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Hormonal pathology of the uterus and endometrial carcinogenesis

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The uterus is a sensitive target for steroid sex hormones, capable to modify its structure and function with promptitude and versatility. Hormone therapy is widely used as contraceptives, ovulation stimulation, treatment of postmenopausal symptoms (controversial), adjuvant therapy of benign and malignant uterine tumors. Endometrial Carcinoma (EC), is known to be associated with prolonged and unopposed (by Progesterone) Estrogen. Obesity, nulliparity, late menopause, polycystic ovarian disease and exogenous Estrogen intake without adequate Progestin opposition are the most common risk factors for EC.

Endometrial Carcinoma (EC): EC is presently the most common malignant gynecological tumor in the USA and in the industrialized world, increased by 20% over the past two decades.

EC is classified into type I and II. About 75% are Type I, mostly diagnosed in younger women, with histologically well differentiated endometrioid carcinoma, Estrogen Receptor positive, most often diagnosed in early stages of cancer, therefore amenable to treatment and resulting in low mortality. Type II is less common, affecting elderly women, frequently diagnosed in late stages, non-endometrioid, poorly differentiated, usually Estrogen Receptor negative. The prognosis of type II EC is poor as most tumors are invasive and metastatic. Type I EC patients are often infertile, overweight, with a history of Estrogen intake. Type II EC patients may first present with vaginal bleeding, are usually not overweight. It appears that Type I EC is a hormonally-related neoplasm related to estrogenic stimulation while Type II EC is a more aggressive tumor possibly arising in a non-estrogenic stimulated endometrium. Recurrence of Type I EC after surgery as a Type II EC occurs occasionally. The biological progression to a more aggressive tumor phenotype suggests an epigenetic mutation.

Tamoxifen is a non-steroidal synthetic estrogen successfully used in Breast Cancer for its antiestrogenic effect on breast tissue; on the Endometrium it has both agonist and antagonist effects. Some elderly patients develop polyps and cancer as shown by this author and team in the largest series (700 cases) published. While hormonal effects are the most common etiologic factor in EC, a possible cofactor has recently been demonstrated by this team: Human Mammary Tumor Virus (HMTV) identified in23.3%of EC containing env. gene sequence, absent in all control benign endometrial tissue.

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