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*version 2008-05-26*

# **WHI-THE WOMEN'S HEALTH INITIATIVE**

## **How July 2002 changed menopausal management and what the Women's Health Initiative Study really says.**

In July of 2002, headlines in every newspaper and all the major television and TV news networks spread the word that menopausal hormone replacement was to be feared. While hormone replacement was terrific for everyone the week before, protecting against heart disease, osteoporosis, colon cancer, and Alzheimer's disease, now, these same hormones caused breast cancer, heart disease and stroke. The study was stopped before completion. **What happened?**

**Why was the WHI done?:** In the 1990s it was known that Estrogen replacement protected against coronary heart disease. The company that makes Premarin, an extract of pregnant mare's urine, wanted to prove that their product was heart protective so they could advertise it as such.

**What was the WHI, and who participated?** WHI was actually two studies that were to last eight years.

**Group 1:** Contained 16,000 menopausal women with an intact uterus. Half the women received **Prempro**, consisting of **Premarin** 0.625mg (horse urine estrogens) and **Provera** (synthetic imitation progesterone, a progestin). Half received a look-alike placebo. **Group 2:** Contained 8,000 women who had a prior hysterectomy. Half received Premarin alone and half placebo. No one had been taking hormones for at least three years prior to the start of either study. Neither the doctors nor the patients knew who received the real medicine. Since estrogen alone is known to promote cancer of the lining of the uterus and Provera protects against this, women with no uterus did not have to receive Provera.

**Was this group of women representative?** Since half these women would be receiving 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 **participants tended to be overweight**. In addition, because they had to be off hormones at least three years, **they tended to be older**. Only about 500 of the study women were 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 whom average ten or fifteen years younger. In addition, as a group of somewhat overweight women, they would have had higher than average rates of breast cancer, atherosclerosis and lower rates of osteoporosis.

**Why was the WHI stopped early?** In July of 2002, the code was broken for the Prempro Group 1 only. They were found to have a small, but provably higher rate of breast cancer than the placebo group. They were also found to have higher rates of heart attack and stroke than the placebo group. The Premarin Only Group 2 was still OK and that part of the study continued until 2004.

**How dangerous was the Premarin + Provera?** With 16,000 participants, small differences in active vs. 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 detectable difference. The heart attack rates were slightly higher in the Prempro takers as were strokes. Oral estrogens of all kinds tend to induce the liver to make more blood clotting factors. If a woman already has clogged arteries, a stroke was more likely in the first year of therapy.

**Were there any benefits?** Yes. The hormone takers 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 for the Prempro takers was LOWER than the all-cause mortality rates for the placebo group.** I have never seen that reported in any news reports, but it is in the original, 36 page WHI report.

**What about the Premarin only part of the study?** Their numbers looked better and the study continued another 2 1/2 years. The report on the Premarin only group was published in 2004, in the same week as the Abugrabe prison scandal story. I never saw a single report in any news media on TV, the Atlanta Journal or the New York Times. Good news is often not reported at all.

**How did those women do?** The breast cancer rates in the Premarin only group were **lower** than for the placebo group. Heart attack was essentially the same. Stroke rates were slightly higher. Osteoporosis and colon cancer were lower.

**What can we learn?** There was a small but provable difference between the Premarin only and the Premarin + Provera group. Provera seems to increase the detection or growth of breast cancer and also slightly increased heart attacks over the short time of this study.

**Provera is NOT the same as Progesterone!!** Progesterone is the natural human hormone. In addition to reducing cancer of the endometrium, the lining of the uterus, which Provera does do, real progesterone promotes bone growth, improves sleep, promotes thyroid function and probably reduces breast cancer. Provera, synthetic altered progesterone, has been known for decades to reduce bone growth, that is, it promotes osteoporosis. There is a boxed warning in the PDR. Also, Provera has been shown in dogs to increase breast cancer. This has also been known for decades.

**What about Premarin?** Premarin is a blend of many hormones derived from pregnant mares urine. 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 given human estrogens do.

**Were the news media correct?** Mostly, **NO**. The news media kept blaming the problems seen in WHI only on estrogens. WHI proved instead that **Provera** might slightly increase detection or growth of **breast cancer**, and that starting **oral estrogen** on older women who have been **off hormones for years**, increases the risk of heart attack and stroke.

**WHAT DOES WHI TEACH US?** **Starting a woman on oral Estrogens who has been off hormones for many years increases 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. It also doesn't address **younger**, peri-menopausal and early menopausal **women** who take human estrogen and progesterone instead of synthetic Provera. It doesn't address the safety of carefully monitored topical hormone cream or patches instead of oral preparations for older women. It doesn't address continuous hormone use, as opposed to starting hormones after many years off. It also doesn't show a risk for estrogen use and breast cancer.

**What about breast cancer? That's why they stopped the Prempro study.** It has been theorized for many years that it takes about a decade for a breast cancer to reach a size detectable by 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**. We really need a similar study using natural Progesterone instead of Provera. In theory, natural Progesterone should reduce the rates of breast cancer growth. Also, we don't know how controlled levels of natural estrogen compare to Premarin 0.625mg, which was given to everyone regardless of baseline levels. No hormone levels were taken on any of the women. Everyone got the same dose regardless of individual need.

**One more thing.** Most of the new hormone starts are women in their late 30s to early 50s. How long to stay on hormones is an important question. American women are living longer; many are physically more active and sexually active much later in life, than any prior generation. Breast cancer rates might be pre-programmed decades before cancer is 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 different, and are aging differently than their parents and grandparents. **I write prescriptions one at a time, for individual women, to help with their current needs. There is still much to learn. Take HRT one year at a time.**