Women's Hormonal Health Assessment

Premenopausal - Luteal

Great Smokies Diagnostic Laboratory℠

63 Zillicoa Street
Asheville, NC 28801-1074

Patient: **Sample Patient**

Age: 31
Sex: F
MRN:

Order Number:

Completed:
Received:
Collected:

Precursors/Modifiers

Progesterone
Ref Range ng/mL: 1.61 – 16.85
40.00

Sex Hormone-Binding Globulin (SHBG)
Ref Range nmol/L: 39 – 208
220

Androgens

DHEA-S
Ref Range ug/dL: 39 – 307
10

Testosterone
Ref Range ng/mL: 0.11 – 1.08
0.20

Estrogen Metabolism

Estrone (E1)
Ref Range pg/mL: 14.6 – 81.8
50.0

Estradiol (E2)
Ref Range pg/mL: 34 – 299
60

Estriol (E3)
Ref Range pg/mL: 17 – 66
70

2-Hydroxyestrone
Ref Range pg/mL: 59 – 363
20

16-alpha-Hydroxyestrone
Ref Range pg/mL: 236 – 522
530

2:16-alpha-Hydroxyestrone Ratio
Ref Range: 0.40 – 1.40
0.04

Estrogen Distribution

% Estrone (E1)
Ref Range: 6 – 45
28

% Estradiol (E2)
Ref Range: 35 – 74
33

% Estriol (E3)
Ref Range: 9 – 29
39

Ratios/Indices

Progesterone/ Estradiol Ratio
Ref Range: 18.1 – 122.3
666.7

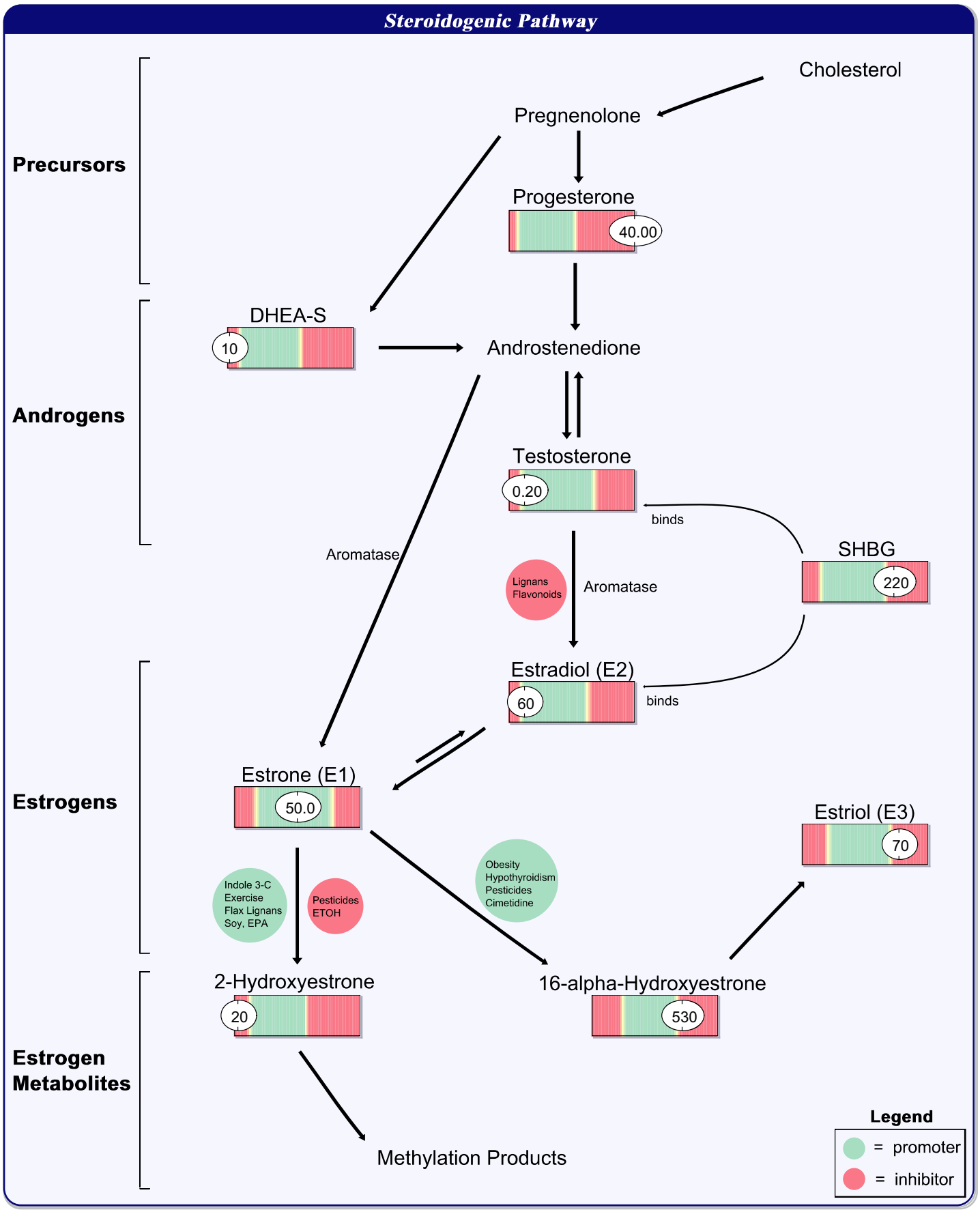
Estriol / (Estradiol + Estrone) Ratio
Ref Range: 0.10 – 0.41
0.64

Free Androgen Index
Ref Range: 0.39 – 3.57
0.32

Estrogen Metabolism Index

Estrogen Metabolism Index
Ref Range: <= 4
8

Histograms represent idealized data based upon large populations



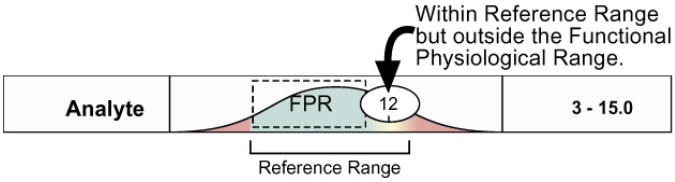
Commentary

Women's Hormonal Health Assessment (Premenopausal Patient)

All reference ranges and functional physiologic ranges for this profile were determined with luteal serum samples from women in their reproductive years.

The **Reference Range** is a statistical interval based upon those values between the 2.5th percentile and the 97.5th percentile of the reference population.

The **Functional Physiological Range (FPR),** represented by the dotted box within the reference range, depicts an optimal target interval. Values within the reference range but outside the **FPR** are not necessarily abnormal. Rather the **FPR** has been established by the Department of Medical Science, based upon current medical literature, scientific analysis of reference range study data points and clinical experience. **(See example of FPR below)**



*note ref range is marked by the red color transition on histogram

Precursors/Modifiers

Progesterone is an ovarian hormone produced by the corpus luteum. Some is also produced by the adrenal glands. It is needed for preparation of the endometrium and is responsible for the cyclic breast changes.

Elevations of this hormone may represent increased adrenal activity or persistent corpus lutea. Higher than normal progesterone may be found in some cases of PMS, particularly if depression or blood sugar fluctuations are present. Prolonged menstrual bleeding or polycystic ovary syndrome may also occur, along with a potential for elevated testosterone and estradiol levels via enzymatic conversion. In some populations, elevated progesterone, especially in the follicular/periovulatory phase, may relate to an increased risk of breast cancer, and evaluation of mammograms can be more difficult due to increased breast density under the influence of high progesterone.

Sex hormone-binding globulin (SHBG) levels were above the reference range. This protein is derived primarily from the liver, but in women also from breast and endometrial tissue. SHBG has a major regulatory effect on circulating levels of testosterone, estradiol and dihydrotestosterone. SHBG has a binding affinity in the order dihydrotestoterone >testosterone> estradiol. SHBG's relationship with thyroid hormones, particularly T3, indicates it may a useful gauge of thyroid function & response, with high SHBG possibly indicating a hyperthyroid state. High levels of SHBG may occur with excess circulating estrogens. This is generally viewed as protective since there is greater E2 binding and less stimulation of estrogen-sensitive tissues such as the breast. Dietary phytoestrogens may help raise SHBG levels in some women, while in others these compounds actually lowered SHBG.

Androgens

DHEA-S was below the reference range. DHEA is the major adrenal androgen and is derived from pregnenolone. DHEA may be enzymatically converted to estrone, the last step being dependent on the aromatase enzyme present

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in the adipose and adrenals. DHEA-S at normal levels is associated with maintenance of libido, lean body mass and balanced immunity. Low levels of DHEA-S may be related to conditions such as lupus, fatigue, decreased libido and difficulty with maintaining lean body mass and in women may be associated with an increased cortisol/DHEA-S ratio.

Testosterone is within the reference range. Testosterone in premenopausal women is derived from adrenal and ovarian activity. In adipose cells, testosterone is converted into estrone and estradiol via the aromatase enzyme. Normal levels provide protection against osteoporosis, and help maintain libido and lean muscle mass. Testosterone has strong binding with SHBG, so the relationship between these two analytes is reflected in the free androgen index.

Estrogen Metabolism

Estrone (E1) levels are within the reference range. Estrone comprises the major reversible metabolite with estradiol and is bound primarily to albumin rather than SHBG. After its production from aromatase activity on androstenedione or conversion from estradiol, E1 may be processed via either the 2 or 16-hydroxylation pathways to form the secondary metabolites. Normal levels of estrone imply adequate conversion from estradiol and from aromatase activity. Secondary metabolism should be checked via the 2-hydroxyestrone and 16alpha-hydroxyestrone levels.

Estradiol (E2) is within the reference range. Estradiol is the major estrogen secreted by the active ovaries. It may also arise from adrenal and peripheral adipose sources via enzymatic action (aromatase) on the androgens androstenedione and testosterone.

Estrogens stimulate growth and development of tissues related to female reproduction such as the breasts, vagina and uterus. Some vasodilatory and bone/ cartilage stimulating effects are evident too. E2 levels are cycle-dependent and while variable from person to person, tend to be quite consistent for one individual over time; thus single measurements are typically reflective of long-term patterns.

Estriol (E3) is above the expected range. The least potent of the estrogens, E3 levels are used clinically to gauge the viability of pregnancies. In the context of this profile, estriol is least likely to be associated with high-estrogen problems (PMS, breast cancer etc.) and is generally viewed as a ""protective"" estrogen. Conversion of the 16alpha-hydroxyestrone to estriol is important to consider. High estriol implies a potential for elevated 16alpha-hydroxyestrone, generally considered a negative estrogen metabolite. There appears to be an association of elevated estriol and elevated 16alpha- hydroxyestrone levels with patients having systemic lupus erythematosus, implying shifted metabolism in that condition.

2-Hydroxyestrone (2-OHE1) levels were below the expected range. As this metabolite represents a beneficial direction in estrogen metabolism, low levels are viewed as suboptimal for most conditions, although some literature suggests this may be of benefit in relation to osteoporosis, at least in Asian populations. Metabolic shifting away from the 2-OHE1 pathway may occur with exposure to pesticides. Low levels of this beneficial metabolite may be due to genetic/racial factors, poor exercise habits, obesity, and dietary influences such as imbalanced fatty acids and a low intake of cruciferous vegetables and lignans. Monitoring of 2-OHE1 may be of particular importance when initiating any hormone treatment (such as contraceptives or estrogen replacement therapies) as there appears to be benefits if the 2-OHE1 level and 2:16alpha-hydroxyestrone ratio increases appropriately with increased estrogen exposure.

Commentary

16alpha-Hydroxyestrone (16alpha-OHE1) is above the reference range. This finding represents a non-beneficial shift in estrogen metabolism. This metabolite may be associated with a number of problems, including lupus, breast cancer and other estrogen-dependent diseases. Paradoxically there may be some protective association between this metabolite and osteoporosis, at least in non-obese, Asian women. There are genetic/racial, dietary and exposure factors that may relate to an elevated 16alpha-OHE1 level. Obesity may contribute to high levels. In vitro cellular studies also suggest that pesticide exposure may lead to increased levels. Fortunately, there are a number of strategies that appear to minimize the influence of the 16alpha-OHE1 level: increased intake of cruciferous vegetables, normalizing body weight, exercise, omega 3 fatty acids, and flaxseed lignans. All of the latter factors act to increase production of 2-hydroxyestrone and raise the 2:16alpha-hydroxyestrone ratio.

The **2:16alpha-Hydroxyestrone ratio** is for investigational use only. The 2:16alpha-hydroxyestrone ratio appears to be an important gauge of estrogen metabolism. In general, the higher the ratio, the less association there is with estrogen-dependent diseases such as breast cancer and lupus, and the more likely the person has a beneficial hormone metabolism. A 2:16alpha-hydroxyestrone ratio in serum greater than 0.4 is generally thought to be beneficial. There are numerous modifiers of this value, most of which induce changes in the level of 2-OHE1. These include intake of indole-3-carbinols from cruciferous vegetables, flaxseed, soy, omega-3 fatty acids, and vigorous exercise. All are shown to improve the levels of 2-OHE1 in most individuals. It is to be emphasized that some individuals in clinical studies have exhibited a paradoxical response to treatments that would typically raise the 2-OHE1 levels. Therefore, follow-up testing after treatment is strongly suggested.

There may be an increased likelihood of osteoporosis with excessive 2-OHE1 production. It is important to note that the ideal upper limit of 2-OHE1 is not apparent from the existing literature. Attention to bone loss processes in the urine is perhaps warranted in individuals with a very high 2:16alpha-hydroxyestrone ratio.

Estrogen Distribution

The **Estrogen Distribution** is for investigational use only. The relative percentages of E1, E2, and E3 will vary for each individual. Many factors influence these percentages but in general a lower estrogenic effect is realized with lower E1 and E2 levels. These percentages will fluctuate according to stage of cycle, diet, exercise and various therapeutic regimens including HRT. Generally the E3 has the weakest estrogen influence. E2 is the strongest and E1 is prevalent in post-menopausal women.

Ratios/Indices

The **Progesterone: Estradiol ratio (P: E2)** is for investigational use only. The P: E2 ratio is indicative of the relative balance of these two hormones at the time of collection. This can vary significantly according to the stage of the menstrual cycle, with generally higher ratios in the luteal phase. The P: E2 ratio may show tendencies with symptoms such as PMD, anxiety, insomnia, uterine fibroids, and seizures, as well as menstrual symptoms such as dysfunctional bleeding or menorrhagia. In general, high progesterone in the follicular/periovulatory phase may be due to some residual corpus luteum activity but is not uncommon. High P: E2 ratio in the luteal phase may relate to depressive forms of PMS and carbohydrate cravings, whereas if the P: E2 ratio is relatively low in the luteal phase, it may be consistent with infertility or premenstrual irritability/anxiety.

The **Estriol/(Estradiol + Estrone)** ratio or estrogen quotient is for investigational use only. The relative strength of

Commentary

estrogenic stimulation is highest for E2 and E1 while the E3 acts as somewhat of an antagonist to the other estrogens. This hypothesis was presented in 1969 as a means to gauge the breast cancer potential for a young (<25 years of age) woman throughout her lifetime. While finding a number of proponents, the formula has remained in relative obscurity due to many variables. This calculation may be a viable determinant of overall estrogen balance in the body, and may be used for investigational purposes in the context of clinical signs, history and other laboratory values.

The **Free Androgen Index (FAI)** is for investigational use only. FAI is a computed estimate of the free testosterone present in the sample. While not representing ALL the androgenic effects present, the FAI is a reasonable means to determine the effects of androgens in women. This value is calculated by multiplying the testosterone value by a unit conversion factor, dividing by the SHBG value, and multiplying by 100. The FAI tends to increase after menopause, and may be particularly significant in relation to PCOS, hirsuitism, acne and breast cancer.

Estrogen Metabolism Index

The **Estrogen Metabolism Index** is for investigational use only. This index assigns a numeric value to the combined results of the 2-OHE1, 16alpha-OHE1 and the 2:16alpha-OHE1 ratio. We provide this value to assist the practitioner and patient in evaluating response to lifestyle, nutritional and therapeutic regimens that may modify estrogen metabolism.

One or more of the values for 2-OHE1, 16alpha-OHE1, and the 2:16alpha-OHE1 ratio fall outside of the reference range, indicating that estrogen metabolism is shifted in a non-beneficial direction. This represents a situation whereby adjustments to health, lifestyle, and supplement regimens would be expected to benefit the individual. Adjustments made to lower the Estrogen Metabolism Index may decrease the likelihood of estrogen-dependent conditions such as lupus, breast cancer and osteoporosis. Monitoring of these analytes and the ratio is suggested if significant changes to health and lifestyle factors occur or if there is a change to or addition of hormone-modifying therapies.