

## We Are What Our Hormones Allow Us To Be

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Friends and Patients,

Our subject this time moves to what constitutes a major fight against the accelerated process of aging: Hormones. This subject is necessarily long in its presentation.

Yes, I was going to address the Chinese Connection and will do so in the future. However, this subject seems to have come to the forefront of inquiries and appointments to the office, so let's cover it now. I apologize for the complexity, but it is what it is.

Hormones are produced by endocrine glands throughout the body from cholesterol. They are chemical messengers that circulate through the bloodstream and regulate activities throughout our bodies. Enzymes convert cholesterol into many different hormones but as hormone levels decline, we have three choices. We can do nothing, take synthetic hormones, or take *bioidentical* hormones. Taking nothing is certainly natural but the medical profession in general, has the idea that we are not meant to live as long as we are really capable of living so they encourage us to wind down the clock; for women, not too far beyond menopause.

Before the end of the 19<sup>th</sup> century, most women died before menopause. Nowadays however, women live a substantial part of their lives in menopause. Whether endocrine specialists like it or not, *Bioidentical* hormones are structurally and chemically equivalent to the hormones made by the endocrine organs. *Bioidentical* hormones do require a prescription from a physician (physician, by the way, just means healer-not MD or DO), PA or Nurse Practitioner, they really are not medicines. The natural production of a particular hormone is low because of chronological and cellular age. Male or female hormone deficiencies have been theorized to be a major cause of aging. In our mid-thirties, hormones begin to progressively decline because of many unknown and some known factors.

Many health professionals have referred to *Bioidentical* hormones as “natural” hormone replacement. Granted, the basic matter for these hormones are derived from plants but changed in a laboratory into human hormones. Some people consume soy, yams, or other plants, thinking that they are getting human estrogen from these plants. We do not have the enzymes in our bodies to convert plant hormones into human hormones. Before we had the ability to synthesize plant hormones in the laboratory, the easiest way to get hormones was from animal species, like horses. Foreign or synthetic hormones are completely different molecules than the original hormone. When these molecules act on

the hormone receptors, they do not fit properly, thus many times, producing an abnormal effect.

The reason why synthetic hormones are used so widely today is because pharmaceutical companies are still producing them, and aggressively marketing them to physicians. These companies do not produce bioidentical hormones because they did not invent them, thus they cannot patent them.

It is amazing that today, medical physicians prescribe foreign or synthetic hormones when they could prescribe the exact molecule that the human body produces. Unfortunately there are no large randomized controlled studies on bioidentical hormones. This translates to: “No way will I recognize them as safe and useful” for the standard-trained medical provider.

The three main estrogens produced by the human body are estrone (E1), estradiol (E2), and estriol (E3). Estrone accounts for 10% of the circulating estrogen in a reproductive female. Estradiol and estrone can be converted to one another in the body by enzymes. In addition to being produced by the ovary, estrone is also formed from androstenedione in fatty tissue. Androstenedione is in the androgen family of hormones like testosterone. After menopause, when the ovary stops producing estrogen, a woman's only source of endogenous estrogen comes from the peripheral conversion of androstenedione to estrone; hence estrone accounts for the majority of estrogen in a menopausal woman. Estradiol accounts for another 10% of the circulating estrogen in pre-menopausal women. Most traditional prescriptions of estrogen have either estrone or estradiol. Premarin is essentially estrone, as well as thirty other equine estrogens. Estrace and estrogen patches consist of an estradiol substance.

Estriol accounts for the remaining 80% of circulating estrogen. It is the weakest and most benign of the estrogen family. It is also the predominant estrogen in pregnancy. It is felt to be protective by counterbalancing the aggressive effects of estrone and estradiol. Some studies show it has a protective effect against breast cancer. Vegetarians and Asian women have higher levels of estriol and lower levels of breast cancer. Women with breast cancer were found to have lower levels of estriol relative to estrone and estradiol. Sisters and daughters of women with breast cancer were found to have lower than normal levels of estriol. One of the reasons why an early pregnancy is protective against breast cancer is possibly because of high estriol levels. Estriol is extremely effective in preserving the lower genital tract. As a vaginal cream it is very effective at alleviating vaginal atrophy, preventing urinary and vaginal infections, and preventing urinary incontinence. Estriol has not been shown to be protective to the heart or bones. Vitamin E can increase estriol levels. Estriol is often referred to as the forgotten estrogen because it is rarely prescribed. Although research on estriol is limited, all evidence points to its protective nature, so I believe it is a mistake not to prescribe it with the other estrogens.

Those who take supplemental estrogen should probably take either Biest or Triest. Triest is an exact ratio of the hormones in the body. It consists of 10% estrone, 10% estradiol, and 80% estriol. Biest is 20% estradiol and 80% estriol. The theory behind using Biest instead of Triest is that estrone is the most aggressive of the estrogens and menopausal women already have enough estrone in their bodies. In reality, estrone and estradiol are

readily converted to one another so whether you take one or the other, both estrone and estradiol are going to be in the body. I like to use a 50/50 balance of estradiol and estrone.

There are several ways to take estrogens; the most common way is oral administration. Swallowing a pill is very easy and oral administration improves the cholesterol profile more than other routes of administration. Oral estrogen reduces insulin-like growth factor-I (IGF-I) and increases growth hormone. The downside of oral estrogens is the “first pass liver effect”. Anything we ingest immediately goes to the liver. When the liver processes the hormones, it makes sex hormone binding globulin (SHBG). SHBG binds hormones, making them unable to perform their functions. The liver also is responsible for making clotting enzymes, and oral estrogen leads to a greater production of these enzymes. Oral estrogens increase the risk for gallbladder disease and raise triglyceride levels. Oral estrogen showed a reduction in lean body mass and an increase in fat mass, when compared with transdermal estrogen. I prefer transdermal, via creams or gels however, for administration of estrogens.

This causes the estrogen to go right into the bloodstream without the “first pass liver effect”. When the ovary produces estrogen, it immediately gets into the blood stream via the ovarian vessels. The transdermal and sublingual routes closely resembles this physiologic process. Transdermal application of estrogen does not increase the risk of gallbladder disease or raise triglyceride levels like oral administration does. Transdermal estrogen also is less of a risk factor for blood clotting because the estrogen does not initially go through the liver.

Despite what recent studies have led many physicians and women to believe, estrogen is protective to the heart. The American College of Obstetrics and Gynecology (ACOG) now recommends that women no longer take HRT for cardiovascular protection. This is based on the findings from the Women's Health Initiative (WHI) study, but only the effects of synthetic hormones on older women were studied.

More than 40 observational studies have shown that menopausal women receiving estrogen have less heart disease than menopausal women not on estrogen. We cannot just ignore the other studies. Heart disease is the leading cause of death in women and they usually do not develop heart disease until after menopause, when estrogen is deficient. In multiple studies, estrogen also has been shown to prevent atherosclerosis. It does this by lowering total cholesterol, lowering low density lipoprotein (LDL) cholesterol, raising high density lipoprotein (HDL) cholesterol, and lowering lipoprotein (a), homocysteine, and C-reactive protein (CRP). Estrogen also has direct vascular effects. It increases vascular dilatation by relaxing the smooth muscle cells within the vessel wall. Estrogen increases endothelial cell growth, increases insulin sensitivity, and decreases coagulation factors. It also decreases uptake of LDL cholesterol in the coronary arteries and inhibits the oxidation of LDL. This results in a decrease in atherosclerosis and an overall protection to the coronary arteries.

The biggest fear of women who use estrogen is breast cancer. Among women surveyed, 40% felt that the leading cause of death in women is breast cancer, where as in reality it is 4%. Whether or not estrogen causes breast cancer is still not known. Prior to the WHI study, there were more than fifty case control and cohort studies with mixed findings; thus the findings have been inconclusive. If there is an increased risk, the risk must be

small. (See the chapter on research on hormone replacement therapy.) The largest cohort study looked at 46,355 women who were evaluated for 15 years in the Breast Cancer Demonstration Project. There were 2,082 incidents of breast cancer. Women taking estrogen alone had a 1.2 fold increase in breast cancer, whereas women taking estrogen and a progestin had a 1.4 fold increase in breast cancer. Progestins (synthetic progesterone) have recently been shown to be more responsible than estrogen in the rising incidence of breast cancer. These risks are shown to decrease after stopping HRT, and are almost nonexistent five years after stopping.

Nothing is better than estrogen at preventing osteoporosis. The majority of bone loss occurs in the first five years of menopause without estrogen supplementation. Without estrogen women lose approximately 3-5% of their bone mass per year for the first five years, and then approximately 1% per year thereafter. Not only does estrogen prevent osteoporosis by reducing bone resumption, studies have shown that it helps to rebuild bone mass as well. Estrogen has also been shown to reduce the chance of a fracture in weaker bones. Menopausal women have a 15% chance of developing a hip or wrist fracture, and a 20% chance of developing a vertebral fracture.

When long-term estrogen replacement is complemented with adequate calcium intake, hip and wrist fractures are reduced by 55% and vertebral fractures are reduced by 80%. Hip fractures are so serious that approximately 20% of women hospitalized because of a hip fracture die within a year. We also forget many times that vitamin D is absolutely necessary for proper bone health, remembering that too much D can cause phosphorus problems.

Colon cancer is the third leading cause of cancer deaths in women, after lung cancer and breast cancer. The risk for developing colon cancer is reduced by 50% with estrogen use. The longer one uses estrogen, the more protection they receive. This risk reduction is maintained for approximately ten years after discontinuation of estrogen. The WHI did not see as great a result, but patients were observed for only five years. Between 1960 and 1990, mortality rates from colon cancer rose in men by 16%, whereas in women they fell by 21%. This time period is when women started using more estrogen replacement, so estrogen could account for these findings or it could also be related to the relative low amounts of vitamin D<sub>3</sub>.

Since this is such a timely topic, but can be a little complex, I will continue next time from this point, finishing points on estrogen and move on to progesterone.