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Breast Cancer Survivors and the Role of Hormone Therapy

What are the Risks?

In the United States, one out of nine women will have developed breast cancer by the time they reach their 90's. Although the incidence of breast cancer is rising, the cure rate of early-detected invasive disease (lymph nodes negative for tumor) is excellent (97%). The role of estrogen as a possible risk factor for breast cancer has and continues to be a subject of major concern. This article will try to sort out fact from fiction.

It is clear that once ovarian function has ceased, significant changes occur within a woman's body. This 'estrogen deficiency state' can affect her future risk of chronic diseases and therefore, alter the quality and the longevity of her life. Estrogen replacement therapy helps prevent the development of osteoporosis and its subsequent complications of hip fracture, wrist fracture and spinal fractures. Only estrogen therapy eliminates completely the vaso-motor symptoms of hot flashes and night sweats, and prevents the thinning of the vaginal tissue leading to vaginal dryness, painful intercourse and overactive bladder. Estrogen combined with progesterone in any form is no longer indicated for the prevention of cardiovascular disease events in women known to have existing cardiovascular disease. Its preventative role in the risk of atherosclerosis in otherwise healthy women is under current investigation.

A few definitions:

- **ERT** means '*estrogen replacement therapy*' and refers to taking estrogen without progesterone, either cyclically (usually the first 25 days of each calendar month) or continuously (daily without stopping)
- **HRT** means 'hormone replacement therapy' and refers to taking estrogen plus a progestin (synthetic) or progesterone (bio-identical). HRT is indicated when a woman has her uterus. HRT is taken either cyclically or continuously.

Hormone Therapy in Women with No Personal History of Breast Cancer

In women *without* a personal history of breast cancer there is contradictory evidence as to the risk of developing breast cancer while taking ERT or HRT. The increased risk that has been reported appears to be related more to long-term use (over 5 years) of HRT, rather than ERT. Other risk factors for developing breast cancer have been studied. The following is a summary from a re-analysis of 51 epidemiological studies of the association of HRT and breast cancer diagnosed between the ages 50 to 70. The baseline risk in women who never used HRT was 45 breast cancers/1000 women or 4.5%. The risk of breast cancer per 1000 women over a 20-year period was as follows:

▪ Never Used HRT	45/1000
▪ Used HRT for >5 years	47/1000
▪ Used HRT for >10 years	51/1000
▪ Used HRT for >15 years	57/1000
▪ Late menopause (>5 years)	59/1000
▪ Alcohol (2 drinks/day)	72/1000
▪ No daily exercise	72/1000
▪ Weight gain (over 45 lbs)	90/1000

The *Women's Health Initiative* (WHI)–Part I and the *Heart and Estrogen/Progestin Replacement Studies* (HERS I & II) were reported in the summer of 2002. Both of these studies indicated a minimal increased risk of breast cancer associated with HRT, specifically PremPro. The WHI Study included 16,608 healthy women between the ages of 50 and 79 who were followed for an average of 5.2 years. The *relative risk* of developing breast cancer in the PremPro group of women was 1.26, or 26% higher than the placebo group. In order to put this risk % into perspective it is important to understand the *absolute risk* in the study. The actual number of women who developed breast cancer in both the PremPro and the placebo groups are expressed in terms of *10,000 women/year*. In the WHI Study–Part I the number of women who developed breast cancer was reported as follows:

- Placebo Group 30 cases of breast cancer per 10,000 women/year
- PremPro Group 38 cases of breast cancer per 10,000 women/year

Therefore, the additional absolute risk of developing breast cancer in the PremPro (HRT) group was 8 cases per 10,000 women/year. In the HERS I & II articles the relative risk for breast cancer in 1383 women taking PremPro as compared to 1380 women taking a placebo for 6.8 years was 1.27 or 27% higher. The absolute risk was 39 cases in the placebo group and 49 cases in the PremPro group.

The *Women's Health Initiative* (WHI) – Part II included an additional 10,739 women who had a previous hysterectomy and were given Premarin 0.625 mg. alone (ERT). This study was reported in the spring of 2004, and the incidence of breast cancer was 23% less than the placebo group.

Hormone Therapy in Breast Cancer Survivors

When a post-menopausal woman on ERT or HRT is diagnosed with breast cancer she is routinely advised to stop her hormones, usually with no consideration or discussion of the impact from quitting. When a breast cancer survivor enters menopause, or if she is already post-menopausal, she will usually not be offered the option of hormone replacement. The reason is a long-standing concern among the medical profession that administering estrogen in any form might stimulate a recurrence of her disease. However, a double-blinded clinical trial has never been conducted to determine if, in fact, there is any increased risk of recurrence of disease in women who elect to initiate or restart ERT or HRT.

In spite of the absence of a prospective double-blind study as to the risk of estrogen use in women with a personal history of breast cancer, there are clinical studies and observations, which provide support for the consideration of estrogen replacement in appropriately selected patients:

1. When breast cancer is detected during a pregnancy, termination of the pregnancy is no longer recommended. Exposure to high levels of female hormones while pregnant has no adverse impact on either the course of the disease or the incidence of a future recurrence.
2. Previously treated breast cancer patients who become pregnant do well.
3. Pre-menopausal patients who are diagnosed with breast cancer do not have their ovaries (the source of estrogen) removed. There is an exception, if recurrent disease occurs and the tumor is estrogen receptor positive.
4. There is no evidence of an increased risk of breast cancer in women who have used oral contraceptive pills or estrogen alone (without progesterone) after the menopause.
5. Women who develop breast cancer while taking estrogen have a better outcome compared to non-users of estrogen.
6. A review of 15 studies comprising a total of 1,416 breast cancer survivors and 1,998 women without a history of breast cancer found no increase in the risk of cancer recurrence with hormone replacement therapy.

If menopausal symptoms of hot flashes or night sweats are interfering with the quality of her life, only estrogen will reliably relieve her symptoms. If vaginal dryness or painful intercourse is an issue, estrogen in the form of a vaginal tablet (Vagifem) or a vaginal ring (Femring) inserted every 3 months may be a good option as the blood levels of estrogen are not significantly elevated. If osteopenia or osteoporosis is a risk issue as determined by a bone mineral density scan (DEXA), Evista is an excellent estrogen substitute for

prevention and treatment of osteoporosis (but it does not relieve hot flashes, night sweats or vaginal dryness). For a more complete review of '*Osteoporosis: The Risks and Treatment*', visit our website: www.gunntowbincenter.com

Each woman is unique and deserves a thorough risk assessment that includes her quality of life (QOL). In the final analysis, it is the patients' right to choose whether she will initiate or continue her hormone replacement program. We view our professional responsibility to assess, educate, and counsel our patients and then to respect and support their decisions. Any decision can always be changed, and in the future further investigational data and newer alternatives will be available.

For a current review of the risks of ERT & HRT and coronary heart disease (heart attacks), stroke, breast cancer, venous blood clots, uterine (endometrial) cancer, colorectal cancer, and osteoporosis, review our updated article "*Menopause and Hormone Therapy, What We Recommend and Why*" at our website:

www.gunntowbincenter.com.

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