

## **Hormone Replacement Therapy Update – 2002**

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Like so many issues in medicine, the information on HRT continues to be debated and re-examined. Data from the WHI study continues to slowly be made available to a group of advisors. Several additional issues have developed. The debate of whether this was indeed a study of primary prevention seems to be divided between gynecologists and the researchers. Most gynecologists view primary prevention as beginning HRT at menopause, usually for treatment of symptoms, and continuing it for several years. The average woman in the WHI was 63 years old, 1/3 were over 70 years old, 15% had previously existing heart disease, the patients had a body mass index of 28 (bordering on obesity), and IF YOU HAD HOT FLASHES YOU WERE NOT ALLOWED TO BE IN THE STUDY. This, in my opinion is not a primary prevention study. We are now discovering that estrogen receptors in the heart and probably other organs (there are over 400 estrogen receptor sites or places estrogen can act, in your body) are gradually lost in the years following menopause. The addition of ERT many years after menopause may not have the desired effects. Certainly, in the WHI study most women were in this category.

The exclusion of women with hot flashes is also a problem. Hot flashes are increased in women with the lowest estrogen levels. To do a study on estrogen replacement and eliminate the group of women who exhibit a symptom of low estrogen, does not provide a balanced or representative study group. Also, the patients in this study on average were almost obese. Fat produces its own estrogen, and therefore obese women make more estrogen. Incorporating a group of women with higher estrogen levels while eliminating women with lower levels does not provide a representative study population and skews the results.

There is an ongoing review of the women who have been on HRT the longest, the first group of women to enroll in the WHI. Despite the supposed increase in risks, the group

of women on Prempro the longest, have the lowest mortality, and the mortality curves are separating with time, in favor of the Prempro group.

Perhaps, the most critical mistake of the Women's Health Initiative, is it's total lack of any questions on quality of life questions. How can a health initiative on HRT ignore the main reason most women initiate estrogen therapy? This is an insult to women. There were no questions regarding hot flashes, insomnia night sweats and sleep quality, vaginal dryness and the ability to have sexual intercourse, pain with sex, interest in sex, cognitive functioning, multitasking, depression (estrogen increases serotonin), eye dryness, skin dryness, palpitations, and other symptoms of estrogen deficiency. Can you imagine a study on male sex hormones not asking men about their sexual function and sense of wellness and making conclusions about male hormone replacement's risks and benefits. If a man's penis were to shrink, dry up, not work, and bleed, hurt, and crack if he tried to use it, wouldn't this be a topic of concern. Remember, almost all women have urogenital atrophy without ERT.

Two recent studies again show good news for estrogen users. A recent study in The Journal of the American Association, showed a 50% reduction in Alzheimer's risk in the women who took estrogen for 10 years. Remember, if you live to 90, there is an approximately 50% chance of getting Alzheimer's, so this is a huge reduction in a very common and severe medical problem. Please realize this study agrees with many other previously done studies and a lot of European studies. If you are a thin white woman, your risk of Alzheimer's is much higher as is your risk of osteoporosis, so estrogen may be more important for you. There was also a recent study in the Journal of Psychiatry that demonstrated estrogen was comparable to antidepressants in the treatment of perimenopausal depression. Estrogen increases serotonin in the brain just as antidepressants do. Around menopause some women experience a new onset of depression and those with a history of depression experience exacerbations. Since the cause may be decline in estrogen levels, supplementing what is low may be more effective and with less side effects than adding a new drug with more interactions. Again, these positive studies are minimally reported in the media.

As you continue to learn more about estrogen therapy, you realize it is not a one size fits all and there is a need for a discussion with your gynecologist. Unfortunately, most primary care physicians cannot keep track of the data and should abdicate to those who specialize in hormone therapy. I can no longer keep up with anti-hypertensive meds and other meds used by internists as medicines continue to be developed.

There is a small group of women who should not take estrogen because the risk is greater for them than others. Unfortunately, due to the premature cessation of part of the WHI, we may not be able to identify this small group. For most women, the individual risks are low and the benefits for some great. We will have to stay tuned to the European, Canadian, and Australian studies. There is some solace in knowing, I do not know one expert on menopause who has stopped her hormones, or one male expert who has had his wife stop.