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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

MICRO SAMPLE ASSAYS

DRIED URINE	Result	Range	Units
Estrogen Essential, Dried Urine			
Dried Urine Hormone Comments	Please refer to PDF attached.		

Patient Name: TEST TEST **Samples Collected** Urine - 00:00 Urine - 00:00 Urine -00:00 Urine - 00:00

TEST NAME	RESULTS | 11/17/18	RANGE
Urinary Estrogens		
Estradiol	0.80	0.78-1.79 µg/g Cr Premeno-luteal or ERT
Estrone	6.38 H	2.27-5.22 µg/g Cr Premeno-luteal or ERT
Estriol	1.06	0.78-1.98 µg/g Cr Premeno-luteal or ERT
E3/(E1+E2)	0.15 L	>0.3 (> median value)
2-OH Estradiol	0.32	0.17-0.70 µg/g Cr Premeno-luteal or ERT
2-OH Estrone	0.93	0.70-2.54 µg/g Cr Premeno-luteal or ERT
4-OH Estradiol	0.08 L	0.10-0.18 µg/g Cr Premeno-luteal or ERT
4-OH Estrone	0.14 L	0.17-0.47 µg/g Cr Premeno-luteal or ERT
16α-OH Estrone	0.56	0.35-1.07 µg/g Cr Premeno-luteal or ERT
2-OH (E1 + E2)/16-α-OH E1	2.30	1.29-5.49 Premeno-luteal or ERT
2-MeO Estradiol	0.04	0.03-0.08 µg/g Cr Premeno-luteal or ERT
2-MeO Estrone	0.29	0.26-0.68 µg/g Cr Premeno-luteal or ERT
2-MeO E1/2-OH E1	0.31	0.21-0.38 Premeno-luteal or ERT
4-MeO Estradiol	0.01	<0.04 µg/g Cr
4-MeO Estrone	0.02	<0.04 µg/g Cr
4-MeO E1/4-OH E1	0.14 H	0.05-0.13 Premeno-luteal or ERT
4-MeO E2/4-OH E2	0.12	0.10-0.29 Premeno-luteal or ERT

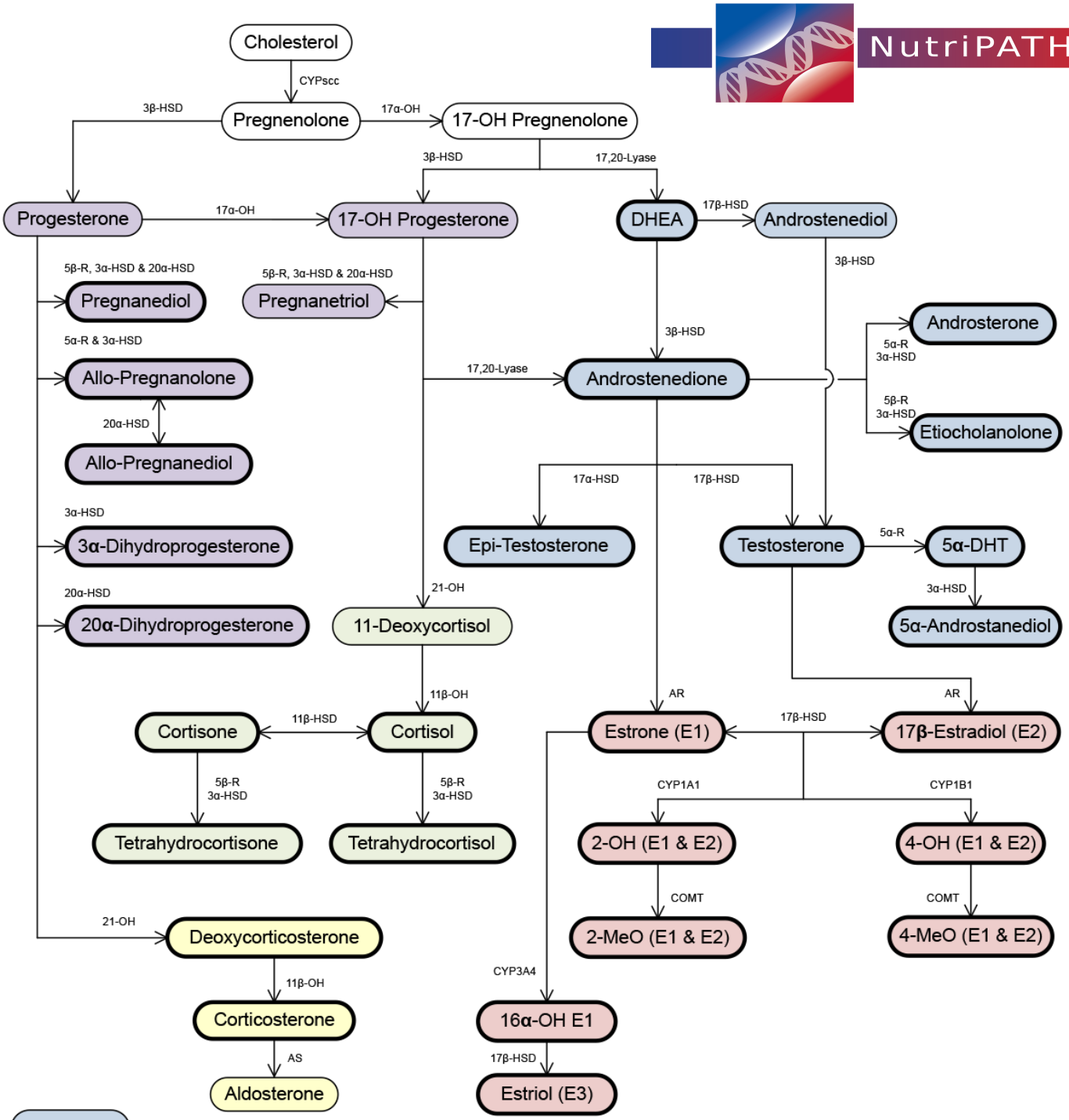
TEST NAME	RESULTS | 11/17/18	RANGE
Urinary Creatinine		
Creatinine (pooled)		0.3-2.0 mg/mL

<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.* ***H*** *= High.* ***L*** *= Low.*

Therapies

None Indicated

The Steroid Hormone Cascade

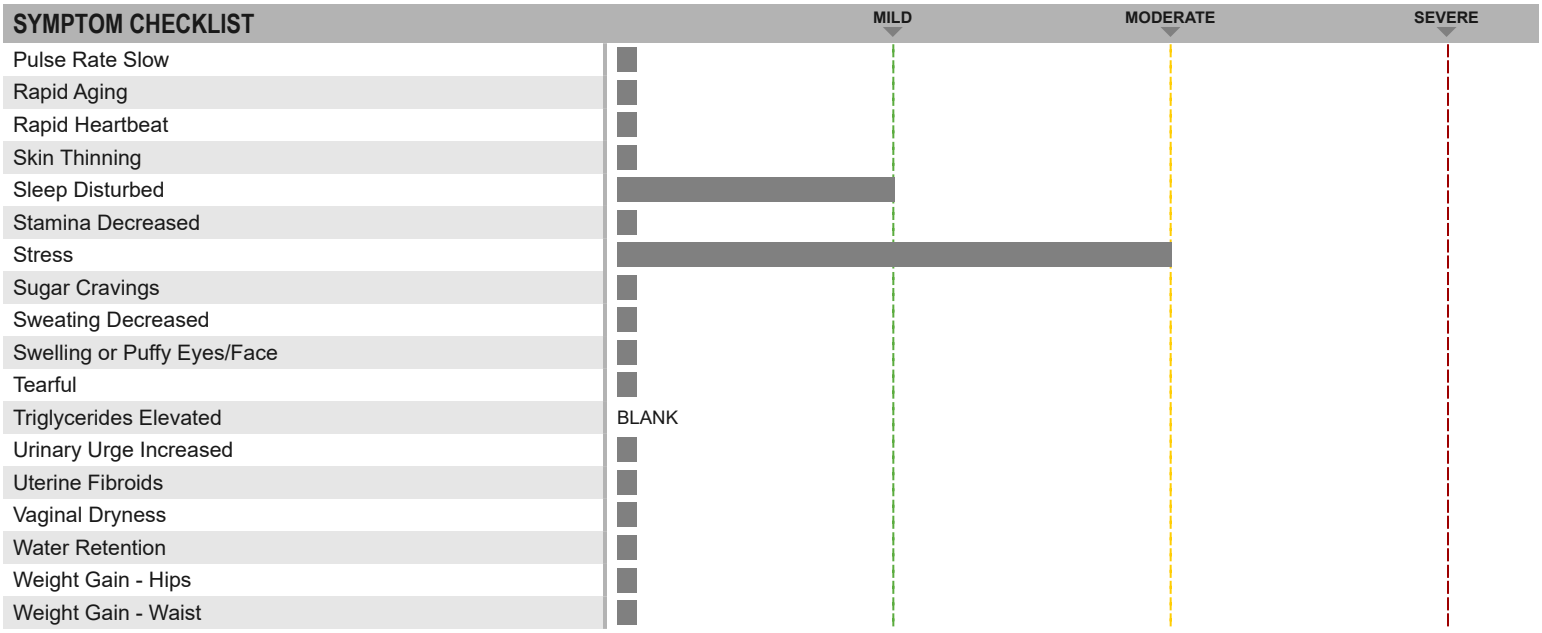


Enzyme Abbreviations

(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

SYMPTOM CATEGORIES	RESULTS | 11/17/18
Estrogen / Progesterone Deficiency	5%
Estrogen Dominance / Progesterone Deficiency	4%
Low Androgens (DHEA/Testosterone)	7%
High Androgens (DHEA/Testosterone)	1%
Low Cortisol	13%
High Cortisol	9%
Hypometabolism	5%
Metabolic Syndrome	0%

SYMPTOM CHECKLIST	MILD / MODERATE / SEVERE
Aches and Pains	
Acne	
Allergies	
Anxious	
Bleeding Changes	
Blood Pressure High	
Blood Pressure Low	
Blood Sugar Low	
Body Temperature Cold	
Bone Loss	BLANK
Breast Cancer	
Breasts - Fibrocystic	
Breasts - Tender	
Chemical Sensitivity	
Cholesterol High	
Constipation	
Depressed	
Fatigue - Evening	
Fatigue - Morning	
Fibromyalgia	
Foggy Thinking	
Goiter	
Hair - Dry or Brittle	
Hair - Increased Facial or Body	
Hair - Scalp Loss	
Headaches	
Hearing Loss	
Heart Palpitations	
Hoarseness	
Hot Flashes	
Incontinence	
Infertility	
Irritable	
Libido Decreased	
Memory Lapse	
Mood Swings	
Muscle Size Decreased	
Nails Breaking or Brittle	
Nervous	
Night Sweats	
Numbness - Feet or Hands	



Lab Comments

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

The parent estrogens are within/near the reference ranges seen in premenopausal women. When estrogens are within the normal reference intervals, or slightly higher, it is worthwhile to consider means to lower the estrogens (e.g. improved diet, more exercise, natural progesterone) iff symptoms of estrogen imbalance (dominance or deficiency) are problematic. If progesterone is low relative to estradiol (low PgDiol/E2 ratio) consider progesterone restoration therapy as this often helps accelerate estrogen clearance and balance symptoms of both estrogen deficiency and excess. Estradiol should be well balanced with progesterone (optimal PgDiol/E2 ratio = 1300-2000 ug/g Cr; only applies to endogenous pregnanediol and not in women treated with exogenous oral, topical or vaginal progesterone).

HYDROXYLATED ESTROGENS (2-OH E2 & E1, 4-OH E2 & E1, 16-OH E1)

The 2-hydroxylated (catechol) estrogens (2-OH-E2 and 2-OH-E1) are within reference ranges, whereas the 4-hydroxylated estrogens (4-OH-E2 and 4-OH-E1) are lower than reference ranges (considered beneficial).

The 2-hydroxylated estrogens are considered a safer form of catechol estrogens because their down-stream 2-quinone estrogens are not mutagenic. In contrast, the 4-hydroxylated estrogens, when they are oxidized further to 4-quinone estrogens are very mutagenic, damage DNA, and increase risk for cancer. Thus, higher levels of 2-hydroxyestrogens relative to 4-hydroxyestrogens should be considered as beneficial and carry a lower lifetime risk for development of breast cancer. Any increase in 4-OH-E2 or 4-OH-E1 beyond reference ranges should be considered as a potentially higher risk for breast cancer, especially if they are not neutralized by methylation (see below-methylation of 4-hydroxyestrogens).

The hydroxylation of estradiol and estrone at the 2, 4, or 16 positions on E2 and E1 represents the first phase of metabolism and elimination of these estrogens via urine. Following hydroxylation the estrogens undergo further Phase 2 modification (methylation, sulfation, glucuronidation) that inactivates them (eliminates their estrogenic potential and prevents them from further oxidizing to more toxic estrogen quinones) and increases their solubility and excretion in urine and bile/feces.

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), the latter of which bind to and damage DNA, leading to mutations that are associated with increased breast cancer risk (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). Therefore, maintaining low estrogen hydroxylation, or increasing 2-hydroxylation relative to 4-hydroxylation, should be considered as a long-term strategy to prevent damage to breast epithelial cells that could potentially lead to breast cancer.

The safer 2-hydroxylated estrogen metabolism is increased by consumption of cruciferous vegetables and/or extracts of them. The most commonly used extracts 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. Heavy metals, via the creation of excessive Reactive Oxygen Species (ROS) in tissues accelerate oxidation of 4-catechol estrogens to 4-quinones; therefore, means to reduce heavy metal exposure, should it be problematic, or preventing heavy metal stimulation of ROS with antioxidants or essential elements (e.g.

selenium) should help reduce formation of toxic and mutagenic 4-estrogen quinones.

16-OH-E1 is a precursor to estriol (see Steroid Hormone Cascade). Early clinical research 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-OH-E1 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 (2-MeO-E2, 2-MeO-E1, 4-MeO-E2, 4-MeO-E1)

The methylated forms of the 2-hydroxyestrogens (2-MeO-E2, 2-MeO-E1) and 4-hydroxyestrogens (4-MeO-E2, 4-MeO-E1) are low or lower than the median of the reference ranges. When the hydroxyestrogens are within range or higher this indicates poor methylation. This is also apparent from the low 4-MeO-E2/4-OH-E2 ratio. Increased urinary levels of the 4-hydroxyestrogens (4-OH-E2 and 4-OH-E1), in the absence of their methylation, are associated with increased risk for cancers of reproductive tissues such as breasts and uterus in females and prostate in males.

The 2- and 4- hydroxyl estrogens are methylated by the enzyme Catechol-o-Methyl Transferase (COMT), which renders them inert (Cavalieri EL, Rogan EG Future Oncol 6(1): 75-79, 2010). In this form the methylated catechol estrogens are rapidly excreted in urine. When methylation of catechol estrogens is inadequate, due to low levels of COMT, or lack of precursors of methylation (i.e. vitamins B6, B12, folate, betaine), the 2- and 4-hydroxylestrogens can further oxidize to more highly reactive 2- or 4-estrogen quinones. The 4-quinones of estradiol and estrone, formed from 4-OH-E2 and 4-OH-E1, are highly electrophilic and bind to DNA forming adducts that lead to permanent mutations in the DNA. The 2-quinones of estradiol and estrone, formed from 2-OH-E2 and 2-OH-E1, will also form covalent adducts with DNA, but this is repaired without DNA damage (mutations).

Formation of 2- and 4-estrogen quinones occurs more readily in the presence of oxidized lipids such as trans-hydrogenated fats, heavy metals, and other conditions that enhance reactive oxygen species (ROS) in tissues. Estrogen quinones are inactivated by many different types of sulfur- or selenium-containing antioxidants, such as N-acetyl cysteine, glutathione, and glutathione peroxidase. Glutathione, the most ubiquitous antioxidant in the body, binds to and inactivates estrogen quinones; therefore, means to maintain high levels of this antioxidant are key to preventing estrogen quinones, as well as other ROS from causing DNA mutations that potentially can lead to cancer. 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).

Consider means to reduce the estrogen burden (e.g. lower therapies that increase estrogen levels-e.g. estrogen replacement therapies in women and testosterone therapies in men) and consider diets that will help with estrogen clearance (lower consumption of meats and increase vegetables with color and fiber). Consumption of vitamins that decrease ROS (all forms of antioxidants) and increase methylation (e.g. folate, B6, B12, betaine) may also be helpful.