

Alternatives to Premarin®

ASPCA and Dr. Ray Kellosalmi, M.D

A Conversation with Ray Kellosalmi, M.D.

A medical doctor answers questions about estrogen, menopause, women's health...and horses.

What is estrogen? Where is it found?

Estrogens are hormones that control the development and function of female sexual characteristics. They also have profound effects on other body tissue and organ systems, including bones, skin, blood vessels and the brain. In mammals, estrogens are primarily produced by the ovaries. They can be found in plants, as well.

How many different kinds of estrogen are there?

Besides being found in mammals, estrogen can also be:

1. Produced from plants, most commonly soybeans or Mexican yams. These are plant-based estrogens, available only with a prescription;
2. Made synthetically in laboratories from chemicals. These are synthetic estrogens, also available only with a prescription;
3. Found in weaker concentrations in edible plants and herbs. These are called phytoestrogens.

Although strictly speaking, only prescription estrogens are used in Estrogen Replacement Therapy (ERT), phytoestrogens have also been shown to be beneficial to menopausal and post-menopausal women. Additionally, Remifemin™, an extract from the herb black cohosh that also contains non-estrogenic compounds, has proven to be beneficial in relieving symptoms such as hot flashes. Phytoestrogens can be obtained through the foods you eat, while concentrated forms are available at health food stores and some pharmacies.

What does estrogen have to do with horses?

When scientists first conducted hormone-replacement research in the 1930s, they used the estrogen from the urine of pregnant women. As this proved increasingly impractical, stallions were tried because their estrogen levels actually exceed those of pregnant women. But the intact male horses were found to be too unmanageable for the prolonged confinement required for collection. Attention then shifted to pregnant mares. Their estrogen levels were a little lower than the stallions, but their relatively docile nature made the process of urine collection- the apparatus, narrow stalls, infrequent exercise and six months out of a year in confinement- easier. Thus, in 1942, the pharmaceutical company Wyeth-Ayerst introduced Premarin® (for PREgnant MAREs' urINE). Even though it was a relatively crude mixture of estrogens, the complete absence of competition, along with aggressive marketing, ensured its success as a treatment for hot flashes.

What's the most "natural" estrogen for women?

In the mid-'50s, plant-derived estrogens began making their way into the ERT market. They match the chemistry of the most active human estrogen, called beta-estradiol. This is the form

that is truly natural to the human female and is available today through many different brands, including Estrace®, Ogen®, Ortho-Est®, Estraderm®, Vivelle®, Climara® and Estrin®.

Are there ERT drugs similar to Premarin?

More complex plant-based estrogens - the main ingredients of which are similar to those in Premarin yet contain no hormones from equine sources - are available. These include Estratab® and Menest®. The newest plant-derived estrogen in the United States is Cenestin®. Made from soybeans and yams, its nine estrogens closely mimic the formulation of Premarin, minus the host of unknown ingredients and impurities in the horse urine product. Determining which regimen is most effective depends on each woman's genetic history, lifestyle and symptoms.

Which forms of estrogen increase a woman's risk of getting breast cancer? Which don't?

A growing number of studies have shown that standard prescription estrogens (Premarin, plant-based and synthetic estrogens) can begin to raise breast cancer risk after several years of use. From their formulation and mode of action, all standard prescription estrogens could be expected to contain this downside.

One recent study found that when progestins are added to the estrogen regime- which is done to help prevent cancer of the womb- the risk of breast cancer may be higher than with estrogen alone, but the study suggests this is only true for slender women.

Selective estrogen receptor modulators (SERMS), one of a new class of bone protector drugs, appear to escape the breast cancer worry, but Evista, the first widely used drug in this class, is not effective against hot flashes. Phytoestrogens seem to be sufficiently different from standard prescription estrogens in that they do not increase breast cancer risk, but are still effective for treating hot flashes. The herb black cohosh (Remifemin™) has not been associated with an increased cancer risk.

Does ERT help keep a woman's bones strong? Does this mean that all menopausal women ought to be on ERT?

It is well established that standard prescription estrogens can protect bone. In the United States, studies supporting this benefit have been accepted by the Food and Drug Administration for Estrace, Ogen, Estraderm and Premarin. It has been shown that the dose of estrogen needed to keep bones strong is less if calcium is taken. Studies have also suggested that bone protection can be enhanced by eating a diet high in soy, exercising and refraining from alcohol, caffeine and smoking.

Relatively new on the market are other classes of drugs that benefit bone strength but do not carry the cancer risks common to estrogens. These include diphosphonates (e.g., Didronel® and Fosamax®) and selective estrogen receptor modulators, or SERMS (e.g., Evista®). Other possibilities include calcitonin, once produced from salmon but now available as a synthetic. It is also important to remember that only 25 percent of women are at risk of osteoporosis, so it would be difficult to support 100 percent of women taking ERT for bone protection alone.

Does ERT protect a woman against heart disease?

It appears that ERT increases the ratio of "good" to "bad" cholesterol. Consequently, it has been thought that this should lower the incidence of heart problems. However, the recently released Heart and Estrogen/Progestin Replacement Study (HERS) - which used the equine drug Premarin - failed to show any significant benefit. The study followed women with prior heart

disease for four years. If future studies show ERT to be beneficial in the long-term prevention of heart disease, it is likely to be true of all standard prescribed estrogens and not specific to Premarin.

What about Alzheimer's? Does ERT guard against that, too?

Studies that look at the possible protective effects of ERT in warding off Alzheimer's are not in agreement, so the final verdict is still out. Again, any benefit would likely be an estrogen class effect.

Can you explain more about phyto-estrogens and herbals?

Phytoestrogens are present in just about all plant foods. The highest concentrations are in kudzu, soy and flaxseed, with significant amounts in lentils, chickpeas and beans. Minor amounts exist in fruits, vegetables, seeds and many cereals. A new supplement in pill form called Promensil®, available at health food stores, utilizes multiple phytoestrogens from red clover to arrive at reportedly the highest concentration presently available.

Some herbs used as an alternative to ERT have been shown to contain phytoestrogens. Others appear to have different natural ingredients that mimic some of estrogen's effects on menopausal symptoms. Remifemin™, an extract from black cohosh, is the most widely used herb for ERT because of its effectiveness in treating hot flashes.

How do I know which, if any, to take? It's important to realize that lifestyle choices can make a big difference. Abstaining from smoking, caffeine, alcohol, overeating and high-meat diets, while including regular exercise, adequate calcium and more phytoestrogens could actually make taking a prescription ERT unnecessary for many women. Aerobic exercise and deep-breathing exercises have been shown to decrease hot flashes by up to 40 to 50 percent. If herbals are preferred, Remifemin™ and Promensil® are available without any added risk of cancer. Every person has a different genetic history and lifestyle, so be sure to consult with your doctor.

Dr. Kellosalmi is a practicing family physician and surgeon in Peachland, BC, Canada. He has written articles on ERT for Family Practice magazine and ASPCA Animal Watch.

FACTS ON PREMARIN®

Premarin® (including Prempac®, Prempro® and Premphase®) is made from pregnant mares' urine (PMU) by Wyeth-Ayerst Laboratories. It is the most widely prescribed drug in the United States. Sales of Premarin-based drugs reach nearly \$1 billion annually.

From 45,000 to 50,000 mares in Canada, and hundreds in the United States, are currently being used in the production of Premarin. Every fall, foals born to these mares- a by-product of the drug industry-are sent to auction. The majority end up being sold for slaughter to provide meat for markets in Japan and Europe.

For information on how to adopt or sponsor a PMU foal, contact:

ASPCA/Lucky Fund New York, NY (212) 876-7700, ext. 4650 United Pegasus Foundation
Arcadia, CA (626) 279-1306

GFW Equine Assistance Maysville, GA (706) 335-2422

E.P.O.N.A. Epping, NH 03042 (603) 679-1896

T.R.A.C.S. Westbank, BC, Canada V4T 2G3 (250) 768-4803 American Sanctuary
Association Las Vegas, NV (702) 804-8562

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