

Hormone Replacement Therapy (HRT)

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It is hard to think of a health issue that has had as much controversy and concern as Hormone Replacement Therapy (HRT). For the first time, a study has shown convincing evidence that prolonged use of HRT increases the risk of breast cancer as well as heart attacks (<http://jama.ama-assn.org/issues/current/fful/joc21036.html>). The results of this study, called the Women's Health Initiative were long awaited. The study was planned to go on for 8.5 years but was stopped after 5.2 years because the results to date indicated that the potential benefits of HRT were outweighed by the risks. This was the first randomized study (people enrolled in the study had an equal chance of receiving HRT or a placebo- a pill without any active ingredient) that was designed to answer the question of whether or not HRT would protect women from heart disease who did not have any pre-existing heart disease. A previous randomized study (The Heart and Estrogen/Prosterin Replacement Study- HERS) showed that HRT does not have any benefit and has short term harm in patients with pre-existing heart disease who received HRT.

The Women's Health Initiative was stopped prematurely because the women in the treatment arm (those receiving HRT) did worse than those receiving placebo. Specifically, there was a 29% increase in heart attacks, a 26% increase in newly diagnosed breast cancer, a 41% increase in strokes, and a 1.13% increase in serious bloods clots that traveled to the lung (pulmonary embolus). For every 10,00 women receiving HRT, this meant an absolute increase of 7 heart attacks, 8 strokes, 8 more invasive breast cancers, and 8 more pulmonary emboli. The study also showed benefits of HRT. For every 10,000 women on HRT, there were 6 fewer colon cancers, and 5 fewer hip fractures. Nevertheless, the investigators concluded that the risks exceeded the benefits to a degree that the study should be terminated prematurely to protect those who were in the study and receiving HRT. What are the risks of HRT? We have always known that HRT can cause blood clots and should not be used in people that have serious blood clots in the past. We also knew that HRT did not have any benefits for women with pre-existing heart disease. We now know that HRT, despite the fact that it lowers cholesterol levels, has a increased risk of heart attacks when used for at least 5 years in women who did not have pre-existing heart disease. We also now know that there is a small but significant risk of newly diagnosed invasive breast cancer.

What are the known benefits of HRT? HRT improves bone density and this study also showed a reduction in the incidence of hip fracture. Because there are other treatments that do not have the risks shown in this study, HRT should not be the primary treatment for osteoporosis. This study also showed a benefit in preventing colon cancer. Again, this would not be a primary reason to take HRT. Folic acid as well as low dose aspirin (81 mg. per day) have both been shown to have benefits in terms of preventing colon cancer. Folic acid has virtually no side effect. The major side effect of aspirin is bleeding, especially from the intestines. But most people tolerate aspirin fairly well. There are other medications that are being researched that have the potential to reduce one's chances of

developing colon cancer. HRT also has effects on the vagina to prevent or treat excessive dryness associated with menopause.

Because of the results of this study, it makes sense to use lubricating agents instead, if this is the primary reason for using the HRT. Other potential benefits of HRT have been less well researched and are very speculative. These include vision preservation and prevention of Alzheimer's disease. Because of the problems that we now know occur with HRT, it is unlikely that we will know the answers to these issues any time soon and therefore, these are not reasons to take HRT.

What is the reason to consider HRT? The major indication for HRT is the same as it has always been, treatment of the effects of menopause that cause hot flashes, chills, and sweats (vasomotor symptoms). What has changed now is that physicians will be more conservative in recommending HRT for this option. When we thought that HRT had benefits in terms of reducing the chances of heart disease, we were quicker to recommend it. Now that we know that HRT increases the risk of heart disease, other treatments will be tried first. The symptoms of menopause (hot flashes) should not be minimized. For many women, these symptoms are incapacitating and can significantly impair the quality of life. Some women, who have tried all other options, will opt for HRT, despite the risks. For others, the risks will outweigh the benefits. For the other proven indication for use of HRT (prevention of osteoporosis), there are other medications that have a safer profile. What about using estrogen only? HRT refers to the use of estrogen along with progesterone. It is possible that estrogen alone would not have some of the harmful side effects shown in the Women's Health Initiative. The reason that we prescribe estrogen along with progesterone is that estrogen alone has been shown to increase the risk of cancer of the uterus (endometrial cancer). A recent retrospective study (JAMA.2002;288) showed an increase in the risk for developing ovarian cancer in women that received estrogen alone. There was not an increased risk in women who received estrogen and progesterone. Since ovarian cancer is hard to detect at an early and treatable stage and is also hard to treat, these results, although in a retrospective study, need to be taken seriously. Given all of the evidence that we now have, we should be conservative and assume that estrogen alone has the same problems with heart disease and breast cancer as HRT, until proven otherwise. In addition, estrogen alone has unique risks with respect to uterine cancer and probably ovarian cancer.

What should I do if I am on HRT? First and foremost, you need to speak to your physician. You need to understand what the reasons were for placing you on HRT to begin with. The researchers in the Women's Health Initiative concluded that "this regimen should not be initiated or continued for primary prevention of CHD." (coronary heart disease). If you were placed on HRT primarily to prevent heart disease, you should discontinue the medication. You need to speak to your physician about how to do so. This is not an emergency and it is possible that you and your physician may want to taper you off to minimize side effects. If you are on HRT primarily to prevent osteoporosis, you should have a discussion with your physician of other treatment options. If you are on HRT for hot flashes, the decision needs to be individualized. Some of the issues that you and your doctor will take into account are: How severe are my symptoms? How well

is the HRT relieving the symptoms? How long have I been on HRT? Have I tried to go off in the past? What happened? Have I tried all other options (other medications, herbs, not medication options such as biofeedback?) Once you have discussed these issues you and your doctor can weight the risks and benefits to help you make an informed decision that is right for you.

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