

## Hormones and Cancer Risk

Patients often have questions regarding hormone replacement and cancer risks. While not all cancers are influenced by hormone levels, malignancies that arise from hormone sensitive tissues often are. These hormone sensitive cancers include ovarian, endometrial, breast and prostate cancers.

One of the primary risk factors for endometrial cancer is unopposed estrogen. This relationship came to light in the years following the introduction and widespread prescription of conjugated estrogens (Premarin) to millions of women in the US, resulting in an eight-fold increase in endometrial cancer. Since 1976, Premarin, and other medications that contain estrogen are required to carry a label warning about the risk of endometrial cancer. Conventional prescribing practices have been changed to include a progestin along with estrogen for women who have not had a hysterectomy. The primary progestin prescribed to most women in this situation is medroxyprogesterone acetate (Provera), a synthetic molecule that binds to progesterone receptors in the endometrium, but does not have the same effects in the rest of the body. While Provera may reduce the risk of endometrial cancer, it has multiple side effects including an increased risk of breast cancer and cardiovascular disease.

The impact of medroxyprogesterone acetate along with conjugated estrogens was not fully understood until 2002 when one arm of the Women's Health Initiative was halted prematurely due to the increased incidence of breast cancer, heart disease and strokes in the study subjects. At this time millions of women stopped taking hormones altogether, and the information that came from this study has left many patients and their health care providers confused about hormone replacement and the potential effects.

When exploring the relationship between hormones and cancer it is important to distinguish between the various types of hormones and to look at their relationship to each other. Estrogen is a proliferative hormone, and causes growth of the endometrium, breast tissue and development of ovarian follicles. Progesterone plays an important role in supporting the differentiation and complete development of these tissues. When there is not sufficient progesterone to balance these effects of estrogen, there is an increased risk of uncontrolled growth, or cancer. This is especially true for exogenous hormones that are foreign to the body such as Premarin, but is also true for increased endogenous production. For example, women who have an early menarche or late menopause have an increased risk of breast cancer as do women who are overweight, as fat tissue is a source of estrogen. Though synthetic progestins and progesterone have similar sounding names and act on the same receptors in the body, their differences far outweigh their similarities. After the WHI report in 2002, a French study compared women using an estrogen and **progestin** combination with women who were using estrogen and **progesterone**. Researchers found a significant increase in the incidence of breast cancer with women in the progestin group and no increase in the group using progesterone when compared with controls.

### References:

***Influences of percutaneous administration of estradiol and progesterone on human breast epithelial cell cycle in vivo.*** Chang KJ, et al. *Fertil Steril* (1995) 63(4):785-91.

***Breast Cancer Risk in Relation to Different Types of Hormone Replacement Therapy in the E3N-EPIC Cohort.*** Fournier A et al. *Int J Cancer* (2005); 114(3):448-54.