Does Hormone Therapy Increase Risk of Breast Cancer?

Fear of Hormone Therapy Arose From the WHI Study

In 2002, the Women's Health Initiative (WHI) study claimed that hormone therapy (HT) increased the risk of breast cancer. The claim was released in a 2002 press conference before even being published in a medical journal, committing a serious breach of scientific procedure. Headlines alarmed the public and health professionals alike, causing an immediate and sharp decline in the numbers of women receiving HT.

The WHI Study was Seriously Flawed and Irresponsibly Reported

WHI findings reported by investigators and in the press were often distorted, oversimplified, or inaccurate. For example, breast cancer increase in users of HT did not reach clinical significance as defined by standard scientific method. Moreover, careful analysis of the data reveals there was not really an increase in breast cancer for the HT users in the study, but rather a lower incidence than expected in the control group (HT nonusers). An affirmation to the benefit of HT was revealed when it was recognized that some of the nonusers had a history of HT use prior to entering the study (that in itself a grievous flaw in study design), and when these subjects were removed from the data pool, the difference in breast cancer vanished. (Where was the press conference when this finding was released?) Other problems with the WHI have been detailed in the 2009 review article referenced below, *Hormone Replacement Therapy: Real Concerns and False Alarms.*

BOTTOM LINE: WHI should not have claimed an increased risk in breast cancer, because the actual data found no true increase in breast cancer between HT users and nonusers.

Benefits of Hormone Therapy

In decades before WHI, and in the 2 decades since, there have been dozens of clinical studies demonstrating the opposite of WHI's claims. Hormone therapy is associated with reduction in the development of cardiovascular disease, Alzheimer disease, osteoporosis, colon cancer, and diabetes. Hormone therapy has been shown to reduce all cause mortality, meaning those who use HT have longer lives. For most women, these benefits are most likely realized if HT is initiated within about ten years of the menopausal transition, before conditions of aging begin to develop. That's why it's important to start HT early in perimenopause.

Hormone therapy initiated at any time, from perimenopause to later years, has been shown to improve emotional health as well as sexual health and sexual satisfaction in postmenopausal women. Hormone therapy relieves symptoms related to hormonal depletion such as hot flashes, night sweats, insomnia, brain fog, depression, anxiety, fatigue, hormone withdrawal headaches, muscle atrophy, joint/muscle aches, bladder symptoms, vaginal dryness, decreased libido, and less common symptoms, such as dry eye, itchy crawly skin, burning tongue, and heart palpitations.

Risks of Hormone Therapy

Use of <u>oral</u> estrogen may slightly increase the risk of stroke or blood clots. This is not the case with use of transdermal patches, creams, or subcutaneous implants. Oral estrogen may increase risk of liver tumors or gallbladder disease. Again, not so with subcutaneous implants or transdermal delivery. Synthetic progestin, a progesterone like substance that binds to progesterone receptors (ex. Provera), have been associated with slight increase in blood clots, cardiovascular events, and breast cancer. This is not the case with bioidentical progesterone, the safety of which has been clearly demonstrated in numerous clinical trials. For women who start HT well after the menopausal transition (>10 yrs), some studies suggest HT may slightly increase risk of a cardiovascular event during the first year of use; after the first year, risk falls back to the same risk as nonusers. For the vast majority of women it will be safe to start HT any time after hormonal depletion, provided oral estrogen or synthetic progestin are avoided.

How Long Should a Woman Continue Hormone Therapy?

As soon as HT is discontinued, the body is susceptible to all the conditions and symptoms that HT had been preventing and controlling for the duration of use of HT. The North American Menopause Society (NAMS), in a 2017 position statement, noted that "hormone therapy does not need to be routinely discontinued in women older than 65…. There are no data to support routine discontinuation in women age 65 years." This position statement was endorsed by over 30 medical professional organizations.

Is Hormone Therapy Safe for Breast Cancer Survivors?

In most cases HT can be considered safe for breast cancer survivors. Of the 20 clinical studies conducted between 1980 and 2008 examining HT in breast cancer survivors, only one claimed to find an increase in breast cancer risk, and some studies found a reduced recurrence risk. Regarding the one outlier, the study was terminated early, after only 2 years, claiming increased breast cancer recurrence. Leading oncologists and other scientists immediately weighed in and found that like WHI, this study was riddled with flaws in design, interpretation, and conclusions. Also like WHI, the one outlier remains the most often quoted study regarding hormone treatment in breast cancer survivors, contributing further to the everlasting persistence of misleading messages received by women and their healthcare providers.

After WHI, research all but stopped on HT in breast cancer survivors. However, a meta-analysis of 15 studies was conducted, examining a total of 1,416 women who used HT after breast cancer treatment, compared to 1,998 controls who did not use HT after breast cancer. After an average of 3 years of hormone use, the group using HT had 10% fewer breast cancer recurrences than the group not using HT. In addition, the hormone users had a lower 7-year mortality rate from invasive breast cancer (4.5%) than for women not using HT (17.9%). By the way, most breast cancer survivors die of cardiovascular disease, which is responsible for over seven times as many deaths as breast cancer every year.

BOTTOM LINE: Withholding HT from breast cancer survivors increases their risk of cardiovascular disease, the number one killer above all cancers, accidents, and all causes of death. HT reduces all cause mortality, meaning it prolongs life.

The myth is commonly repeated that estrogen causes breast cancer, and that the more estrogen a woman is exposed to in her lifetime, the higher her risk of breast cancer. However, this belief is not supported in the medical literature, and there are studies to refute the "cumulative exposure" argument. Besides the lack of good scientific evidence supporting the estrogen myth, consider the following:

1. If estrogen were an important cause of breast cancer, we would expect rates of breast cancer to decline after menopause when estrogen levels naturally diminish. Instead, breast cancer rates increase after menopause, even for women not using HT.
2. Historically, high doses of estrogen have been effectively used to treat metastatic breast cancer (*yes, it's true*).
3. Women currently using HT when breast cancer is diagnosed have a much better prognosis than those diagnosed while not using HT.
4. During pregnancy, estrogen levels are at their highest, yet women diagnosed with breast cancer in pregnancy have a similar prognosis as non-pregnant women. Moreover, with a breast cancer diagnosis, termination of pregnancy, thus reducing excess estrogen, does not improve the prognosis.
5. Normal breast cells have receptors for estrogen, androgen, and progesterone. If these receptors are found on a breast cancer cell, it usually means the breast cancer is growing slowly enough to adopt this normal cell characteristic. In most breast cancers, estrogen receptor positive cells are not the ones proliferating, but rather the cells with no estrogen receptors are generally ones that multiply. The presence of estrogen, androgen, or progesterone receptors on a cancer cell does not mean the cancer was caused by the hormone.

Testosterone therapy is another option to control menopausal symptoms, and can be considered safe in breast cancer survivors. Testosterone has been used historically as an effective treatment for breast cancer. The practice did not cease because it didn't work (it did). However, along came the advent of pharmaceuticals for breast cancer treatment. Bioidentical testosterone, being a compound found in nature, is not patentable, and therefore would not be profitable for the pharmaceutical industry to research, develop, and market.

For those interested in medical references and more reading, much of the material above was taken from:

1. *Hormone Replacement Therapy: Real Concerns and False Alarms*. The Cancer Journal, Mar 2009. This review article highlights the history of research on HT, discusses how to distinguish important, robust findings from those that are trivial; closely examines the WHI findings on HT and breast cancer, most of which are weak or statistically insignificant; and reports research on the benefits of HT. The article lists 210 references from the medical literature – further reading indeed!
2. *Estrogen Matters.* This 2018 book takes on the controversial topic of hormone therapy. The author, Avrum Bluming, MD, a medical oncologist at USC, has spent his career devoted to studying the benefits and risks of HT, particularly for those with a history of breast cancer. Coauthor Carol Tavris, PhD, has written extensively on gender bias in healthcare and cognitive bias in scientific research.
3. *Testosterone Matters… More!* A book by Gary Donovitz, MD, Ob/Gyn and a pioneer in subcutaneous hormone therapy.

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