**ESTROGENS: E1, E2, E3**

Estrogen is a general term used to describe one of the hormones produced in a woman’s body. Estrogens are normally produced by the ovaries from puberty through menopause. When one hears the term “estrogen” in medical dialogue, it is used to define both the natural and synthetic manufactured hormones. Primarily there are three forms of estrogen, lesser variations and sub-variations found in the woman’s body through the reproductive years. The first of these estrogens is E1 (Estrone), a “weak” estrogen produced by the ovaries and fat tissue. It is also converted from other hormones and external environment precursors. E2 (Estradiol) is the most active estrogen produced by the ovaries before menopause. E3 (Estriol) is the weakest of the three forms of estrogen and is made in the body from other estrogen. The amounts of the differing estrogens in the body vary not only over the course of the menstrual cycle, but over the years of reproductive life.

After menopause, E1 (Estrone) becomes the predominantly produced estrogen in women’s bodies from secondary hormone productive sites, even though the ovaries continue to produce small amounts of E2 (Estradiol). The adrenal glands continue to produce androstenedione which can be converted to E1 (Estrone) and E2 (Estradiol) by body fat, the muscles, and skin cells. The ovaries may continue making small amounts of T2 (Testosterone) which can also be converted to E2 (Estradiol).

Estrogens exert powerful influence in a woman’s body, including the development of her reproductive capabilities, bone formation, overall cardiovascular health, and what most people judge empirically as “feminine” characteristics. Estrogens are dispersed in the body through the blood stream and travel to the tissue to seek out estrogen receptors. Estrogen receptors are found in the brain, breasts, heart, blood vessels, uterus, vagina, bladder, liver, bones, skin and gastrointestinal tract. Estrogen binds to these estrogen receptors, and this binding determines the effects that vary from one body part to another.

However, not all parts of the body have estrogen receptors and not all estrogen receptors are alike. For example, estrogen receptors in bone tissue do not react to estrogen the same as estrogen receptors in breast tissue. Environmental factors also influence the differing effects the receptors have in different parts of the body, but there is limited knowledge of these factors and their results. Since estrogen plays such an important role in numerous body tissues and their functions in a woman’s body, the results of lower estrogen levels can manifest themselves in negative ways. Significant estrogen loss can lead to some, a few or all of the following results: the end of menses, hot flashes, night-sweats, disturbed sleep, vaginal dryness, loss of vaginal tissue elasticity, loss of sexual desire and arousal, urinary tract infections, incontinence, change in mood, depression, cognitive problems, breast changes, skin changes, bone loss (osteoporosis), and an increase in cholesterol levels. This is simply to name a few possibilities.

It has been an accepted view that because a woman’s body has had a percentage of these major estrogens at different stages throughout her fertile life, this represents a model to return to at the onset of menopausal symptoms. This is the adage “just return to those similar levels, and the body would be perfectly normal, again.” There arises a more fundamental problem with this line of thinking: the notion that all estrogens must be supplemented. A better approach to hormone replacement therapy is achieved by understanding the nature of each estrogen, and the role it plays in the functioning of the body. This understanding, coupled with blood level readings (as ordered by a physician) of a woman’s individual levels, can aid in deciding which estrogen(s) to provide to the body through hormone replacement therapy.
What are the different types of Estrogens?

There are three primary estrogens produced by the female through her fertile years. E2 (Estradiol) is the major estrogen produced by ovaries and is the “strongest” (the most effective for the least quantity dose) form. E2 (Estradiol) is instrumental in over 400 functions in the female body. The depletion of E2 (Estradiol) in the middle years helps to explain why the body goes through such dramatic changes. E2 (Estradiol) replacement may be very effective for the symptomatic relief of hot flashes, genitourinary symptoms, osteoporosis prophylaxis, psychological well-being and reduction of coronary artery disease. E1 (Estrone) is the “weakest” estrogen that is capable of a full range of estrogen effects, because it is the one that actually binds in high levels with the estrogen receptors. Actually, it binds to estrogen breast receptors by a ratio of five to one, versus the E2 (Estradiol) binding ratio of one to one.

In addition to having been made in non-menopausal women, E1 (Estrone) also can be produced by conversion from a number of precursors from the adrenal glands. However, this conversion cannot solely be relied on to produce a specific estrogen, because certain nutrients, at specific levels (and other factors,) have to be present to determine the metabolite that is produced. When the ovaries begin to fail, the circulating E2 (Estradiol) levels drop. This drop in the E2 (Estradiol) level is what the physician often measures as a serum E2 (Estradiol) concentration test to determine estrogen levels. Ruling out other causes or diseases, the drop in estrogen level may yield the detection of ovarian failure, or in other words “early menopause.”

Because hormone levels can and do fluctuate, it becomes difficult for the practitioner to issue a foolproof diagnosis of menopause. Other external factors that can cause a drop in E2 (Estradiol) level include excessive exercise, low body fat, or diminished ovarian reserves. Other benchmark hormone levels are needed to further aid the physician to rule for certainty whether the patient is experiencing post-menopause, perimenopause, pre-menopause, or possibly diseases of the endocrine glands.

Some physicians recommend the saliva testing to measure hormone levels. This is not as frequently used as blood testing, but advocates claim that it is quicker, less expensive and reliable. Unlike the blood test, the saliva method tests the levels of “free hormones” in the body. That is, the hormones that aren’t bound to protein, but instead are able to move into cells. Because about 95% or more of the blood level hormones are protein bound, the saliva test measures only the remaining 1-5%. The results from saliva testing may be markedly lower than those which could be detected from blood test results.

During the first 2-5 years of menopause, blood levels of E2 (Estradiol) drops to an average of about 25-35pg/ml. This drop continues yearly to often below 25pg/ml. Therefore, blood levels of E2 (Estradiol) below 36pg/ml is considered post-menopause, but some women with levels 40-50pg/ml may still be having a period. They also can be experiencing symptoms of low E2 (Estradiol). Since hormone levels can and do fluctuate, remember that the blood test or any test for hormone levels will be far from foolproof. The wisest choice would be to submit to being tested more than once.

Other endocrine glands also produce different hormones that have profound effects on the ovaries. It is beyond the scope of this text to discuss the many pituitaries, thyroid hormonal secretions and their effects on the ovaries and hormonal balance. However, it should be pointed out that elevation of the hormone FSH (Follicle) and LH (Luteal) hormones during and after menopause are thought to be responsible for the “hot flashes”. Laboratory reference ranges are for FSH, during the follicular phase is 19 -144ng/ml and LH, during the luteal phase is 55-214ng/ml.
E1 (Estrone) is considered a weaker form of estrogen. It is typically produced by special belly fat cells, and is a major estrogenic form found in naturally menopausal women. It is most commonly found in increased amounts in post-menopausal women. The body derives it from the hormones that are stored in the body fat. E1 (Estrone) may do the same work that E2 (Estradiol) does, but it is considered weaker in its effects. E1 (Estrone) is not directly active in tissue, but can be readily converted by most women to E2 (Estradiol) for actual use, because it is considered to be an E2 (Estradiol) precursor. The conversion can go both ways, though meaning that E1 (Estrone) can also be considered a breakdown or even a storage form of estrogen. It is sometimes considered “safer” than E2 (Estradiol) by virtue of its weakness, but since large quantities and high doses are required to get the same effect as a smaller quantity of E2 (Estradiol), other experts consider it no more or less safe than E2 (Estradiol). Some experts suspect that E1 (Estrone) may be responsible for the higher risk of breast and endometrial cancer, due to a high receptor binding rate and production in women who are obese.

E3 (Estriol) is the weakest of the three major estrogens. In fact, it is 1,000 times weaker in its effect on tissue than other estrogens. E3 (Estriol) is a metabolic waste product of E2 (Estradiol) metabolism or produced by conversion from the progesterone concentration during pregnancy. E3 (Estriol) usually is the culprit for morning sickness during pregnancy. However, it can still have some effects on a limited number of estrogen receptors. It is formed in the liver and is 8% as potent as E2 (Estradiol) and 14% as potent as E1 (Estrone). Once E3 (Estriol) is bound to an estrogen receptor, it blocks the stronger E2 (Estradiol) from acting there. Therefore, it is considered to have both estrogenic and anti-estrogenic actions. There is also some evidence that because it is so weak and blocks the stronger forms, E3 (Estriol) can be considered to have effects comparable to E2 (Estradiol) in regard to occupying as many receptors as a “need share level” of E2 (Estradiol). Yet the risk rises to the same level with E3 (Estriol), when compared to the other estrogens. One of the metabolic products of elevated E3 (Estriol) is associated with an increased risk of developing breast and cervical cancer. At other times, E3 (Estriol) can be implicated as a source of interference in lab tests for E2 (Estradiol,) as it may lead to clinical testing error.

Please note, that E3 (Estriol) is not FDA approved and pharmacies have been notified to stop using it, although it has been used widely in Europe for 50 years. Therefore, E3 (Estriol) is not going to be an effective component of hormone replacement therapy because it is not a convertible contributor to E2 (Estradiol).

Is Bio-Identical Hormone Therapy the right choice for me?

When considering using hormone replacement therapy, a myriad of questions and choices must be considered by the individual in cooperation with one’s physician. It can take some time to reach the goal of determining which estrogen and dosage is the true candidate for the body’s needs. Remember that each individual’s particular hormone needs will change over time. This is especially true in the early years of menopause. Women should not be fooled by someone insisting that this procedure, product, or hormone replacement approach is the perfect fit. When considering hormone replacement therapy, remember there are no “one size fits all” answers concerning which estrogen(s) a woman will need. The best answer is to get the hormone replacement therapy that meets the individual’s needs. Those are best determined in tandem with one’s physician.

Contact your physician to learn if our patented hormone replacement drops will meet your treatment plan that fulfills the menopausal wellness goal.