*Physician Copy*

GENOVA DIAGNOSTICS EUROPE

Parkgate House
356 West Barnes Lane
New Malden, Surrey KT3 6NB

63 Zillicoa Street
Asheville, NC 28801 USA

Patient:
DOB:
Sex: M
MRN:

**Order Number:**
Completed:
Received:
Collected:

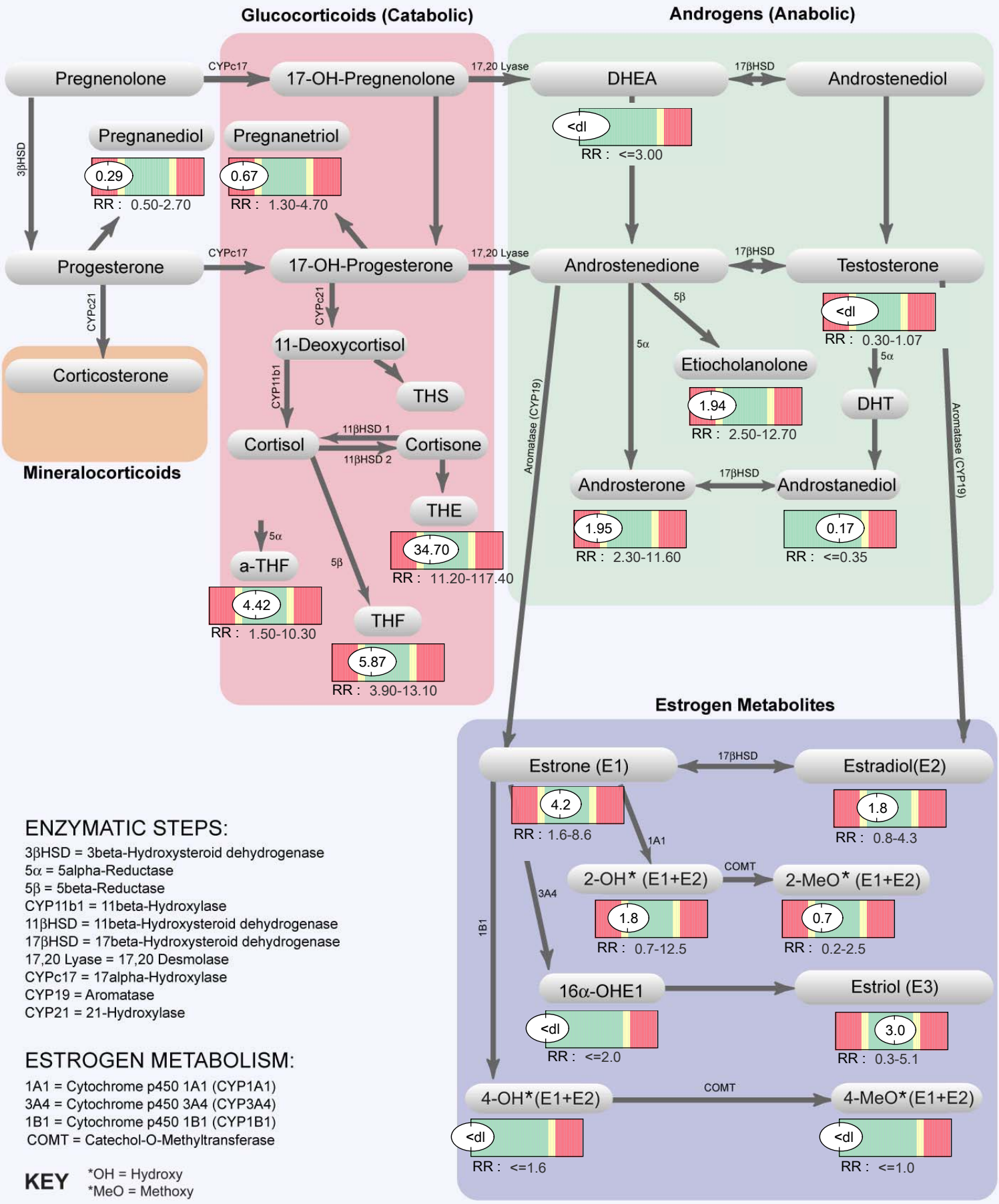
# Complete Male Hormones

Patient:

ID:

Complete Male Hormones

## Pathway At-A-Glance




## ENZYMATIC STEPS:

3βHSD = 3beta-Hydroxysteroid dehydrogenase
5α = 5alpha-Reductase
5β = 5beta-Reductase
CYP11b1 = 11beta-Hydroxylase
11βHSD = 11beta-Hydroxysteroid dehydrogenase
17βHSD = 17beta-Hydroxysteroid dehydrogenase
17,20 Lyase = 17,20 Desmolase
CYPc17 = 17alpha-Hydroxylase
CYP19 = Aromatase
CYP21 = 21-Hydroxylase

## ESTROGEN METABOLISM:

1A1 = Cytochrome p450 1A1 (CYP1A1)
3A4 = Cytochrome p450 3A4 (CYP3A4)
1B1 = Cytochrome p450 1B1 (CYP1B1)
COMT = Catechol-O-Methyltransferase

**KEY** *OH = Hydroxy
*MeO = Methoxy

Patient: ID:

Complete Male Hormones

## *Interpretation At-A-Glance*

# Anabolic/Catabolic Balance

### 17-Ketosteroids/17-Hydroxysteroids Ratio

| Anabolic/Catabolic Balance (24hr urine) | 0.1 | 0.1-1.5 |
|---|---|---|

Catabolic (Wear & Tear) ⟷ Anabolic (Growth & Healing)

## Catabolic

| 17 - Hydroxysteroids Total* | 46.0 | 21.0-154.1 micromol/24 hr |
|---|---|---|

## Anabolic

| 17 - Ketosteroids Total* | 5.8 | 12.6-35.5 micromol/24 hr |
|---|---|---|

* Total values equal the sum of all measurable parts

## Enzymatic Activity

### Estrogen Metabolism

2-OH (E1+E2) / 16α-OHE1

Lower 2/16 Ratio — >UL — Higher 2/16 Ratio

RR : 0.8-12.9

### Methylation Activity

2-OH (E1+E2) / 2-MeO (E1+E2)

More Methylation — 2.6 — Less Methylation

RR : 1.0-8.8

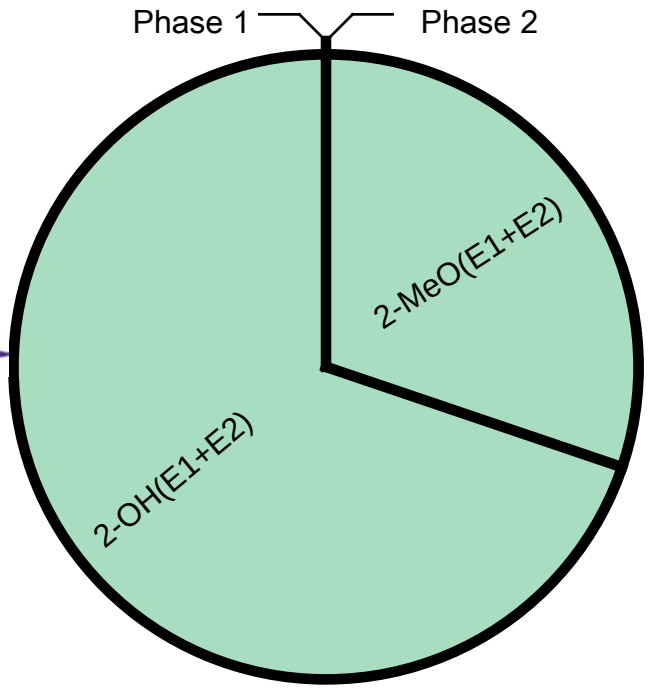
### 5α-Reductase Activity

Etiocholanolone/Androsterone (E/A) Ratio

More 5α-Reductase — 1.0 — Less 5α-Reductase

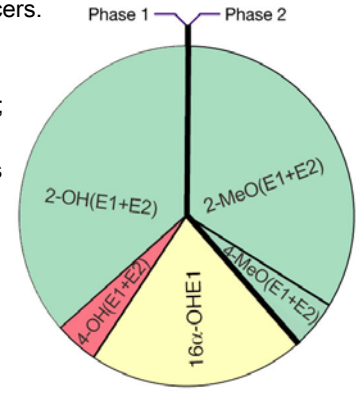
RR : 0.4-1.7

## Estrogen Metabolism




Estrogen metabolite values <DL cannot be depicted in the pie-chart.

This sample pie-chart reflects current scientific understanding of the association of specific estrogen metabolites with disease risk for hormone related cancers. Metabolites in green have been associated in the literature with decreased risk; those in red, with increased risk. 16-OHE1 (in yellow) has mixed findings, some studies showing an association and many finding no association. The dark line separates Phase 1 and Phase 2 detoxification pathways.




**Key**

# Complete Hormones (24hr)

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Parkgate House
356 West Barnes Lane
New Malden, Surrey KT3 6NB

63 Zillicoa Street
Asheville, NC 28801 USA

Patient:
DOB:
Sex: M
MRN:

**Order Number:**
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Collected:

Methodology: GC-MS and LC-MS/MS; Specimen: 24 hour urine; Results normalized to volume

## Progesterone

| | | Reference Range |
|---|---|---|
| Pregnanediol (24hr urine) | 0.29 | 0.50-2.70 micromol/24 hr |

## Androgens

### 17-Ketosteroids

| | | Reference Range |
|---|---|---|
| DHEA (24hr urine) | <dl | <= 3.00 micromol/24 hr |
| Androsterone (24hr urine) | 1.95 | 2.30-11.60 micromol/24 hr |
| Etiocholanolone (24hr urine) | 1.94 | 2.50-12.70 micromol/24 hr |
| 11-Keto-androsterone (24hr urine) | <dl | 0.10-2.40 micromol/24 hr |
| 11-Keto-etiocholanolone (24hr urine) | 0.29 | 0.40-2.10 micromol/24 hr |
| 11-Hydroxy-androsterone (24hr urine) | 0.99 | 2.00-7.50 micromol/24 hr |
| 11-Hydroxy-etiocholanolone (24hr urine) | 0.59 | 0.50-2.40 micromol/24 hr |
| 17-Ketosteroids, Total* (24hr urine) | 5.8 | 12.6-35.5 micromol/24 hr |

* Total values equal the sum of all measurable parts

| | | |
|---|---|---|
| Testosterone (24hr urine) | <dl | 0.30-1.07 micromol/24 hr |
| Androstanediol (24hr urine) | 0.17 | <= 0.35 micromol/24 hr |

## Glucocorticoids

### 17-Hydroxysteroids

| | | Reference Range |
|---|---|---|
| Pregnanetriol (24hr urine) | 0.67 | 1.30-4.70 micromol/24 hr |
| allo-Tetrahydrocortisol, a-THF (24hr urine) | 4.42 | 1.50-10.30 micromol/24 hr |
| Tetrahydrodeoxycortisol, THS (24hr urine) | 0.32 | <= 1.20 micromol/24 hr |
| Tetrahydrocortisone, THE (24hr urine) | 34.70 | 11.20-117.40 micromol/24 hr |
| Tetrahydrocortisol, THF (24hr urine) | 5.87 | 3.90-13.10 micromol/24 hr |
| 17-Hydroxysteroids, Total* (24hr urine) | 46.0 | 21.0-154.1 micromol/24 hr |

* Total values equal the sum of all measurable parts

Methodology: LC-MS/MS; Specimen: 24 hour urine; Results normalized to creatinine

## *Estrogens*

### Estrogens

| | | Reference Range |
|---|---|---|
| Estrone (E1) | 4.2 | 1.6-8.6 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | 2.0-26.2 mcg/g Creat. |
| Menopause | 1.1-26.2 mcg/g Creat. |
| Male | 1.6-8.6 mcg/g Creat. |

| | | |
|---|---|---|
| Estradiol (E2) | 1.8 | 0.8-4.3 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | 0.6-11.2 mcg/g Creat. |
| Menopause | 0.6-15.4 mcg/g Creat. |
| Male | 0.8-4.3 mcg/g Creat. |

| | | |
|---|---|---|
| Estriol (E3) | 3.0 | 0.3-5.1 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | 0.6-19.9 mcg/g Creat. |
| Menopause | 0.7-30.8 mcg/g Creat. |
| Male | 0.3-5.1 mcg/g Creat. |

### Estrogen Metabolites

| | | |
|---|---|---|
| 2-Hydroxyestrone + 2-Hydroxyestradiol [2-OH(E1+E2)] | 1.8 | 0.7-12.5 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | 1.3-36.3 mcg/g Creat. |
| Menopause | 0.9-43.8 mcg/g Creat. |
| Male | 0.7-12.5 mcg/g Creat. |

| | | |
|---|---|---|
| 16α-Hydroxyestrone (16α-OH E1) | <dl | <= 2.0 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | 0.5-8.9 mcg/g Creat. |
| Menopause | 0.4-7.7 mcg/g Creat. |
| Male | <=2.0 mcg/g Creat. |

| | | |
|---|---|---|
| 4-Hydroxyestrone+4-Hydroxyestradiol [4-OH(E1+E2)] | <dl | <= 1.6 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | <=5.9 mcg/g Creat. |
| Menopause | <=8.8 mcg/g Creat. |
| Male | <=1.6 mcg/g Creat. |

| | | |
|---|---|---|
| 2-Methoxyestrone+2-Methoxyestradiol [2MeO(E1+E2)] | 0.7 | 0.2-2.5 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | 0.2-8.6 mcg/g Creat. |
| Menopause | 0.3-5.9 mcg/g Creat. |
| Male | 0.2-2.5 mcg/g Creat. |

| | | |
|---|---|---|
| 4-Methoxyestrone+4-Methoxyestradiol [4MeO(E1+E2)] | <dl | <= 1.0 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | <=1.0 mcg/g Creat. |
| Menopause | <=1.0 mcg/g Creat. |
| Male | <=1.0 mcg/g Creat. |

## Estrogens

### Ratios

| | | Reference Range |
|---|---|---|
| Anabolic/Catabolic Balance (24hr urine) | 0.1 | 0.1-1.5 |
| E/A: 5β/5α Ratio (24hr urine) | 1.0 | 0.4-1.7 |
| 2-OH(E1+E2) / 16α-OHE1 | >UL | 0.8-12.9 |

| | Reference Ranges |
|---|---|
| Premenopause | 0.3-13.7 |
| Menopause | 0.3-15.1 |
| Male | 0.8-12.9 |

| | | |
|---|---|---|
| 2-OH(E1+E2) / 2-MeO(E1+E2) | 2.6 | 1.0-8.8 |

| | Reference Ranges |
|---|---|
| Premenopause | 1.6-10.7 |
| Menopause | 0.4-11.6 |
| Male | 1.0-8.8 |

## Lab Comments

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. Unless otherwise noted with ◆, the assay has not been cleared by the U.S. Food and Drug Administration.

<dl = Unable to calculate results due to less than detectable levels of analyte.

Please note the reference range for Tetrahydrocortisone (THE), Total 17-OH Corticosteroids, and the Anabolic/Catabolic Balance have been updated.

Please note analysis of estrogens and estrogen metabolites is now performed using LC/MS/MS. The reference ranges for these biomarkers have been updated.

## *Commentary*

Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or treatment recommendations. Diagnosis and treatment decisions are the responsibility of the practitioner.

### Pregnanediol

Progesterone rapidly metabolizes by the time it reaches the urine, and its direct metabolite, pregnanediol, is a reflection of circulating progesterone concentrations. Progesterone is important for normal reproductive and menstrual function, and influences the health of bone, blood vessels, heart, brain, skin, and many other tissues and organs. As a precursor, progesterone is used by the body to make other steroid hormones, including DHEA, cortisol, estrogen and testosterone. In addition, progesterone plays an important role in mood, blood sugar balance, libido, and thyroid function, as well as adrenal gland health. Progesterone is primarily produced in the ovaries in premenopausal women and in the adrenal cortex in postmenopausal women. Although progesterone is found in both women and men, the physiologic role in men is poorly understood.

•In women, lower levels of progesterone have been associated with dysfunctional uterine bleeding, and may play a role in osteoporosis and impaired neurological function. Excessive amounts can result in problems such as dysglycemia, alopecia, acne, and breast tenderness.

•The clinical significance of elevated or low levels in men is poorly understood. Low progesterone levels may be involved in male infertility. Increased levels of progesterone have been found in states of stress and anxiety in men and women: this may relate to its sedative or stress-countering effects.

### Glucocorticoids & Cortisol

The glucocorticoids, or 17-hydroxysteroids, are cortisol-related metabolites that have traditionally been assessed to provide insight into catabolic activity in the body. Assessment of total 17-hydroxysteroid metabolites gives a better sense of overall glucocorticoid production compared to cortisol alone. Cortisol (optional add-on) is the main glucocorticoid produced by the adrenal cortex and plays a central role in glucose metabolism and the body's response to stress. In addition, cortisol has significant effects on protein, carbohydrate, and lipid metabolism, muscle tissue maintenance, myocardial integrity, and suppression of inflammatory responses.

•An elevated 17-hydroxysteroids total and/or cortisol total may be caused by stress, strenuous exercise, inflammation, hypoglycemia, insulin resistance, hypothyroidism, or licorice ingestion. Indicated therapeutics include stress management, adequate sleep, reducing stimulants such as caffeine, reducing high glycemic load foods, as well as considering adrenal nutritional and botanical (adaptogenic) support.

•A low 17-hydroxysteroids total and/or cortisol may be a result of endogenous suppression from exogenous glucocorticoid supplementation or adrenal or pituitary insufficiency. Treatment might include stress management, managing inflammation, infections, and hypoglycemia, as well as considering nutritional and botanical (adaptogenic) support for the adrenal glands.

### Cortisol

Cortisol (optional add-on) is the main glucocorticoid produced by the adrenal cortex and plays a central role in glucose metabolism and the body's response to stress. In addition, cortisol has significant effects on protein, carbohydrate, and lipid metabolism, muscle tissue maintenance, myocardial integrity, and suppression of inflammatory responses.

•An elevated cortisol total may be caused by stress, strenuous exercise, inflammation, hypoglycemia, insulin resistance, hypothyroidism, and/or licorice ingestion. Indicated therapeutics include stress management, adequate sleep, reducing stimulants such as caffeine, reducing high glycemic load foods, as well as considering adrenal nutritional and botanical (adaptogenic) support.

•A low cortisol may be a result of endogenous suppression from exogenous glucocorticoid supplementation or

## Commentary

adrenal or pituitary insufficiency. Treatment might include stress management, managing inflammation, infections, as well as considering nutritional and botanical (adaptogenic) support for the adrenal glands.

### Androgens (Testosterone and DHEA)

Testosterone and DHEA are metabolized into what are collectively known as the 17-ketosteroids. Testosterone and DHEA are parent hormones that are rapidly metabolized by the time they reach the urine, therefore assessing total 17-ketosteroids in addition to testosterone and/or DHEA levels gives a better sense of overall androgen production. Testosterone is an androgenic sex steroid/hormone that helps maintain libido, influences muscle mass and weight loss, and plays a role in the production of several other hormones. During the aging process, testosterone levels gradually decline in both sexes, which can lead to loss of bone density. Testosterone concentrations tend to be higher in men versus women.

•In women, imbalances of testosterone have been associated with various forms of coronary heart disease and cardiovascular events, including myocardial infarction in postmenopausal women. Excessive amounts are associated with PCOS, acne, oily skin, and hirsutism.

•In men, lower levels of testosterone are associated with aortic, peripheral vascular, and cardiovascular disease in middle-aged and older men. In some but not all studies, lower levels of testosterone predict increased incidence of cardiovascular events and mortality. Additionally, elevated testosterone can be associated with CVD risk. Men with excessive testosterone may exhibit aggressive behavior or increased irritability, and hair loss (scalp).

•In men and women, low levels of testosterone have been associated with lower coital frequency and loss of sexual desire in men and women. Low levels are also associated with reduced stamina and lean muscle mass, anxiety, depression and cognitive decline in both men and women.

### Dehydroepiandrosterone (DHEA)

Dehydroepiandrosterone (DHEA) is a hormone produced by both the adrenal gland and brain. DHEA leads to the production of androgens and estrogens. DHEA levels in the body begin to decrease after age 30. Levels decrease more quickly in women.

•Lower levels of DHEA have been associated with immune dysregulation, heart disease, osteoporosis, insomnia, depression, inflammation and decreased libido. Corticosteroids, birth control pills, and some medications used to treat psychiatric disorders may reduce DHEA levels.

•High levels are usually due to supplementation and can cause side effects related to DHEA’s influence on downstream androgens and estrogen production. Symptoms mimic those of elevated testosterone and/or estrogens.

### Etiocholanolone/Androsterone (E/A) Ratio

The Etiocholanolone/Androsterone (E/A) Ratio assesses androgen metabolism by comparing the enzymatic activity of 5β-reductase/5α-reductase. Etiocholanolone is produced via the 5β-reductase pathway, and androsterone is produced via the 5α-reductase pathway. The ratio aids in assessing dihydrotestosterone (DHT) production from testosterone. While DHT is measurable in serum, it is not measurable in urine. However, biomarkers that provide insight into 5α-reductase activity in the urine give an approximation of the level of production of DHT in the body.

•A low E/A ratio indicates more 5a-reductase activity and greater production of DHT from testosterone. Symptoms in a male might include BPH and lower urinary tract symptoms. Symptoms in a female might include hirsutism, acne, infertility, polycystic ovary syndrome (PCOS), and oily skin. Both men and women may experience androgenic alopecia as a result of higher DHT production. Therapeutic strategies for 5α-reductase inhibition may be considered, and include pharmaceutical intervention with 5α-reductase inhibitors (such as Finasteride) or botanical inhibitors (such as saw palmetto).

## 3 Commentary

•An elevated E/A ratio indicates less 5α-reductase activity, which is not thought to be a clinically relevant finding – though physiologically induced 5α-reductase blockade states via pharmaceuticals (such as Finasteride) may be associated with side effects such as impotence, decreased libido, depression and anxiety in men. Robust inhibition of 5α-reductase activity decreases the production of DHT, resulting in increased levels of testosterone - and subsequently estradiol (via aromatization pathways). As a result of increased substrate flow through the aromatization pathways, gynecomastia has also been described in men.

### Anabolic/Catabolic Balance (A/C Balance)

The Anabolic/Catabolic Balance refers to the balance between "growth and healing" (anabolic) and "wear and tear" (catabolic) activity in the body. Both anabolic and catabolic metabolism are essential to health. For example, a healthy body requires sufficient time and androgens to rebuild/repair cells and tissue (anabolism), but also requires sufficient corticosteroids to respond to stressors and to discharge cellular debris/toxins (catabolism). While there are no established set of biomarkers in the urine to assess the balance between anabolic and catabolic activity, combinations of various 17-ketosteroids and 17-hydroysteroids have been described to assess this balance in the peer-reviewed literature. The "Anabolic/Catabolic Balance" has traditionally been described to serve as an indication of imbalances between these opposing metabolic actions in a given patient.
•An elevated A/C ratio indicates a preponderance of anabolic activity, and may be associated with conditions consistent with androgen excess including metabolic syndrome, acne, PCOS, prostatism, and male pattern baldness.
•A low A/C ratio indicates a preponderance of catabolic activity, and may be associated with aging, insomnia, hypoxia, chronic stress, chronic illness, hyperadrenalism, hypoandrogenism, hyperglycemia, and diabetes. A prolonged catabolic shift may result in poor healing, cognitive decline, muscle and tissue degeneration, cardiovascular disease, pro-inflammatory immune dysregulation, anxiety, and depression.
•The clinical approach to managing a high or low A/C balance involves ruling out or treating associated underlying conditions. Supportive therapeutics include stress management, adequate sleep, reducing stimulants such as caffeine, reducing high glycemic load foods, and adrenal nutritional and botanical support.

### Estrogens

Estrogens play a critical role in female sexual development, menstrual function, protein synthesis, cardiovascular function, bone formation and remodeling, cognitive function, emotional balance and other important health factors. The estrogenic potency of estradiol (E2) is 12 times that of estrone (E1) and 80 times that of estriol (E3). Estradiol (E2) is the primary estrogen in premenopausal women. Estrone (E1) is the second most potent estrogen compared to estradiol. After menopause, estrone (E1) becomes the primary estrogen as the ovary loses its ability to manufacture estradiol, and it is synthesized in the adrenal glands and fat cells. Estriol (E3) is considered to be the mildest and briefest-acting of the three estrogens. Estrogen metabolism and synthesis in men appears to remain relatively stable across the life course.
•In women, lower levels of estrogens have been associated with a variety of clinical symptoms: peri/menopausal symptoms (vasomotor symptoms; mood and memory alterations; diminished skin tone, atrophic vaginitis – a condition associated with decreased vaginal lubrication and thinner vaginal epithelial lining); altered lipid metabolism; accelerated rate of bone loss. Excessive estrogen levels have been associated with increased risk of some hormone-dependent cancers.
•In men, low levels of estrogen may be associated with decreased bone density, cognitive decline and cardiovascular disease. Excessive estradiol levels have been associated with greater risk of stroke and cardiovascular disease, as well as BPH, gynecomastia, decreased sexual function and weight gain. Men who have a higher body fat percentage may also have increased estrogen levels, as increased aromatization of testosterone to estradiol can occur in adipose tissue.

## Commentary

### Estrogen Metabolites

Estrogens are metabolized by two main pathways: (1) formation of the catechol estrogens 2-hydroxyestrone/estradiol (2-OHE1/E2) via the CYP1A1 pathway and 4-hydroxyestrone/estradiol (4-OHE1/E2) via the CYP1B1 pathway; and (2) formation of 16α-hydroxyestrone (16α-OHE1) via the CYP3A4 pathway.

### 2/16 Ratio and Hydroxylation pathways

2/16 Ratio - The clinical utility of the ratio of 2-hydroxyestrone (2-OHE1) to 16α-hydroxyestrone (16α-OHE1) – the 2/16 ratio or Estrogen Metabolite Ratio (EMR) – historically reported lower 2/16 ratio levels among breast cancer cases compared to controls (particularly in premenopausal women). Recent studies have been mixed: there appears to be no strong evidence in the literature that a higher urinary 2/16 ratio protects postmenopausal women from breast cancer, and only weak evidence of a protective effect in premenopausal women.

Higher 2-OH (E1+E2)/16α –OH ratios in males have been associated with reduced risk of prostate cancer.

**2-OH (E1+E2)** - While traditional 2/16 ratio clinical utility may not be as robust as previously thought, a majority of findings indicate that metabolism of parent estrogens through 2-hydroxylation (independent of any relationship to 16α-OHE1) may be considered as a benign or even protective pathway. (Of note: one study found increased breast cancer risk with higher 2-OH levels, but only in a small subgroup of ER-/PR- cases.)

Studies suggest that women with predominant metabolism through the 2-hydroxyl pathway have accelerated postmenopausal bone loss and lower BMD compared to those with predominant 16α-hydroxylation who appear to have reduced risk of bone loss. Increased 2- hydroxylation has been noted in women with a positive family history of osteoporosis suggesting that increased risk of osteoporosis in those with a family history may be related to inherited differences in estrogen metabolism.

**16α-OH** - Recent findings in the peer-reviewed literature are mixed, with some studies finding an association with increased risk (cancers of the cervix, breast, endometrium, and head and neck, as well as in people with tumors related to the human papilloma virus), but many finding no significant association.

**4-OH (E1+E2)** - Research focus is shifting toward 4-hydroxyestrone which is thought to have greater estrogenic and genotoxic potential than either 2-hydroxyestrone or 16α-hydroxyestrone. Metabolites of 4-hydroxyestrone may induce DNA damage through redox cycling, which generates reactive oxygen species and form reactive semiquinones and quinones capable of forming adducts with glutathione and purines in DNA. However, studies demonstrate that when DNA is incubated with quinones in the presence of an antioxidant, the formation of the DNA adducts is reduced.
•In patients with a low 2-hydroxylation result, metabolism may be shifted toward this pathway by dietary interventions rich in cruciferous vegetables; flax; soy; rosemary and turmeric; exercise that increases lean body mass and decreases BMI; and supplementation with broccoli derivatives indole-3-carbinol (I3C) or diindolylmethane (DIM), as well as omega-3 fatty acids, and vitamins B6, B12 and folate.
•Support of antioxidant activity appears to be a reasonable proactive step for reducing risk of hormone-related disease. Several natural compounds have exhibited the ability to minimize DNA adduct formation/damage including, resveratrol, N-acetylcysteine, lipoic acid, and melatonin. Cruciferous and allium vegetables also demonstrate the ability to induce glutathione S-transferases.

### Methoxylated Estrogens

## *Commentary*

**2-OH(E1+E2)/2-MeO(E1+E2) ratio** - There is evidence that methoxylated estrogens, especially the 2-pathway methoxylated estrogens (E1 and E2), are associated with decreased breast cancer risk; 2-MeOE2, produced from 2-OHE2, has been described to have anti-proliferative, antiangiogenic, and pro-apoptotic activity in multiple types of cancer. A high 2-OH (E1+E2)/2-MeO (E1+E2) ratio may indicate less methylation activity and/or a robust amount of hydroxylated compared to methylated analytes.

**4-MeO (E1+E2)** - Most recent studies also find an increased breast cancer risk associated with the ratio of 4-pathway catechols to 4-pathway methylated catechols. This increased risk has been seen in cases with less extensive methylation of potentially genotoxic 4-hydroxylation pathway catechols; thus, increased relative levels of 4-methoxyestrogens would be considered favorable.

Catechol-O-methyltransferase (COMT) is the enzyme responsible for catalyzing methylation of catechol estrogens to methoxy estrogens, which simultaneously lowers the potential for DNA damage and increases the concentration of 2-methoxyestradiol (2-MeOE2), an anti-proliferative metabolite. Genetic polymorphisms (SNPs) may impact COMT catalytic activity, and as a result, may be associated with significant differences in catechol estrogen and methoxy estrogen levels – thereby contributing to differences in risk for estrogen-mediated breast cancer amongst individuals.
•Numerous factors support methylation including S-Adenosyl-l-Methionine (SAMe); methionine; magnesium; vitamins B2, B6 and B 12; folate (or folinic acid, 5-formyl THF or 5-methyltetrahydrofolate); trimethylglycine (TMG); glutathione; and stress management strategies that reduce catecholamine production.

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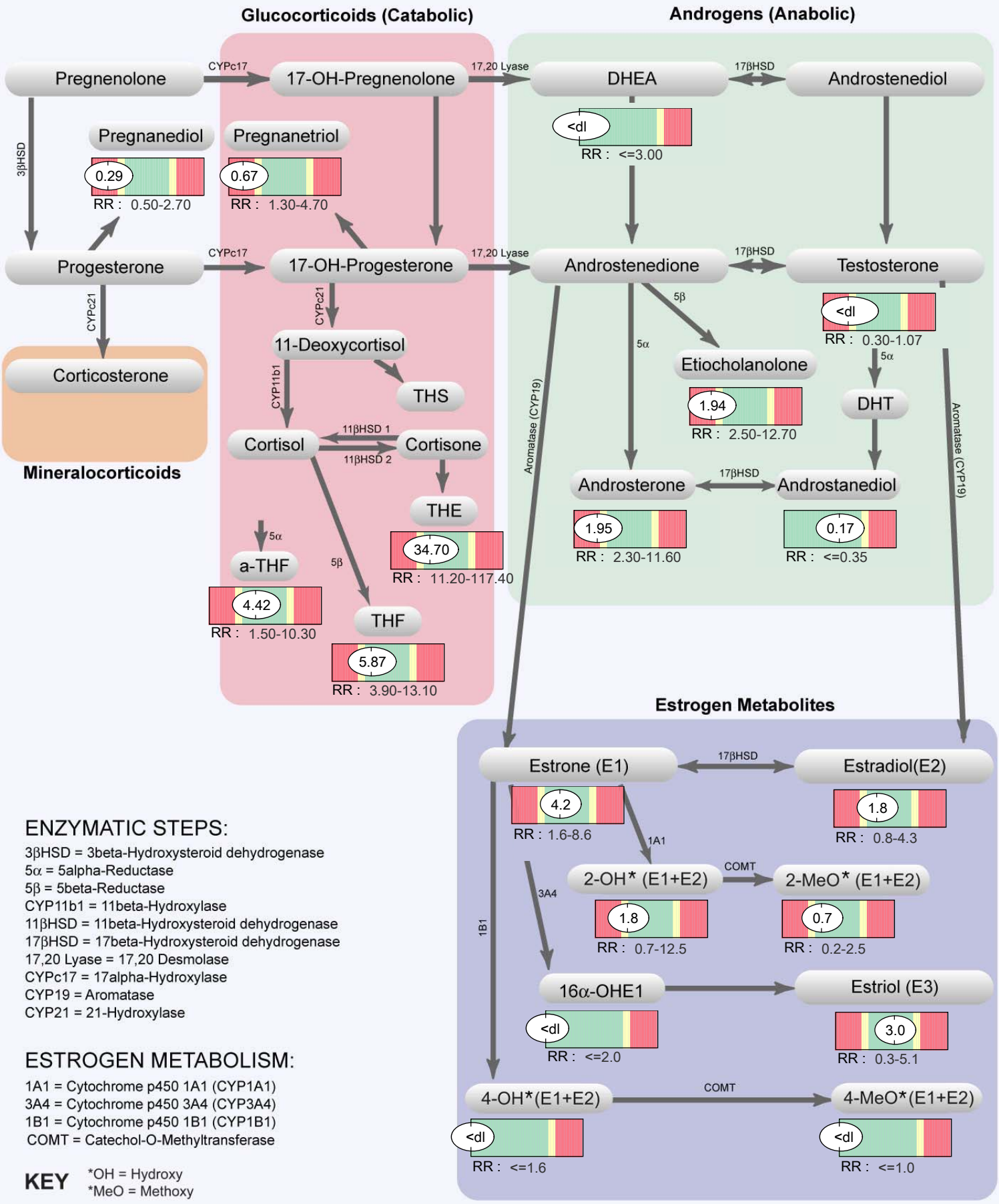
## Pathway At-A-Glance




## ENZYMATIC STEPS:

3βHSD = 3beta-Hydroxysteroid dehydrogenase
5α = 5alpha-Reductase
5β = 5beta-Reductase
CYP11b1 = 11beta-Hydroxylase
11βHSD = 11beta-Hydroxysteroid dehydrogenase
17βHSD = 17beta-Hydroxysteroid dehydrogenase
17,20 Lyase = 17,20 Desmolase
CYPc17 = 17alpha-Hydroxylase
CYP19 = Aromatase
CYP21 = 21-Hydroxylase

## ESTROGEN METABOLISM:

1A1 = Cytochrome p450 1A1 (CYP1A1)
3A4 = Cytochrome p450 3A4 (CYP3A4)
1B1 = Cytochrome p450 1B1 (CYP1B1)
COMT = Catechol-O-Methyltransferase

**KEY** *OH = Hydroxy
*MeO = Methoxy

Patient: ID:

Complete Male Hormones

## *Interpretation At-A-Glance*

# Anabolic/Catabolic Balance

### 17-Ketosteroids/17-Hydroxysteroids Ratio

| Anabolic/Catabolic Balance (24hr urine) | 0.1 | 0.1-1.5 |
|---|---|---|

Catabolic (Wear & Tear) ⟷ Anabolic (Growth & Healing)

## Catabolic

| 17 - Hydroxysteroids Total* | 46.0 | 21.0-154.1 micromol/24 hr |
|---|---|---|

## Anabolic

| 17 - Ketosteroids Total* | 5.8 | 12.6-35.5 micromol/24 hr |
|---|---|---|

* Total values equal the sum of all measurable parts

## Enzymatic Activity

### Estrogen Metabolism

2-OH (E1+E2) / 16α-OHE1

Lower 2/16 Ratio — >UL — Higher 2/16 Ratio

RR : 0.8-12.9

### Methylation Activity

2-OH (E1+E2) / 2-MeO (E1+E2)

More Methylation — 2.6 — Less Methylation

RR : 1.0-8.8

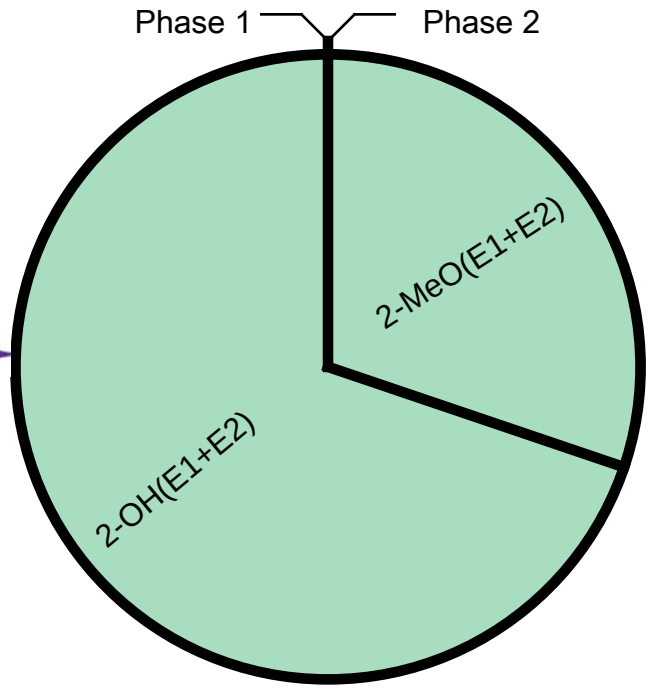
### 5α-Reductase Activity

Etiocholanolone/Androsterone (E/A) Ratio

More 5α-Reductase — 1.0 — Less 5α-Reductase

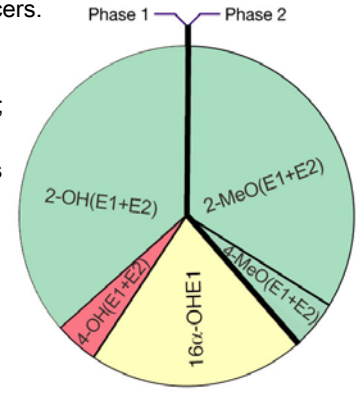
RR : 0.4-1.7

## Estrogen Metabolism




Estrogen metabolite values <DL cannot be depicted in the pie-chart.

This sample pie-chart reflects current scientific understanding of the association of specific estrogen metabolites with disease risk for hormone related cancers. Metabolites in green have been associated in the literature with decreased risk; those in red, with increased risk. 16-OHE1 (in yellow) has mixed findings, some studies showing an association and many finding no association. The dark line separates Phase 1 and Phase 2 detoxification pathways.




**Key**

# Complete Hormones (24hr)

GENOVA DIAGNOSTICS EUROPE

Parkgate House
356 West Barnes Lane
New Malden, Surrey KT3 6NB

63 Zillicoa Street
Asheville, NC 28801 USA

Patient:
DOB:
Sex: M
MRN:

**Order Number:**

Completed:
Received:
Collected:

Methodology: GC-MS and LC-MS/MS; Specimen: 24 hour urine; Results normalized to volume

## Progesterone

| | | Reference Range |
|---|---|---|
| Pregnanediol (24hr urine) | 0.29 | 0.50-2.70 micromol/24 hr |

## Androgens

### 17-Ketosteroids

| | | Reference Range |
|---|---|---|
| DHEA (24hr urine) | <dl | <= 3.00 micromol/24 hr |
| Androsterone (24hr urine) | 1.95 | 2.30-11.60 micromol/24 hr |
| Etiocholanolone (24hr urine) | 1.94 | 2.50-12.70 micromol/24 hr |
| 11-Keto-androsterone (24hr urine) | <dl | 0.10-2.40 micromol/24 hr |
| 11-Keto-etiocholanolone (24hr urine) | 0.29 | 0.40-2.10 micromol/24 hr |
| 11-Hydroxy-androsterone (24hr urine) | 0.99 | 2.00-7.50 micromol/24 hr |
| 11-Hydroxy-etiocholanolone (24hr urine) | 0.59 | 0.50-2.40 micromol/24 hr |
| 17-Ketosteroids, Total* (24hr urine) | 5.8 | 12.6-35.5 micromol/24 hr |

* Total values equal the sum of all measurable parts

| | | |
|---|---|---|
| Testosterone (24hr urine) | <dl | 0.30-1.07 micromol/24 hr |
| Androstanediol (24hr urine) | 0.17 | <= 0.35 micromol/24 hr |

## Glucocorticoids

### 17-Hydroxysteroids

| | | Reference Range |
|---|---|---|
| Pregnanetriol (24hr urine) | 0.67 | 1.30-4.70 micromol/24 hr |
| allo-Tetrahydrocortisol, a-THF (24hr urine) | 4.42 | 1.50-10.30 micromol/24 hr |
| Tetrahydrodeoxycortisol, THS (24hr urine) | 0.32 | <= 1.20 micromol/24 hr |
| Tetrahydrocortisone, THE (24hr urine) | 34.70 | 11.20-117.40 micromol/24 hr |
| Tetrahydrocortisol, THF (24hr urine) | 5.87 | 3.90-13.10 micromol/24 hr |
| 17-Hydroxysteroids, Total* (24hr urine) | 46.0 | 21.0-154.1 micromol/24 hr |

* Total values equal the sum of all measurable parts

Methodology: LC-MS/MS; Specimen: 24 hour urine; Results normalized to creatinine

## *Estrogens*

### Estrogens

| | | Reference Range |
|---|---|---|
| Estrone (E1) | 4.2 | 1.6-8.6 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | 2.0-26.2 mcg/g Creat. |
| Menopause | 1.1-26.2 mcg/g Creat. |
| Male | 1.6-8.6 mcg/g Creat. |

| | | |
|---|---|---|
| Estradiol (E2) | 1.8 | 0.8-4.3 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | 0.6-11.2 mcg/g Creat. |
| Menopause | 0.6-15.4 mcg/g Creat. |
| Male | 0.8-4.3 mcg/g Creat. |

| | | |
|---|---|---|
| Estriol (E3) | 3.0 | 0.3-5.1 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | 0.6-19.9 mcg/g Creat. |
| Menopause | 0.7-30.8 mcg/g Creat. |
| Male | 0.3-5.1 mcg/g Creat. |

### Estrogen Metabolites

| | | |
|---|---|---|
| 2-Hydroxyestrone + 2-Hydroxyestradiol [2-OH(E1+E2)] | 1.8 | 0.7-12.5 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | 1.3-36.3 mcg/g Creat. |
| Menopause | 0.9-43.8 mcg/g Creat. |
| Male | 0.7-12.5 mcg/g Creat. |

| | | |
|---|---|---|
| 16α-Hydroxyestrone (16α-OH E1) | <dl | <= 2.0 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | 0.5-8.9 mcg/g Creat. |
| Menopause | 0.4-7.7 mcg/g Creat. |
| Male | <=2.0 mcg/g Creat. |

| | | |
|---|---|---|
| 4-Hydroxyestrone+4-Hydroxyestradiol [4-OH(E1+E2)] | <dl | <= 1.6 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | <=5.9 mcg/g Creat. |
| Menopause | <=8.8 mcg/g Creat. |
| Male | <=1.6 mcg/g Creat. |

| | | |
|---|---|---|
| 2-Methoxyestrone+2-Methoxyestradiol [2MeO(E1+E2)] | 0.7 | 0.2-2.5 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | 0.2-8.6 mcg/g Creat. |
| Menopause | 0.3-5.9 mcg/g Creat. |
| Male | 0.2-2.5 mcg/g Creat. |

| | | |
|---|---|---|
| 4-Methoxyestrone+4-Methoxyestradiol [4MeO(E1+E2)] | <dl | <= 1.0 mcg/g Creat. |

| Reference Ranges | |
|---|---|
| Premenopause | <=1.0 mcg/g Creat. |
| Menopause | <=1.0 mcg/g Creat. |
| Male | <=1.0 mcg/g Creat. |

## Estrogens

### Ratios

| | | Reference Range |
|---|---|---|
| Anabolic/Catabolic Balance (24hr urine) | 0.1 | 0.1-1.5 |
| E/A: 5β/5α Ratio (24hr urine) | 1.0 | 0.4-1.7 |
| 2-OH(E1+E2) / 16α-OHE1 | >UL | 0.8-12.9 |

| | Reference Ranges |
|---|---|
| Premenopause | 0.3-13.7 |
| Menopause | 0.3-15.1 |
| Male | 0.8-12.9 |

| | | |
|---|---|---|
| 2-OH(E1+E2) / 2-MeO(E1+E2) | 2.6 | 1.0-8.8 |

| | Reference Ranges |
|---|---|
| Premenopause | 1.6-10.7 |
| Menopause | 0.4-11.6 |
| Male | 1.0-8.8 |

## Lab Comments

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. Unless otherwise noted with ◆, the assay has not been cleared by the U.S. Food and Drug Administration.

<dl = Unable to calculate results due to less than detectable levels of analyte.

Please note the reference range for Tetrahydrocortisone (THE), Total 17-OH Corticosteroids, and the Anabolic/Catabolic Balance have been updated.

Please note analysis of estrogens and estrogen metabolites is now performed using LC/MS/MS. The reference ranges for these biomarkers have been updated.