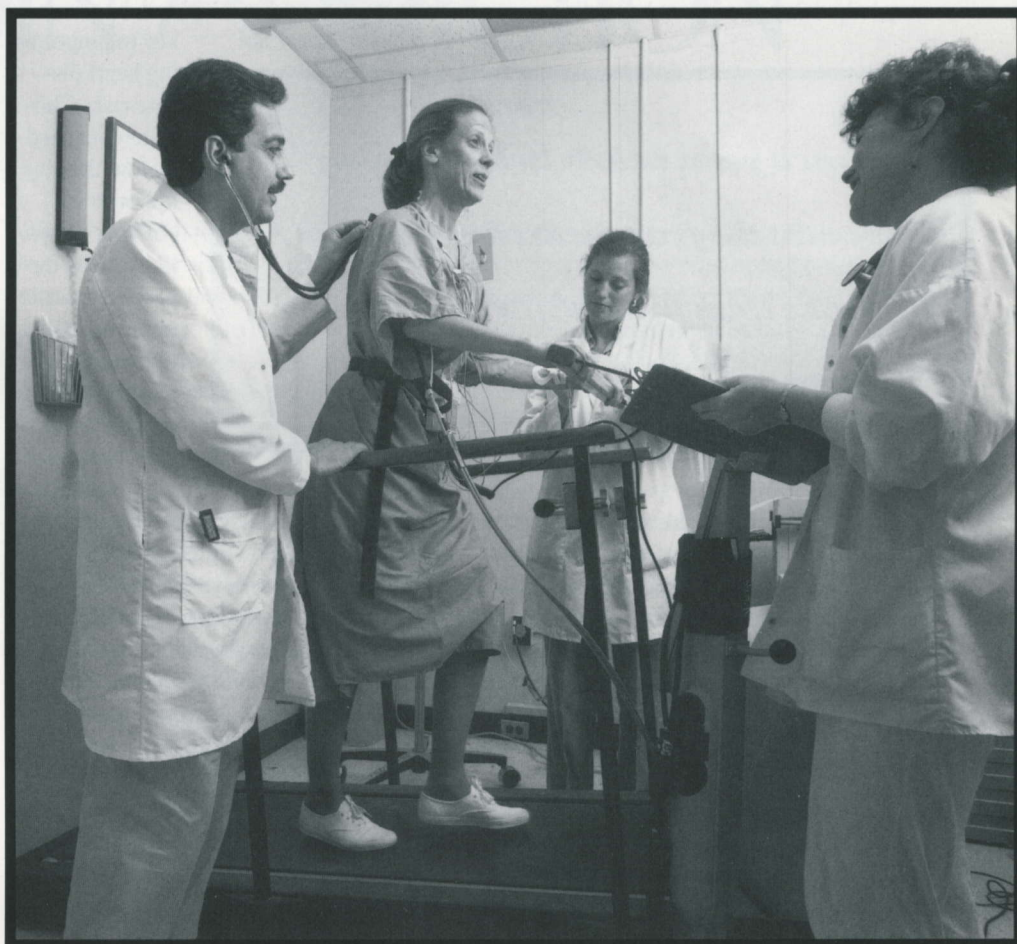
The usually smaller body size and higher body-fat content of women, and the hormones generated or taken by women may alter the effects of drugs, according to Ruth Merkatz, Ph.D., R.N., of FDA.

Recognizing the problems with prescribing drugs for women that have been analyzed mainly in men, FDA recently

issued a guideline that requests women be adequately represented in new drug tests and that the drugs' safety and effectiveness be analyzed for both genders. FDA also recently set up an Office of Women's Health, to focus on women in clinical trials and develop other measures needed to ensure that most drugs are tested and analyzed in

### **Prevention Tactics Vary**

The tricks of the trade for preventing coronary heart disease also vary from men to women. Post-menopausal women may have the option of possibly delaying or preventing the onset of heart disease by taking daily estrogen, in a dose comparable to what their bodies generated before



both men and women, said Merkatz, who heads the office. "We won't close the loop and have all the answers tomorrow," she added, "but over the next few years we'll have much more information on cardiovascular treatments for women."

FDA is also working with academic institutions to further test in women some commonly used cardiovascular drugs already on the market, such as propranolol and quinidine, two heart drugs.

*In the first part of a thallium stress test, the patient (here played by a staff member) walks or runs on a treadmill, while Vasken Dilsiban, M.D. (left), monitors her heart rate. After the treadmill, a patient would receive an injection of thallium 201, a radioactive material that allows imaging of the heart muscle. The patient then would rest for two to three hours before another image of the heart muscle is taken in a resting state. A comparison of the two images is used to diagnose coronary artery disease. (This photo was taken at the Clinical Center of the National Institutes of Health)*

menopause. Some studies suggest that women who take estrogen during and after menopause have about half the risk of heart attack as women who don't take the hormone. Natural production of estrogen before menopause, some researchers speculate, may explain why women develop heart disease later than men.

Whether estrogen replacement therapy may help delay or prevent heart disease in

heart disease in men is a diet low in cholesterol, a fat-like substance carried in the blood and used by the body to build cell walls, sex hormones, and a variety of other vital substances. (See "Lowering Cholesterol" in the March 1994 *FDA Consumer*.) When too much cholesterol accumulates in the blood, it clogs arteries.

The amount of the two main types of cholesterol found in the blood, however, is key to pinpointing heart disease risk. Cholesterol carried by low-density lipoproteins (LDLs) is more likely to be deposited on artery walls, unlike cholesterol carried by high-density lipoproteins (HDLs), which often is

North Carolina. Because high HDL levels are so much more protective in women than low LDL levels, lowering total cholesterol may not benefit women and may do more harm than good, he claims. The National Heart, Lung, and Blood Institute is conducting several studies to assess if this is the case.

Like men, however, women can help prevent heart disease by using medications or other measures to stem high blood pressure, losing weight if they are overweight, and not smoking. Both sexes should adhere to a low-fat diet and not consume alcohol if they have high blood levels of triglycerides, a type of fat produced by the liver when alcohol is drunk or when excess calories are taken in.

Scientists are studying whether vitamin E and the vitamin A precursor beta carotene may also help stave off heart disease. Women with a high vitamin E consumption had a 34 percent lower risk of heart disease, according to an epidemiological study by Meir Stampfer, M.D., of Brigham and Women's Hospital in Boston. In the same study of more than 87,000 nurses, those with boosted beta carotene consumption had a 22 percent lower risk of heart disease.

Vigorous aerobic exercise is often touted as a heart disease preventive. But regular walking may be equally effective, according to a small epidemiological study at the Cooper Institute for Aerobics Research in Dallas. Women who walked three miles a day, five days a week decreased their risk of heart disease, even if they took 20 minutes to walk a mile.

Much more research needs to be done, however, to paint a complete and accurate picture of the best ways to prevent, diagnose and treat heart disease in women. "It's only been about five years," noted Wenger, "that we've begun to carefully look at heart disease in women, in contrast to 30 years experience looking at it in men—we have a lot of catching up to do." ■

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women, however, remains unproven. Since women selected for estrogen treatment in studies were often healthier, slimmer, and more active than those who didn't receive the hormone therapy, their reduced heart attack risk could have been due to lifestyle characteristics rather than by the estrogen treatment. Because of these uncertainties, FDA has not approved the use of estrogen for prevention of cardiovascular disease.

Use of estrogen after menopause is linked to a greater risk of developing endometrial cancer. To counter that risk, estrogen is often prescribed with the hormone progestin.

Whether this hormone combination also prevents heart disease in women is also unknown. To resolve this question and to prove whether estrogen replacement therapy prevents heart disease in women, the National Institutes of Health has undertaken a randomized clinical trial as part of the Women's Health Initiative. Results are not expected to be available for five to 10 years, however.

A mainstay in treating and preventing

ferried back to the liver where it is processed or removed. High levels of HDL cholesterol and low levels of LDL cholesterol are linked to lower risk of heart disease in both men and women. But HDL levels are a much more powerful predictor of heart disease risk in women than LDL levels, several studies suggest.

A low-cholesterol, low-saturated-fat diet can lower blood cholesterol by more than 15 percent in men. Epidemiological studies of men also found that each 1 percent drop in blood cholesterol was accompanied by a 2 percent drop in the risk of a heart attack.

Research suggests high cholesterol is a risk factor for heart disease in women, too, but experts debate whether women should strive to lower their cholesterol to the levels recommended by the American Heart Association because these levels are based on studies done primarily in men.

A cholesterol-lowering diet in women not only lowers LDL cholesterol, but nearly equally lowers their HDL cholesterol, pointed out John Crouse, M.D., of the Bowman Gray Medical School in