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Cardiovascular Disease Risk Factors Part XIII Gender By James L. Holly, MD<br>Your Life Your Health<br>The Examiner<br>September 22, 2005

Gender is a cardiovascular disease risk factor. Yet, it is obviously a factor which you cannot change, but one which you need to understand in order to know how to address other modifiable risk factors which you may experience.

Men are at higher risk for heart disease at an earlier age than women. The risk of a heart attack begins to increase more rapidly when a man reaches age 45 . His risk goes up steadily as he gets older. A woman's risk of heart attack begins to increase when she reaches age 55 . The hormone estrogen is protective to the heart, so when a woman reaches menopause and her estrogen production reduces, she is more susceptible to heart disease. This would suggest that estrogen replacement might decrease women's risk of cardiovascular disease.

## Hormone Replacement Therapy and Heart Disease

However, in March of 2004, the National Institutes of Health stopped the estrogen-only phase of the Women's Health Initiative (WHI). The WHI found an increased risk of stroke and no reduction in the risk of heart disease in postmenopausal women who have had a hysterectomy.

In February 2004 the American Heart Association updated its Guidelines for Cardiovascular Disease Prevention in Women with new recommendations for Post Menopausal Hormone Therapy (PHT). Combined hormone therapy is not recommended for the prevention of heart disease and stroke in postmenopausal women. The Guidelines recommended a conservative approach to the use of estrogen-alone hormone therapy until further research is available.

Since the recent data from the estrogen only arm of the WHI trial does not support the use of estrogen only to prevent cardiovascular disease, the American Heart Association reinforced its recommendation that hormone therapy not be used for cardiovascular prevention. Its use for other reasons should be cautiously considered with the advice of a physician. Hormones may relieve menopausal symptoms, but women and their healthcare providers should weigh the potential risks of therapy against the potential benefits for menopausal symptom control. For more information on hormones and heart disease see the attached addendum.

## Gender Gap in Diagnosing and Treatment

Heart disease is the leading killer of men and women. But when it comes to diagnosing and treating it, there is a gender gap. Women with heart attacks are more likely to die than men...and that's not just older women. Women of all ages are more likely to die.

According to one Israeli study that adjusted for age, size and other factors, the death risk for women was 1.7 times that of men.

Coronary artery disease is the leading cause of death in women. More than twice as many women die from cardiovascular disease as from all forms of cancer combined. Evaluation for suspected coronary disease differs in women because of frequently misleading results provided by treadmill testing without imaging. Gender differences have been observed in treatment practices, but since more is not necessarily better in this setting, the optimal approach for women has yet to be established. Opportunities remain for the physician to work in partnership with the patient for early intervention in women with symptoms of coronary artery disease, including responding to chest pain.

## Not Just a Man's Disease

Heart disease is more than just a man's disease - much more. One in 9 women between the ages of 45 and 64 has some form of cardiovascular disease, ranging from coronary artery disease to stroke or renal vascular disease. By the time a woman reaches 65 , she has a 1 in 3 chance of developing cardiovascular disease. And a number of studies show that African American women are at even greater risk than these averages.

Heart disease, in its various forms, is the leading killer of American women. The following statistics paint a graphic picture:

- One-third of all deaths of American women each year are attributable to heart disease.
- Heart disease kills more women each year than cancer, accidents, and diabetes combined.
- All forms of cardiovascular disease kill nearly 500,000 American women a year. Stroke alone kills 88,000.
- Myocardial infarction, commonly known as a heart attack, kills 244,000 women a year.
- Forty percent of women with heart disease will eventually die of it.

The reason that so much more attention has been focused on men is that they are much more likely to be stricken with heart disease in their prime middle years, whereas women tend to get it 10 to 20 years later. For most women, it is only after menopause that heart disease becomes a problem. But a woman of 60 is about as likely to get heart disease as a man of 50 , and by time they are in their 70 s , men and women get heart disease at equal rates.

## Exercise Stress Tests and Gender

Treadmills as a screening tool for diagnosing heart disease are accurate in men but not so in women. In one study comparing the accuracy of treadmill tests in women and men, misleading treadmill results occurred in 35 percent of the women studied. When combined with nuclear imaging using thallium (a low-dose radioisotope), the accuracy
rate improved in women, provided the interpreter was trained to take breast tissue and valve plane artifacts into account.

Abnormal treadmill tests have been related to phases of the menstrual cycle and to oral contraceptive use, implicating sex hormones as a factor. It may be estrogen's effect on cardiocytes - the cells of the heart muscle. Another explanation for the variations in test results may be the effect of catecholamines (stress hormones i.e. adrenaline) on the vasomotor tone and the higher prevalence of mitral valve prolapse among women.

## Pharmacologic Stress Tests

Stress tests induced by drugs (dipyridamole, adenosine or dobutamine) rather than with exercise may actually be preferable in women since many elderly women cannot endure the physical demands of treadmill testing and sub-optimal heart rates are achieved. Again, the use of thallium improves the accuracy of this stress test as well.

Either stress test when combined with echocardiography is more accurate for diagnosing heart disease in women with comparable results to nuclear imaging. With a skillful, experienced technician, the graphic images of the functioning heart muscle can be accurately interpreted. By using sound waves, echocardiography has the added advantage of avoiding breast artifacts (inaccurate readings due to breast tissue).

## Angiography

Angiography is a dye study using the cardiac catheterization procedure with x-rays to view blocked vessels. It remains the gold standard for diagnosing coronary artery disease, but, unlike nuclear imaging, it has its risks. Women with heart attacks or unstable or stable angina are less likely to be referred for angiography than are men with the same diagnoses. It is debatable whether this reflects under use of angiography in women or overuse in men.

## Surgical Intervention

When it comes to balloon angioplasty, women should do as well as men but they don't. More women die after angioplasty and their complication rates are higher then for men (The age adjusted death rate for women is 4 times that of men, according to the American Heart Association).

Though women undergoing angioplasty are generally older than the men - and more likely to have other conditions like diabetes and high blood pressure - gender remained an independent predictor of risk, according to a study by the National Heart, Lung and Blood Institute. The track record on bypass surgery isn't any more encouraging. More women die from bypass than men...and that's not because they are older at the time of surgery.

In one study of 6,630 subjects, the death rate for women was significantly higher in all age groups. Four women undergoing bypass surgery died for every man in the 40 to 49 year group. In the 50 to 59 group, it was three women for every man. One possible explanation is women's smaller size. In a study done at the Cleveland Clinic, the death rates for women and men were nearly three to one.

When matched for age, severity of chest pains and extent of disease, the risk was two to one. But once body size was factored, gender was no longer a predictor. Another explanation could be their poorer health status at the time of the surgery. One study found that women were more seriously ill compared with men at the time of surgery. This could mean that women are referred at a later stage of their disease, subjecting them to more risk. But one study from Duke University concluded that, although women with heart disease were less likely in general to be referred for bypass, among patients with higher likelihood of cardiac death, women and men were referred with equal frequency.

## Women's Heart Disease will be a growing problem

The significance of these facts is clear when you consider the aging of the American population. By the year 2000, 38 percent of American women will be 45 years of age or older. By 2015, that percentage will rise to 45 percent. This means that heart disease in women will be an even bigger problem in the future than it is now.

Until now, treatment of women with heart disease has been based primarily on what is known about men. Given the many factors unique to a woman's health, this is not satisfactory. Treatment cannot adequately take account of these factors until they have been systematically studied and evaluated.

Until that happens, it is likely that women will continue to pay with delayed diagnosis, inadequate treatment, and a toll that can be counted in disabilities and deaths. In fact, some studies have shown that despite the fact that women with heart disease are often sicker than men with the same disease, they are frequently treated less aggressively.

The good news is that things are changing. Greater attention to women's health in general and a growing awareness of the risks of heart disease in women are replacing the disregard of the past. An increasing number of scientific studies are focusing on how heart disease affects women. Gradually, doctors are becoming better informed about the dangers to women from heart disease, so that they are less likely to attribute chest pain to anxiety or other non-heart-related problems. And women themselves are learning that their own attention to their health must not be limited to an annual visit to the gynecologist.

In part XIV of Cardiovascular Disease Risk Factors, we will examine more about what women can and should do about preventing and/or treating heart disease. Remember, it is your life and it is your health.

## Questions and Answers About Estrogen Replacement and Heart Disease

Many people have been confused and alarmed by the 2004 news about the Women's Health Initiative Study (WHI). To help understand what it means, the following Questions and Answers offer some perspective. Before you personally make any decisions, though, it's very important to consult your physician.

## What if I'm taking or considering taking estrogen alone or estrogen plus progestin to prevent heart disease or stroke?

Estrogen alone and estrogen plus progestin should not be used to prevent heart disease or stroke. Many established methods are available to lower heart disease risk in women. Lowering cholesterol and controlling blood pressure are two examples. If blood pressure and cholesterol aren't controlled with lifestyle measures such as not smoking, getting regular physical activity and eating a heart-healthy diet, then drug therapy may be indicated. Certain medications, such as aspirin, statins, beta-blockers and ACE-inhibitors, also may benefit women who have cardiovascular disease or are at high risk of developing it.

What if I'm taking another type of hormone therapy to prevent heart disease or stroke?

Until there's clear evidence that other forms of PHT not tested in recent clinical trials are beneficial, women should not use these therapies to prevent heart disease and stroke.

Newer estrogen therapies such as selective estrogen receptor modulators (SERMs) aren't the same as PHT. They don't treat menopausal symptoms and don't seem to increase the risk of breast cancer - but they are effective in treating osteoporosis and preventing fractures. Studies are under way to find out if they lower the risk of heart disease. However, like estrogen plus progestin, these should not be used for this purpose until more research is available.

What if I'm taking hormone therapy for other reasons, such as relief of menopausal symptoms?

For many women, using estrogen alone or estrogen plus progestin for short-term relief of menopausal symptoms may be worth the small absolute increase in risk for heart disease, stroke or breast cancer. Because the risk of these complications rises the longer it is used, PHT should be used for the shortest time necessary. Women who've had premature menopause because their ovaries were surgically removed should consult their physician(s) about when to stop hormone therapy.

## What if I'm taking hormone therapy to prevent osteoporosis?

Estrogen alone and estrogen plus progestin are effective for preventing osteoporosis and bone breaks, but these benefits may not outweigh the risk of breast cancer and cardiovascular disease. Other options should be considered.

Is more research under way to evaluate using other forms of hormone therapy to prevent and treat heart disease?

Yes. The WHI results show that postmenopausal hormone therapy didn't work the way physicians assumed it would. This shows why research studies like the WHI are so important. It also makes scientists more intent than ever to discover new types of estrogens that might help prevent and treat heart diseases. It could be that in the future new and different estrogens or SERMs might help prevent and/or treat heart disease. Many different kinds of estrogens and SERMs are now being tested.

