

# **Hormone Replacement Therapy: Pros and Cons...Natural Alternatives** by Len Saputo, MD

## **Definition**

- Natural
- Synthetic
- ERT vs HRT

## **Reasons for using ERT**

There are two estrogen receptor types...alpha and beta, and there may be others. Alpha receptors are located in the target cell nucleus. Binding affinity to these receptors determines biological activity, but is not the only factor involved. The particular way that chemicals bind to a receptor site may be affected by other chemicals that have preferential affinities for the site. Thus, a single compound may have different activities on each of the receptors.

There are also differences in the number and kinds of ERs in different tissues.

Different ligands (chemicals binding with receptor sites) bind with receptors and force them into different biological activities that can be intermediate between those induced by agonists or antagonists. For example, there are at least three different classes of anti-estrogens. The fact that SERMs bind with receptors to create a shape different from that of another estrogen means that they will have different biological effects in different tissues. Another factor determining the biological effect of a compound is related to the fact that there is an interaction of the ligand/receptor within the cell.

Ligand receptors then bind with proteins (adaptors) that have specific effects on the target gene control region. Adaptor proteins recognize only specific configurations...and there are at least 15 different adaptors expressed in different cells. So, it is clear that “designer estrogens” are possible wherein activity is restricted to specific cell types...this opens up a wide variety of estrogen compounds that would have very specific effects in different tissues.

Some estrogens function as antagonists, and some as agonists. They do not bind at the same place and do not compete for binding sites. Thus, all estrogens cannot be considered interchangeable.

Tamoxifen is a SERM...it is an anti-estrogen in breast tissue and an agonist in bone tissue.

Raloxifene is like Tamoxifen in bone, breast, and cardiovascular tissues, but has minimal agonist activity in the uterus.

## **Early symptoms of menopause include:**

75% of women experience **hot flashes**, and they may last for as much as 40 years. 15% have severe problems with them. Symptoms are increased by hot, humid weather and certain foods such as caffeine, alcohol, and spicy foods, and stress. They are less frequent and severe in obese women. The precise etiology is unknown.

### **Insomnia**

### **Irritability**

### **Mood disturbances including depression**

### **Physical changes**

- Vaginal atrophy
- Stress incontinence
- Skin atrophy

### **Diseases**

- Osteoporosis
- Cardiovascular disease
- Dementia (Alzheimer's)
- Cancers

## **There is research supporting that estrogen exerts beneficial actions on:**

- Bone and teeth
- Brain
- Eyes
- Vasomotor
- Heart
- Breast
- Colon
- Urogenital
- Heart disease prevention
- Effect on Lp(a)
- Osteoporosis
- Prevent Alzheimer's disease

## **Reasons to not use HRT**

- Uterine cancer
- Breast cancer
- Colon cancer
- Ovarian cancer
- Hypertension
- Hypercoagulation: arterial and venous
- Fluid retention
- Not part of natural aging

## Getting through the menopause

- Exercise
- Stress reduction
- Dietary factors...soy, flax,
- Supplements

## Aging of Women

- Since 1960 the older segment of the population has been growing faster than younger age groups. There are 30 million US women now in or past the menopause.
- In 1900 women lived 48 years...today to 80 years. Menopause was at age 47, and now it is at age 51. Nearly 1/3 of life is now beyond the menopause.
- *Forever Feminine* became a concept in about 1960, and now women are demanding whatever is possible to maintain femininity and youth...

## **HRT for Prevention of Fractures. JAMA, June 13, 2001.**

Convention has dictated that estrogen prevents bone loss and fractures. This information comes from two lines of evidence:

- Observational studies. However, these studies are not science based as they compare hormone users to non-users...the users are more apt to be healthier, wealthier, and more active than non-users.
- Randomized trials have shown that estrogen prevents postmenopausal bone loss. However, changes in bone density may not reflect likelihood of non-spine fractures.

An example is that calcium and vitamin D decrease the risk of fracture despite having little or no effect on bone density. Alendronate, which reduces fracture risk in women with osteoporosis, increases bone density but does not reduce non-spine fractures in women without osteoporosis. Clinical trials using fracture rate as the outcome have documented that alendronate, risedronate, raloxifene, and calcitonin reduce fracture risk. No clinical trials have been done on estrogen. So estrogen is approved for prevention, but not treatment of osteoporosis.

Estrogen reduces the risk of fractures by 33% in younger women, but has no significant effect in women over the age of 60. Evidence supporting the efficacy of postmenopausal estrogen for preventing osteoporotic fractures is very weak...

- Biphosphonates reduce the risk of non-spine fractures only in women with osteoporosis.
- Estrogen increases the risk of thrombotic events, gallbladder disease, and breast cancer.

Women in their 50's without osteoporosis have a low risk of fracture and the benefit of long-term treatment with estrogen to prevent bone loss and fractures may not exceed the risks...

*For more information schedule a consultation with Dr. Saputo*