NutriPATH
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**TEST PATIENT**
Sample Test Name
Sex : F
Date Collected : 00-00-0000
111 TEST ROAD TEST SUBURB
**LAB ID: 00000000** UR#:0000000

**TEST PHYSICIAN**
DR JOHN DOE
111 CLINIC STREET
CLINIC SUBURB VIC 3000

# DRIED URINE TESTING-INTEGRATIVE MEDICINE

DRIED URINE

**Estrogen Essential, Dried Urine**

Samples Collected: Urine: 00/00/0000 07:45 Urine: 00/00/0000 10:00 Urine: 00/00/0000 17:00 Urine: 00/00/0000 22:15

BMI: 00
Height: 0 ft in
Weight: 00 kg

Menses Status: Pre-Menopausal
Gender: Female

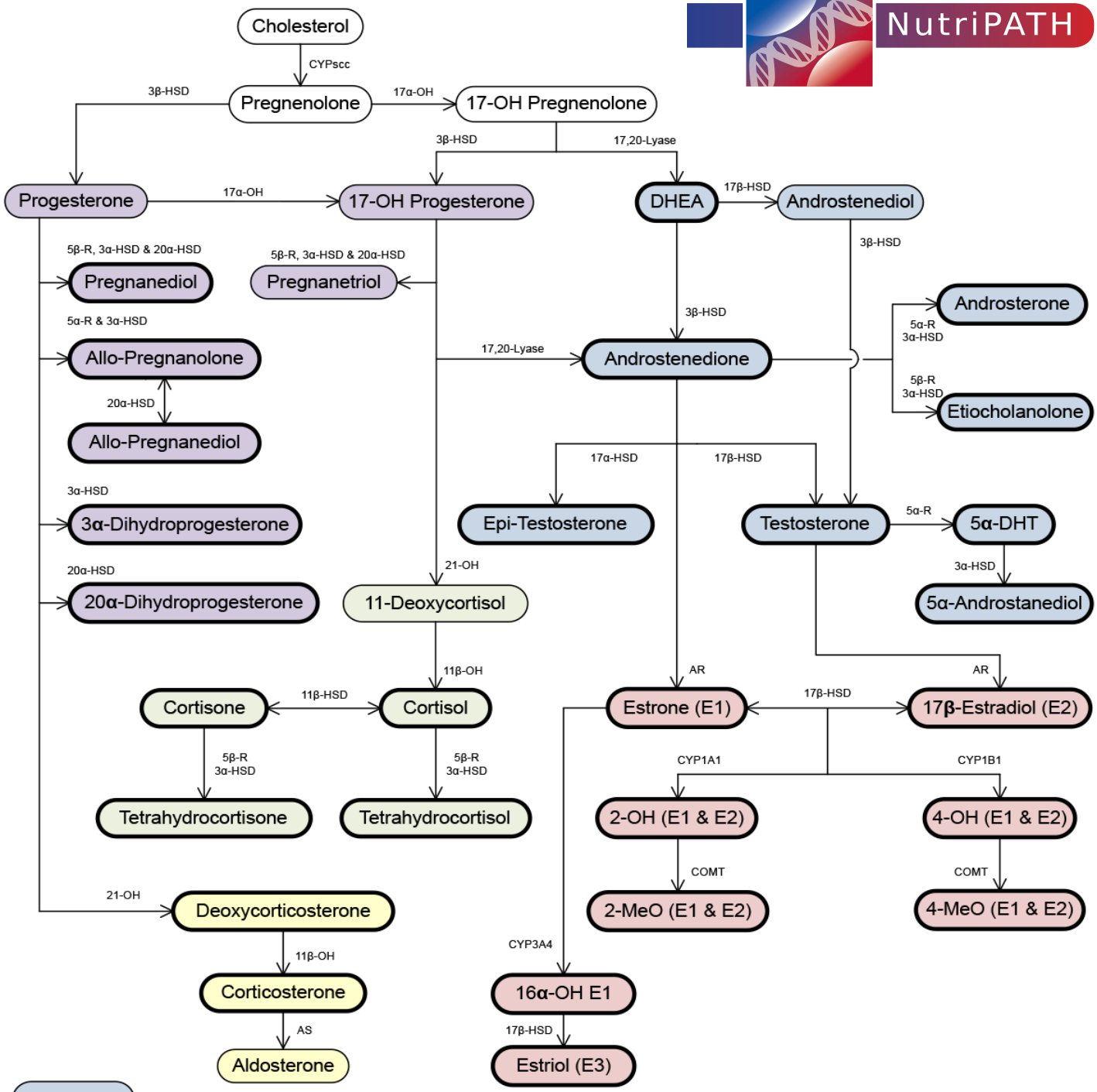
| Test Name | Result | | Range |
|---|---|---|---|
| **Urinary Estrogens (µg/g Cr)** | | | |
| Estradiol (Urine) | 1.49 | | 0.78-1.79 Premeno-luteal or ERT |
| Estrone (Urine) | 6.48 | H | 2.27-5.22 Premeno-luteal or ERT |
| Estriol (Urine) | 1.91 | | 0.78-1.98 Premeno-luteal or ERT |
| E3/(E1+E2) (Urine) | 0.24 | L | >0.3 (> median value) |
| 2-OH Estradiol (Urine) | 0.15 | L | 0.17-0.70 Premeno-luteal or ERT |
| 2-OH Estrone (Urine) | 0.74 | | 0.70-2.54 Premeno-luteal or ERT |
| 4-OH Estradiol (Urine) | 0.19 | H | 0.10-0.18 Premeno-luteal or ERT |
| 4-OH Estrone (Urine) | 0.21 | | 0.17-0.47 Premeno-luteal or ERT |
| 16α-OH Estrone (Urine) | 1.04 | | 0.35-1.07 Premeno-luteal or ERT |
| 2-OH (E1 + E2)/16-α-OH E1 (Urine) | 0.86 | L | 1.29-5.49 Premeno-luteal or ERT |
| 2-MeO Estradiol (Urine) | 0.04 | | 0.03-0.08 Premeno-luteal or ERT |
| 2-MeO Estrone (Urine) | 0.32 | | 0.26-0.68 Premeno-luteal or ERT |
| 2-MeO E1/2-OH E1 (Urine) | 0.43 | H | 0.21-0.38 Premeno-luteal or ERT |
| 4-MeO Estradiol (Urine) | 0.04 | | < 0.04 |
| 4-MeO Estrone (Urine) | 0.03 | | < 0.002 |
| 4-MeO E1/4-OH E1 (Urine) | 0.14 | H | 0.05-0.13 Premeno-luteal or ERT |
| 4-MeO E2/4-OH E2 (Urine) | 0.21 | | 0.10-0.29 Premeno-luteal or ERT |
| **Urinary Creatinine (mg/mL)** | | | |
| Creatinine (pooled) (Urine) | 0.68 | | 0.3-2.0 |

*<dL = Less than the detectable limit of the lab.*
*N/A = Not applicable; 1 or more values used in this calculation is less than the detectable limit.*

## Therapies

None

# The Steroid Hormone Cascade




## Enzyme Abbreviations

(5α-R) 5α-Reductase
(5β-R) 5β-Reductase
(11β-OH) 11β-Hydroxylase
(17α-OH) 17α-Hydroxylase
17,20-Lyase (same enzyme as 17α-OH)
(21-OH) 21-Hydroxylase
(3α-HSD) 3α-Hydroxysteroid dehydrogenase
(3β-HSD) 3β-Hydroxysteroid dehydrogenase
(11β-HSD) 11β-Hydroxysteroid dehydrogenase
(17α-HSD) 17α-Hydroxysteroid dehydrogenase
(17β-HSD) 17β-Hydroxysteroid dehydrogenase
(20α-HSD) 20α-Hydroxysteroid dehydrogenase
(AR) Aromatase
(AS) Aldosterone Synthase
(CYP) Cytochrome p450 (scc, 1A1, 1B1 & 3A4)
(COMT) Catechol-O-Methyl-Transferase

**LAB ID: 000000** **PATIENT NAME**

| **Category | Symptom | None | Mild | Moderate | Severe |
|---|---|---|---|---|---|
| | Hot Flashes | | | | |
| | Night Sweats | | | | |
| | Vaginal Dryness | | | | |
| | Incontinence | | | | |
| | Foggy Thinking | | | | |
| | Memory Lapse | | | | |
| | Tearful | | | | |
| | Depressed | | | | |
| | Heart Palpitations | | | | |
| | Bone Loss | | | | |
| | Sleep Disturbed | | | | |
| | Headaches | | | | |
| | Aches and Pains | | | | |
| | Fibromyalgia | | | | |
| | Morning Fatigue | | | | |
| | Evening Fatigue | | | | |
| | Allergies | | | | |
| | Sensitivity To Chemicals | | | | |
| | Stress | | | | |
| | Cold Body Temperature | | | | |
| | Sugar Craving | | | | |
| | Elevated Triglycerides | | | | |
| | Weight Gain - Waist | | | | |
| | Decreased Libido | | | | |
| | Loss Scalp Hair | | | | |
| | Increased Facial or Body Hair | | | | |
| | Acne | | | | |
| | Mood Swings | | | | |
| | Tender Breasts | | | | |
| | Bleeding Changes | | | | |
| | Nervous | | | | |
| | Irritable | | | | |
| | Anxious | | | | |
| | Water Retention | | | | |
| | Fibrocystic Breasts | | | | |
| | Uterine Fibroids | | | | |
| | Weight Gain - Hips | | | | |
| | Decreased Stamina | | | | |
| | Decreased Muscle Size | | | | |
| | Rapid Aging | | | | |
| | High Cholesterol | | | | |
| | Swelling or Puffy Eyes/Face | | | | |
| | Slow Pulse Rate | | | | |
| | Decreased Sweating | | | | |
| | Hair Dry or Brittle | | | | |
| | Nails Breaking or Brittle | | | | |
| | Thinning Skin | | | | |
| | Infertility Problems | | | | |
| | Constipation | | | | |
| | Rapid Heartbeat | | | | |
| | Hearing Loss | | | | |
| | Goiter | | | | |
| | Hoarseness | | | | |
| | Increased Urinary Urge | | | | |
| | Low Blood Sugar | | | | |
| | High Blood Pressure | | | | |
| | Low Blood Pressure | | | | |
| | Numbness - Feet or Hands | | | | |
| | Breast Cancer | | | | |

| | |
|---|---|
| Metabolic Syndrome | 0.0 |
| Hypometabolism | 3.8 |
| High Cortisol | 7.7 |
| Low Cortisol | 2.3 |
| High Androgens (DHEA/Testosterone) | 1.0 |
| Low Androgens (DHEA/Testosterone) | 0.0 |
| Estrogen Dominance / Progesterone Deficiency | 24.8 |
| Estrogen / Progesterone Deficiency | 0.0 |

***Category refers to the most common symptoms experienced when specific hormone types (eg estrogens, androgens, cortisol) are out of balance, i.e., either high or low.*

**Lab Comments**

PARENT ESTROGENS (ESTRADIOL-E2, ESTRONE-E1, ESTRIOL-E3)

The parent estrogens are within or near the upper limits of the reference ranges seen in premenopausal women, which likely contributes to self-reported symptoms of estrogen dominance. When estrogens levels are within the reference intervals for a premenopausal woman, or slightly higher, it is important that they are well balanced with natural progesterone to prevent excessive proliferation of estrogen-sensitive tissues such as the uterus and breasts. This is especially important if symptoms of estrogen excess (dominance) are problematic, as seen in this individual. In particular, progesterone restoration therapy, regular exercise, eating a healthy diet, and nutritional supplements are often helpful to accelerate estrogen clearance and balance symptoms of both estrogen deficiency and excess.

HYDROXYLATED (CATECHOL) ESTROGENS (2-OH E2 & E1, 4-OH E2 & E1, 16-OH E1) and 2-OH/16-OH RATIO

The hydroxylated estrogens are within reference ranges, with the exception of 4-hydroxy estradiol, which is high. Higher levels of this estrogen metabolite have been associated with increased risk for breast cancer, particularly if this estrogen is not well methylated (4-methoxy estradiol = 4-MeO-E2; please note that the 4-MeO-E2 is also elevated indicating good methylation of this potentially toxic estrogen

When 4-OH-E2 is elevated, a high 4-MeO-E2 would indicate good methylation and inactivation of the potentially dangerous estrogen metabolite. If methylation of the 4-OH-E2 is low, more of this metabolite is available for forming the more reactive 4-E2 quinone that reacts with DNA, causing depurinating adducts that lead to mutations and higher risk for breast cancer.

The hydroxylation of estradiol and estrone represent the first phase of metabolism and elimination of these estrogens via urine. Following hydroxylation at the 2-, 4-, or -16 position, the estrogens undergo further modification (methylation, sulfation, glucuronidation) that increases their solubility and excretion in urine. The sulfate and glucuronide groups are removed by enzyme hydrolysis, which allows for measurement of the different types of hydroxylated estrogens, in addition to methylation of the hydroxyl groups (see below). The 2- and 4-hydroxylated E1 and E2 are referred to as catechol estrogens.

Research and clinical studies show that the 2-hydroxylated estrogens (2-OH E2 and 2-OH E1) are a safer pathway of hydroxylation than the 4-hydroxyestrogens (4-OH E2 and 4-OH E1), which bind to and damage DNA, leading to mutations that are associated with increased breast cancer risk. If either 4-OH-E2 or 4-OH-E1 are higher than reference range, and not well methylated, this may indicate higher risk for DNA damage, mutations, and risk for developing breast cancer. For reviews see: Cavalieri EL, Rogan EG Future Oncol 6(1): 75-79, 2010; and Lee, JR, Zava DT What Your Doctor May Not Tell You About BREAST CANCER: How Hormone Balance Can Help Save Your Life: Chapter 7.

Hydroxylation of estrogens in the 2-position of estradiol (2-OH-E2) and estrone (2-OH-E1) is considered a safer pathway for metabolism than the 4-position hydroxylations of these estrogens. The 2-position hydroxylations (considered safer) are increased with cruciferous vegetables (and extracts of them) as well as iodine. The most commonly used are indole-3-carbinol (I3C) and its metabolite diindolylmethane (DIM). Iodine also increases the 2-hydroxylation of estrogens, with a slight increase in 4-hydroxylation (Stoddard FR et.al. Int J Med Sci 5: 189-196, 2008). The more dangerous 4-hydroxylated estrogen metabolism is enhanced by exposure to environmental toxins, mostly petrochemical-based products but also heavy metals, that induce 4-hydroxylation pathway enzymes (1B1), and cause formation of Reactive Oxygen Species (ROS) that co-oxidize the catechol estrogens to more dangerous estrogen quinones.

16-hydroxyestrone is another pathway of estrone metabolism and is a precursor to estriol (see Steroid Hormone Cascade). Early clinical research in humans suggested that a high urinary level of 16-hydroxyestrone relative to 2-hydroxylated estrogens (i.e. a low 2-OH E1 + 2-OH E2/16-OH E1 ratio), was associated with an increased risk of breast cancer in premenopausal women, but not in postmenopausal women. This has remained controversial and newer research suggests that while higher levels of 16-hydroxy estrone may indeed be slightly associated with increased breast cancer risk in premenopausal women, higher levels are, paradoxically, associated with a decreased risk in postmenopausal women (Huang J et.al. Analytica Chimica Acta 711: 60-68, 2012). Overall, more recent studies have not shown the 2/16 ratio to be useful for predicting breast cancer risk.

METHYLATION OF HYDROXYESTROGENS

The methylated forms of the 2-hydroxyestrogens (2-MeO-E2 and 2-MeO-E1) and the 4-hydroxyestrogens (4-MeO-E2 and 4-MeO-E1) are within or near normal reference ranges for a premenopausal woman. In addition, the ratio of 4-MeO-E2/4-OH-E2 and 4-MeO-E1/4-OH-E1 are within reference ranges (considered beneficial)..

The 2- and 4- hydroxyl estrogens are methylated by the enzyme Catechol-o-Methyl Transferase (COMT), which renders these catechol estrogens inert and harmless (Cavalieri EL, Rogan EG Future Oncol 6(1): 75-79, 2010). In this form the methylated

catechol estrogens are rapidly excreted in urine. However, if methylation pathways are inadequate due to excessive levels of the catechol estrogens, low levels of COMT, or lack of precursors of methylation (i.e. vitamins B6, B12, folate, betaine), the 4-hydroxyl estrogens can take a more insidious and dangerous pathway of metabolism, which is oxidation of the 4-catechol estrogens to 4- estrogen quinones. Estrogen quinones, especially the 4-quinone of estradiol and estrone are highly electrophilic and bind to DNA forming adducts that lead to permanent mutations in the DNA. Many studies have shown that high urinary levels of these 4-quinones of estradiol and/or estrone are associated with increased breast cancer risk if they are not inactivated by methylation or by glutathione sulfation. The 2- and 4-hydroxy estrogens are converted to their more dangerous oxidized quinone forms under oxidizing conditions in the cell, and this occurs rapidly in the presence of oxidized lipids, especially those from trans-hydrogenated fats. These estrogen quinones, like all oxidized and electron-hungry molecules in the body are inactivated when bound to glutathione, the most ubiquitous antioxidant in the body. However, if glutathione is low, due to insufficient levels of minerals (selenium, iodine) and vitamins (C and E), the quinone estrogens are less likely to be detoxified (inactivated) and have potential to damage cells/DNA in close proximity to their formation (i.e. the breast cell/DNA). Neither the quinone estrogens nor their interaction with DNA is measured-only the precursor hydroxyl-estrogens and their methylated metabolites.