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Hormones and Breast Cancer

Breast cancer is the most frequently diagnosed cancer in women. A woman's risk for breast cancer increases with age. Currently, a woman has approximately a 12% chance of developing breast cancer if she lives to be 90 years old; this also means her risk of not getting breast cancer is approximately 88%. Death rates from breast cancer have decreased since 1990. There were more than 180,000 cases of invasive breast cancer diagnosed in the US in 2008 with 40,000 deaths. Breast cancer is the second leading cause of cancer deaths—lung cancer is the first. To some extent, breast cancer may be preventable.

Cancer occurs when cells divide and grow without restraint. The growth and death of cells is usually regulated; however, when normal cell regulators malfunction and cells don't die at the proper rate, they continue to divide, and cancer can develop. Breast cancer usually grows slowly. By the time a tumor is large enough to be felt as a lump, it may have been growing for 10 years and the spread of tumor cells (metastasis) may have already occurred. Therefore, screening methods such as mammography, ultrasound, MRI, or thermography, are important tools in providing early detection. In addition, preventive measures such as a healthy diet and lifestyle, nutritional supplementation, and exercise are crucial.

Knowing the risk factors for breast cancer can help you identify your specific risk. Breast cancer risk factors can be categorized as "modifiable" and "non-modifiable." Although non-modifiable risk factors cannot be altered, modifiable risk factors can be changed based on daily choices regarding diet, exercise, lifestyle habits, and stress management.

Non-modifiable risk factors for breast cancer include:

- Being female
- Advancing age
- Family history (mother, sister, or positive BRCA1 or BRCA2 gene mutation)
- Early menarche (first menstrual period)
- Late menopause
- Diethylstilbestrol (DES) use by mother

Modifiable risk factors for breast cancer include:

- Obesity
- Lack of exercise
- Hormones: conventional HRT—synthetic progestins and, possibly, synthetic estrogens, depending on duration of use; birth control pills (some studies show this, some don't); bioidentical estrogen (depending on duration of use)
- Poor diet: high animal and trans fats, low fiber intake, deficient intake of fruits and vegetables
- Breast trauma
- Late age pregnancy, never having been pregnant, lack of breast feeding
- High alcohol intake (>1 drink per day)

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- Cigarette smoking
- Working the "graveyard" shift
- Environmental toxin exposure (radiation, xenoestrogens, second hand smoke)
- Benign breast disease (fibrocystic breast changes, may or may not increase risk)

Breast cancer and hormones

Currently every 50-year-old woman has about a 2.8% chance of developing breast cancer by age 60. This translates to an absolute risk of 2.8 breast cancer cases out of 100 women.

Most studies show the overall risk of developing breast cancer is higher with the use of synthetic estrogens and synthetic progestins. That means out of 100 women age 50 using synthetic hormone replacement (according to the Women's Health Initiative data), the number who will develop breast cancer by age 60 is 3.5. What this means is that per 100 women who use synthetic estrogen and synthetic progestin (Prempro®) slightly less than one extra woman will develop breast cancer. That increase, from 2.8 to 3.5 per 100 women, represents a 25% increase in risk.

For comparison to other risk factors, some studies show obesity and high insulin levels can cause the risk for breast cancer to go up 200 to 300%.¹⁻³ In addition, some antibiotics used for more than 500 days in a lifetime, or more than 25 prescriptions over 17 years, can increase the risk by 150% to 200%.^{4,5}

When evaluating information regarding hormone use and breast cancer risk, it's imperative to determine

- what hormone is being discussed
 - synthetic estrogen versus bioidentical estradiol or estriol
 - synthetic progestins versus bioidentical progesterone
 - synthetic methyltestosterone versus bioidentical testosterone
- mode of delivery
 - oral
 - transdermal
 - topical
 - pellet
 - vaginal

as the risk varies enormously across these variables. In addition, risk varies based on the number of years of hormone use. Not enough studies have been performed using individualized dosages of compounded hormones (based on lab testing, clinical assessment, and risk factors) since most studies use uniform modes of delivery and dosages of hormones for all women. However, one recently published small study of 189 women reported no increased risk of breast cancer, blood clots, or strokes with bioidentical hormones that were prescribed based on individualized dosages (determined via blood testing and symptom control). Women in this

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study were monitored for one to three years, and most had significant improvements in menopausal symptoms.⁶

The following summary is meant to give you succinct information based on available research regarding estrogens, progestins and progesterone, and testosterone with regard to breast cancer risk.

Estrogens, especially estradiol and estrone, stimulate proliferation of both breast tissue and breast cancer cells. There is much confusion about the use of estrogen replacement therapy (ERT) and breast cancer risk; this is true for the use of bioidentical estrogens as well as synthetic forms, such as Premarin. It's helpful to review the results from three very large, well-conducted studies over the past several years—the Women's Health Initiative, the Million Women Study, and the Nurses' Health Study—to clarify the relationship between ERT and breast cancer risk.

The Women's Health Initiative study found an increased risk of breast cancer in women using the synthetic estrogen Premarin along with the synthetic progestin Provera (Prempro), but not in women using Premarin alone.⁷ The Million Women Study did show an increased risk with ERT (bioidentical and synthetic) and an even higher risk with estrogen plus synthetic progestins.⁸ Lastly, the Nurses' Health Study also found an increased risk with long-term (more than 15 years) estrogen replacement, in women who used estrogen alone.⁹

You may recall from the previous section on pellet implants that a few studies (one with 261 women, one with 508 women) have shown no increased risk of breast cancer,^{10,11} or risk of recurrence in women who've been treated for breast cancer (123 women)¹² with estradiol pellets, especially if used in combination with testosterone.¹³ Note that these studies involved small numbers of women; therefore, it cannot be concluded that there is absolutely no increased risk for breast cancer with estradiol pellets.

As stated earlier, vaginal estrogens, especially estriol, do not increase the risk for breast cancer;^{14–18} vaginal estriol also does not increase the risk for recurrence in breast cancer survivors.¹⁹ There is no accumulation of hormones or metabolites with vaginal estrogen or progesterone therapy.^{20–22}

The data is irrefutable that **synthetic progestins** (such as Provera®) do significantly increase the risk for breast cancer. However, bioidentical **progesterone** is a different molecule than synthetic progestins and has a different effect on breast cancer risk.

Progesterone deficiency (in women who don't ovulate or who don't make enough progesterone) has been shown to increase the risk for breast cancer. In one study progesterone deficient women had a 5.4 times increased risk of pre-menopausal breast cancer, and a 10 times increased risk of death from all malignant cancers.²³ Another study evaluated hormone levels in women under age 45 who developed pre-menopausal breast cancer. There was no association between serum SHBG (sex hormone binding globulin), estradiol, testosterone or androstenedione and premenopausal breast cancer risk. The only link was an inverse relationship between risk and luteal phase progesterone levels—women with the highest

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progesterone levels had the lowest risk.²⁴ The risk of developing breast cancer seems to be decreased in women with high luteal phase progesterone levels.^{25,26}

Breast cancer risk does not increase with the use of **bioidentical progesterone supplementation** (oral micronized progesterone, such as Prometrium,[®] topical progesterone cream, or intravaginal progesterone).²⁷⁻²⁹

The role of **testosterone** in breast cancer is often confusing, due to the use of synthetic, methyltestosterone versus bioidentical testosterone in many studies. In animal and human studies, testosterone supplementation does not increase breast cancer risk.^{30,31}

Testosterone inhibits the growth of breast cancer cells via the androgen receptor.³²⁻³⁶ Testosterone works by preventing breast cells from dividing and multiplying, and by inducing apoptosis (programmed cell death).³⁷⁻⁴¹ Adrenal androgens, such as DHEA and androstenedione, and testosterone counteract the way estrogen stimulates the growth of breast cancer cells.⁴²⁻⁴⁴

Some studies have found that if a woman has androgen-receptor positive breast cancer, her prognosis is better than a woman who doesn't.^{45,46} In women with breast cancer treated with anti-estrogens (such as Tamoxifen[®]), those given androgens have better outcomes.^{47,48} Interestingly, synthetic progestins may increase the risk of breast cancer by blocking the androgen receptor and negating the protective effects of testosterone on breast tissue.⁴⁹

Clinical studies have shown that testosterone given as a patch or pellet can prevent breast proliferation and decrease estrogen receptors.^{50,51} In addition, women who receive testosterone pellets have been shown to have no increased risk of breast cancer even though they were taking estrogen and synthetic progestins.⁵² In one study, testosterone pellets showed no increased risk of recurrence in breast cancer survivors.⁵³

Women with a history of breast cancer deserve to be adequately informed about each individual hormone and the risk of cancer recurrence. I recommend breast cancer survivors do not use estradiol replacement, unless safer forms of estrogen (estriol) or bioidentical testosterone pellet implants (often given along with an aromatase inhibitor to prevent conversion to estrogens) have been unsuccessful at alleviating symptoms.

Lowering your risk for breast cancer

Benjamin Franklin's famous words—*an ounce of prevention is worth a pound of cure*—are certainly applicable to all areas of health. The following recommendations have been shown to lower breast cancer risk:

- **Eat a healthy, Mediterranean-type diet.** This type of diet has been shown to significantly lower breast cancer risk.⁵⁴ A Mediterranean diet consists mainly of vegetables, fruit, whole grains, seafood, nuts, and olive oil. The standard American diet (appropriately called the "SAD" diet) consists mainly of meat, fried food,

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- potatoes, pizza, and white flour products—avoid or significantly limit eating a SAD diet.
- **Drink alcohol in moderation or not at all.** One alcoholic drink per day increases breast cancer risk by 10%, and two drinks increase the risk by 20 to 40%.⁵⁵
- **Exercise!** Sustained physical activity for 30-45 minutes, 3 to 7 times per week, has been shown to decrease the risk of breast cancer between 20 and 60%.^{56,57}
- **If feasible, have children and breast feed at a younger age.** Giving birth before age 25 and having multiple children is known to be breast protective. Most research shows that, regardless of the mother's age, breastfeeding also lowers breast cancer risk.^{58,59}
- **Maintain normal weight**—obesity can double or triple your risk for breast cancer.^{60–62}
- **Don't smoke.** Cigarettes are known carcinogens for many different types of cancer, including breast cancer.⁶³ Smoking also dramatically increases free radicals, shortens telomeres, and accelerates aging.
- **Empty your “stress bucket” daily.** Chronic, prolonged stress impairs your cell's ability to repair DNA damage, leading to an increased possibility of defective cell division and cancer formation.⁶⁴
- **Maintain a serum vitamin D level >30 ng/mL, possibly 40-70 ng/mL.** Vitamin D and sunlight exposure are breast cancer protective.⁶⁵ If you don't know your vitamin D level, consider supplementing with 1000 IU of vitamin D3 per day; this dosage has been shown to lower overall cancer risk by 60%.⁶⁶
- **Go through a yearly detox program.** Many studies have linked environmental toxins to breast cancer.⁶⁷ Yearly detoxification can enable you to minimize exposure and enhance metabolism and excretion of stored toxins. See chapter 9 for detoxification programs and books.

Some nutritional supplements may help lower your risk for breast cancer. They include:

- **Indol-3-carbinol**—200 to 600 mg per day. Indol-3-carbinol enhances estrogen metabolism and has been shown to lower breast cancer risk.⁶⁸
- **Green tea** contains EGCG (epigallocatechin gallate), which helps block vascular endothelial growth factor (VEGF), preventing formation of blood vessels that feed tumors. Green tea has also been shown to inhibit the growth of cancerous tumors, and increase their death.^{69,70} Suggested dosage is 300-1500 mg of green tea capsules per day. For breast cancer prevention, drinking three to five cups of green tea per day is recommended.

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- **Melatonin** is a potent antioxidant that inhibits breast cancer cell growth.⁷¹⁻⁷³ A high percentage of women with breast cancer have low melatonin levels.⁷⁴ As previously mentioned, women who work the "graveyard" shift have a higher risk for breast cancer; therefore, avoid working through the night to prevent disruption of this powerful hormone. If you supplement with melatonin, the recommended dosage depends on prevention (3-5 mg before bed) or breast cancer treatment (beneficial dosage may be significantly higher).
- **Fish oil**—Higher omega-3 (fish oil) to omega-6 ratio may reduce the risk of breast cancer.^{75,76} Fish oil has been shown to retard the growth of breast cancer in the laboratory, and inhibit breast cancer from developing and spreading in animal studies. Take 1,000 to 6,000 mg EPA and DHA per day.
- **Antioxidants**—especially carotenoids (such as beta-carotene, lycopene, lutein, and zeaxanthin), C, E, selenium, and zinc may lower breast cancer risk, as well as improve telomere length.^{77,78}

Understandably, many women are afraid of breast cancer—it is much too common, and is too often fatal. It's essential to remember, however, that women are ten times more likely to die of heart disease than breast cancer. Recall that decreased estrogen and testosterone production are associated with metabolic changes that increase a woman's risk for cardiovascular disease (higher total and LDL cholesterol and triglycerides, and lower HDL cholesterol). In addition, body composition changes that occur with menopause include increased total body fat, especially with accumulation around the waist, and decreased lean body mass. This increased fat to lean body mass and muscle ratio may improve with bioidentical testosterone supplementation. In addition, estrogen replacement can improve cholesterol levels and the health of blood vessels.

Other long-term problems with menopause include bone loss, increased risk of Alzheimer's, thinning skin, urinary frequency, vaginal dryness, tooth and gum disease, weight gain, sleep problems and sexual dysfunction. Considering the fact that bioidentical hormones can help with many of these symptoms and conditions, it's important to weigh your specific risks and benefits when deciding whether to supplement with bioidentical hormones.

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