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## **Women's Health Initiative (WHI) Study**

***How July 2002 changed menopausal management  
and what the study really says.***

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In July of 2002, headlines in every newspaper and news outlet shouted, **“Stay Away From Hormone Replacement Therapy— It Causes Cancer!”** The week before, hormone replacement was terrific for protecting people against heart disease, osteoporosis, colon cancer and Alzheimer’s disease. Articles showed these same hormones now caused breast cancer, heart disease and stroke. The study was stopped before completion.

### **Why was the WHI study done?**

In the 1990s it was well known that estrogen replacement protected against coronary heart disease. The company that makes Premarin (an extract of a pregnant mare’s urine), wanted to promote that their product was heart protective in all of their advertising materials.

### **What is the WHI and who participated?**

WHI was actually two studies that lasted a total of eight years.

**Group 1:** Consisted of 16,000 menopausal women with an intact uterus. 8,000 of the women received Prempro — a combination of *Premarin 0.625mg (horse urine estrogen)* and Provera (*synthetic imitation progesterone-- a progestin*). The remaining 8,000 women received a placebo.

**Group 2:** Included 8,000 women who had a prior hysterectomy. Half of the women received Premarin only and the other half took a placebo. Prior to the start of either study, none of the participants had been taking hormones for at least three years. Neither the doctors nor the patients were aware if they were receiving the actual medicine or placebo. Since taking estrogen alone is known to promote cancer of

the lining of the uterus and Provera protects against this, there was no need for women without a uterus to take Provera.

### **Was this group of women an ideal representation to use in the study?**

Since half of these women would receive placebo for eight years, the volunteers tended to be women with very few menopausal symptoms. Abdominal fat can manufacture estrogen, (which reduces menopausal symptoms), and many of the participants tended to be overweight. Because these women had to be off of hormones for at least three years, many were older. About 500 participants were women under 60 years old. Older women have higher rates of atherosclerosis. These women had more heart disease than a typical group of hormone starters, most of who averaged ten to fifteen years younger. Also, as a group of fairly overweight women, they would have higher than average rates of breast cancer, atherosclerosis but lower rates of osteoporosis.

### **Why was the WHI stopped early?**

In July of 2002, the code was broken for the **Prempro group (Group 1)**. They were found to have a small, but provably higher rate of breast cancer than the placebo group. These women were also found to have higher rates of heart attack and stroke versus the placebo group. **The Premarin only (Group 2) wasn't experiencing** many problems and the study continued until 2004.

### **How dangerous was it to use Premarin and Provera together?**

With 16,000 participants, small differences in active versus placebo groups were detectable. Out of 10,000 women, there were 30 breast cancers in the placebo group and 36 cancers in the Prempro group (a small, but noticeable difference). The heart attack and stroke rates were slightly higher in the Prempro group. Oral estrogens tend to induce the liver to make more blood clotting factors. If a woman already has clogged arteries, a stroke was more likely to happen in the first year of therapy.

### **Were there any benefits?**

Yes. The Prempro group had lower rates of osteoporosis and colon cancer. In fact, the lowered colon cancer rates offset the increase in breast cancer. The all-cause mortality rate for the Prempro users was LOWER than the all-cause mortality rates for the placebo group. I have never seen the report made public in any news media, but it is clearly distinguishable in the original, 36-page report.

## **What was the outcome of the Premarin only (Group 2) study?**

In 2004, the report was published the same week as the Abugrabe prison scandal story. The breast cancer rates were lower than the placebo group. Heart attack was essentially the same. Stroke rates were slightly higher and osteoporosis and colon cancer were lower. I never saw a single reference reported in any of the news media. Often, good news is not reported at all.

## **What can we learn?**

There was a small but unarguable difference between the Premarin only and the Prempro group. Provera seems to increase the detection or growth of breast cancer and slightly increased heart attacks during the short time the study was done.

## **Provera is NOT the same as progesterone!**

Progesterone is a natural human hormone. In addition to reducing cancer of the endometrium, the lining of the uterus (*which Provera does do*), real progesterone builds bone growth, improves sleep, promotes thyroid function and probably reduces the rate of breast cancer. Provera consists of synthetic altered progesterone and has been known for decades to diminish bone growth (which accelerates osteoporosis). There is a direct warning in the Physicians' Desk Reference regarding Provera and has been shown to increase breast cancer rates in dogs.

## **What is in Premarin?**

Premarin is a blend of many hormones derived from the urine of pregnant mares. Although the estrone is identical to human estrone, there are many horse estrogens contained also. Despite this, Premarin probably acts in much the same way that orally dispensed human estrogens do.

## **Was the news media correct to instill warnings and fear?**

Mostly, NO. The media kept focusing on the WHI results relating to women who took estrogen only. Instead, the WHI proved that Provera might slightly increase detection or growth of breast cancer, and to start oral estrogen on an older woman that has been off hormones for years could actually increase the risk of heart attack and stroke.

## **What does WHI teach us?**

Starting women on oral estrogen (after not using hormones for many years) can increase the risk for stroke and possibly heart attack.

## **What doesn't WHI teach us?**

**It doesn't address NATURAL HORMONES.** Real progesterone might actually protect against breast cancer and even improve bone strength. The study does not address perimenopausal and early menopausal women who take human estrogen and progesterone instead of a synthetic like Provera. It does not speak to the safety of carefully monitored topical hormone cream or patches instead of prescribing oral preparations for older women. It does not focus on comparing continuous hormone use versus restarting hormone therapy after a long break. The study doesn't show any risk of estrogen use and breast cancer.

## **What about breast cancer?**

That's why the Prempro study was stopped. For many years, it has been theorized that it takes about a decade for a breast cancer to reach a detectable size when using any method. The Prempro half of WHI was stopped in five years. This means that the breast cancers detected were probably already present before the study began. The Premarin only group had slightly smaller rates of newly discovered cancer than the placebo group. It would seem that Premarin does not stimulate breast cancer growth but Provera does. A similar study should be done using natural progesterone instead of Provera. In theory, natural progesterone should reduce the rate of breast cancer growth. We also don't know how controlled levels of natural estrogen compare to Premarin 0.625mg, the standard dosage prescribed to every woman regardless of baseline levels. Individual hormone levels were not taken prior to the beginning of the study and every participant received the same dose regardless of individual need.

## **One more thing**

Women in their late 30s to early 50s may already need to start on hormone therapy. How long should someone stay on hormones is an important question. American women are living longer and many are physically and sexually active in their later years. Breast cancer rates might be pre-programmed decades before the cancer is actually detected. Breast cancer, heart attack and stroke rates were only slightly altered with or without the Prempro and less by Premarin alone. As Suzanne Somers points out in her book, *The Sexy Years*, quality of life is an important consideration. Doctors also know that lifestyle, exercise, diet, stress, relationships, and enjoyment of life have huge effects of longevity and general health. There is much about growing older that needs to be studied. The current baby boomers are very dissimilar and aging differently than their parents

and grandparents. I write prescriptions for individual women, one at a time, to help with their present, unique needs. There is still much to learn. **Take HRT one year at a time.**