Nordic Laboratories

PATIENT: XXXXXXXXXXXXXXXX
TEST NUMBER: T-NL-XXXXX (XXXXXXXXXX)
GENDER: XYZ
AGE: XX

COLLECTED: XX/XX/XXXX
RECEIVED: XX/XX/XXXX
TESTED: XX/XX/XXXX

TEST REF: TST-NL-XXXX
PRACTITIONER:
XXXXXXXXXXXXX
XXXXXXXXXXXXXXXXXXXX

TEST NAME: Urinary Hormone Metabolites Estrogen Essential

TEST NAME	RESULTS | 12/03/19	RANGE
Urinary Estrogens		
Estradiol	1.86 H	0.78-1.79 µg/g Cr Premeno-luteal or ERT
Estrone	9.11 H	2.27-5.22 µg/g Cr Premeno-luteal or ERT
Estriol	3.25 H	0.78-1.98 µg/g Cr Premeno-luteal or ERT
E3/(E1+E2)	0.30	>0.3 (> median value)
2-OH Estradiol	0.87 H	0.17-0.70 µg/g Cr Premeno-luteal or ERT
2-OH Estrone	4.12 H	0.70-2.54 µg/g Cr Premeno-luteal or ERT
4-OH Estradiol	0.25 H	0.10-0.18 µg/g Cr Premeno-luteal or ERT
4-OH Estrone	0.56 H	0.17-0.47 µg/g Cr Premeno-luteal or ERT
16α-OH Estrone	1.31 H	0.35-1.07 µg/g Cr Premeno-luteal or ERT
2-OH (E1 + E2)/16-α-OH E1	3.81	1.29-5.49 Premeno-luteal or ERT
2-MeO Estradiol	0.19 H	0.03-0.08 µg/g Cr Premeno-luteal or ERT
2-MeO Estrone	1.58 H	0.26-0.68 µg/g Cr Premeno-luteal or ERT
2-MeO E1/2-OH E1	0.38	0.21-0.38 Premeno-luteal or ERT
4-MeO Estradiol	0.03	<0.04 µg/g Cr
4-MeO Estrone	0.06 H	<0.04 µg/g Cr
4-MeO E1/4-OH E1	0.11	0.05-0.13 Premeno-luteal or ERT
4-MeO E2/4-OH E2	0.12	0.10-0.29 Premeno-luteal or ERT

Nordic Laboratories Aps
Nygade 6, 3.sal • 1164 Copenhagen K • Denmark
Tlf. +45 33 75 10 00

UK Office:
11 Old Factory Buildings • Stonegate • E. Sussex TN5 7DU • UK
Tel: +44 (0)1580 201 687

www.nordic-labs.com
info@nordic-labs.com

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PATIENT: XXXXXXXXXXXXXXXX			TEST REF: TST-NL-XXXX
TEST NUMBER: T-NL-XXXXX (XXXXXXXXXX)		COLLECTED: XX/XX/XXXX	PRACTITIONER: XXXXXXXXXXXX
GENDER: XYZ		RECEIVED: XX/XX/XXXX	
AGE: XX		TESTED: XX/XX/XXXX	XXXXXXXXXXXXXXXXXXXX

TEST NAME: Urinary Hormone Metabolites Estrogen Essential

TEST REPORT | Results *continued*

TEST NAME	RESULTS | 12/03/19	RANGE
Urinary Creatinine		
Creatinine (pooled)	0.73	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

TEST NAME: Urinary Hormone Metabolites Estrogen Essential

TEST REPORT | Reference Ranges

Disclaimer: Supplement type and dosage are for informational purposes only and are not recommendations for treatment. For a complete listing of reference ranges, go to www.zrtlab.com/reference-ranges.

TEST NAME	WOMEN
Estradiol	0.15-0.75 µg/g Cr Postmenopausal; 0.78-1.79 µg/g Cr Premeno-luteal or ERT
Estrone	0.64-2.56 µg/g Cr Postmenopausal; 2.27-5.22 µg/g Cr Premeno-luteal or ERT
Estriol	0.28-1.17 µg/g Cr Postmenopausal; 0.78-1.98 µg/g Cr Premeno-luteal or ERT
E3/(E1+E2)	>0.3 (> median value)
2-OH Estradiol	0.08-0.31 µg/g Cr Postmenopausal; 0.17-0.70 µg/g Cr Premeno-luteal or ERT
2-OH Estrone	0.25-1.00 µg/g Cr Postmenopausal; 0.70-2.54 µg/g Cr Premeno-luteal or ERT
4-OH Estradiol	0.03-0.12 µg/g Cr Postmenopausal; 0.10-0.18 µg/g Cr Premeno-luteal or ERT
4-OH Estrone	0.06-0.22 µg/g Cr Postmenopausal; 0.17-0.47 µg/g Cr Premeno-luteal or ERT
16α-OH Estrone	0.10-0.41 µg/g Cr Postmenopausal; 0.35-1.07 µg/g Cr Premeno-luteal or ERT
2-OH (E1 + E2)/16-α-OH E1	1.47-8.17 Postmenopausal; 1.29-5.49 Premeno-luteal or ERT
2-MeO Estradiol	0.02-0.07 µg/g Cr Postmenopausal; 0.03-0.08 µg/g Cr Premeno-luteal or ERT
2-MeO Estrone	0.06-0.29 µg/g Cr Postmenopausal; 0.26-0.68 µg/g Cr Premeno-luteal or ERT
2-MeO E1/2-OH E1	0.19-0.36 Postmenopausal; 0.21-0.38 Premeno-luteal or ERT
4-MeO Estradiol	<0.04 µg/g Cr
4-MeO Estrone	<0.04 µg/g Cr
4-MeO E1/4-OH E1	0.03-0.38 Postmenopausal; 0.05-0.13 Premeno-luteal or ERT
4-MeO E2/4-OH E2	0.14-0.73 Postmenopausal; 0.10-0.29 Premeno-luteal or ERT
Creatinine (pooled)	0.3-2.0 mg/mL

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PATIENT: XXXXXXXXXXXXXXXXX			TEST REF: TST-NL-XXXX
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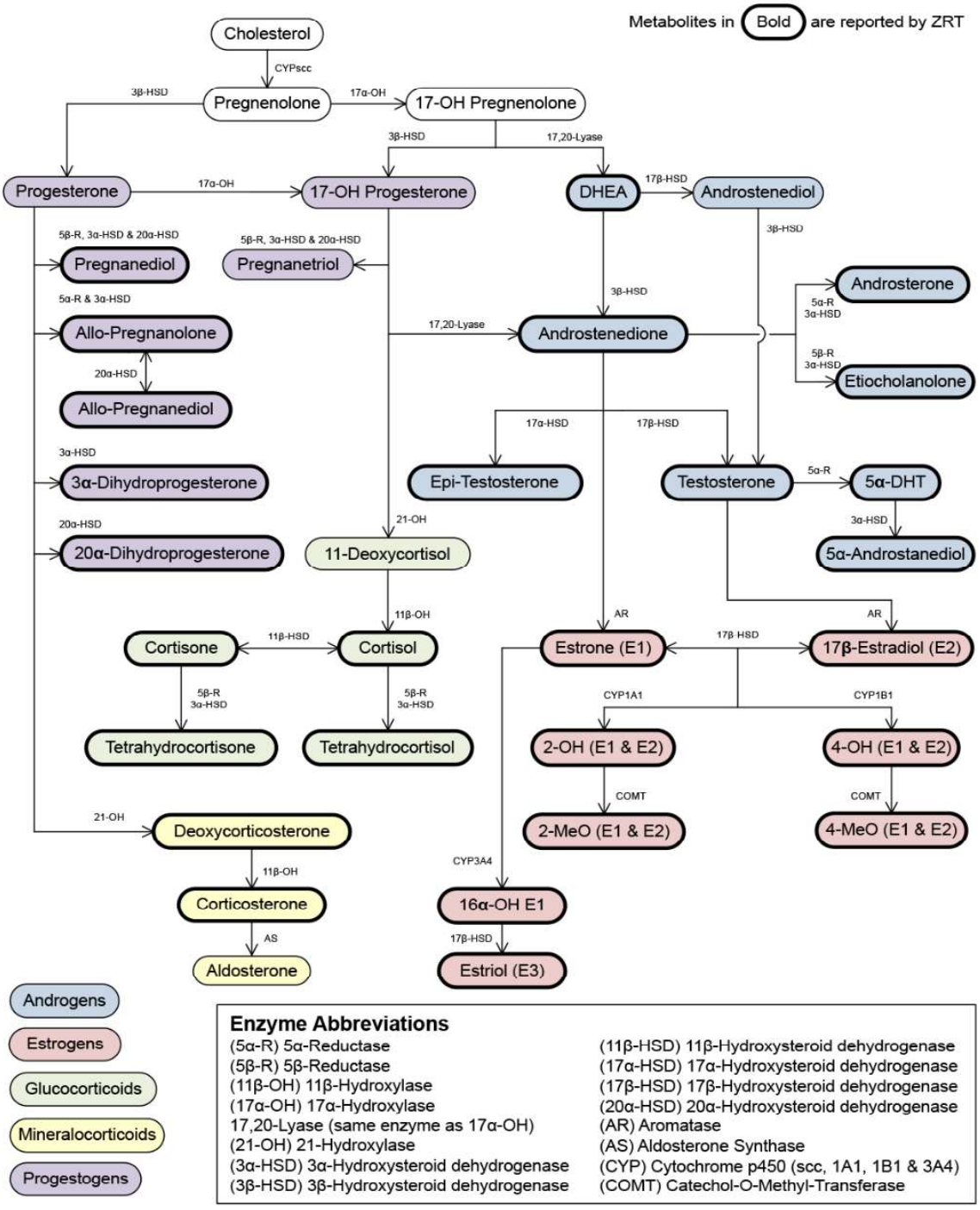
GENDER: XYZ		RECEIVED: XX/XX/XXXX	
AGE: XX		TESTED: XX/XX/XXXX	XXXXXXXXXXXXXXXXXXXX

TEST NAME: Urinary Hormone Metabolites Estrogen Essential

The Steroid Hormone Cascade



TEST NAME: Urinary Hormone Metabolites Estrogen Essential

TEST REPORT | Comments

Lab Comments

PLEASE NOTE: Patient did not indicate hormones used, if any. DBS testing done at same time indicates low estradiol, but high SHBG. Elevated SHBG occurs usually with oral estrogen supplementation, which raises urine estrogen metabolite levels disproportionate to DBS, serum, or saliva levels, which are much lower and more consistent with tissue levels of estrogens.

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

The parent estrogens estradiol (E2), estrone (E1), and estriol (E3) are higher than reference ranges seen in premenopausal women. This is often associated with symptoms of estrogen imbalance (dominance) when progesterone is low (luteal insufficiency or anovulation) and the ratio of pregnanediol/estradiol is low. High estrogens occurs most commonly in the early teens and then again during the 10-15 or so years before menopause (perimenopause-usually about ages 35-50), when estrogens are produced at higher levels relative to progesterone.

Because estrogens are high and symptoms are consistent with estrogen dominance consider means to lower the estrogen burden (diet consisting of more fiber and cruciferous vegetables, less red meat, weight reduction if problematic) and balance the estrogens with natural progesterone (assuming no contraindications) if the urinary pregnanediol is low or the ratio of PgDiol/E2 is low (see results below).

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

The hydroxylated estrogens (2-OH-E2, 2-OH-E1, 4-OH-E2, 4-OH-E1), referred to as catechol estrogens, are all higher than reference ranges.

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 positions, the estrogens undergo further modification (methylation, sulfation, glucuronidation) that inactivates them and increases their solubility and uptake by the kidneys for excretion in urine. In the laboratory the sulfate and glucuronide groups are removed by enzyme hydrolysis, which allows for measurement of the different types of hydroxylated estrogens that formed elsewhere in the body but were excreted in urine.

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 are considered more toxic as they bind to DNA causing 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.

The safer 2-hydroxylated estrogen metabolism is increased, relative to the 4-hydroxylation pathways, with cruciferous vegetables and extracts of them. The most commonly used are indole-3-carbinol (I3C) and its metabolite diindolylmethane (DIM). Eating a healthy diet of plants with beneficial phytochemicals (e.g. leafy vegetables with color, soy foods, flax, foods high in antioxidants such as turmeric) also helps prevent buildup of toxic catechol estrogen metabolites. 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) and serves as a potent antioxidant in concert with selenium to help prevent further oxidation of the catechol estrogens to their highly reactive estrogen quinones that bind and damage DNA, causing mutations that increase risk for cancers of estrogen-sensitive tissues (e.g. breast).

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 much more reactive quinone estrogens. The 4-quinone estrogens, if not inactivated by glutathione, can potentially bind to and damage DNA leading to mutations that increase lifetime risk for cancer.

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 associated with a decreased risk in postmenopausal women (Huang J et.al. Analytica Chimica Acta 711: 60-68, 2012). A meta-analysis of nine studies investigating the relationship of the urinary 2/16 ratio have NOT shown it to be useful for predicting breast cancer risk (Obi N et.al. Int J Women's Health 3: 37-51, 2011).

METHYLATION OF HYDROXYESTROGENS

The methylated forms of the 2-hydroxyestrogens are higher than reference ranges (beneficial). Methylation of the more toxic 4-hydroxyestrogens is within reference ranges or slightly higher, and the ratios of 4-methoxyestrogens to their 4-hydroxyestrogen precursors (i.e. 4-MeO-E2/4-OH-E2 and 4-MeO-E1/4-OH-E1) is within normal reference ranges (beneficial). Adequate methylation of the hydroxyestrogens, and an associated high ratios of 4-methoxyestrogens is considered beneficial as this indicates the toxic 4-hydroxyestrogens are rendered inert via methylation, preventing them from oxidizing further to more dangerous 4-estrogen quinones that potentially can form adducts with DNA, causing mutations that can lead to increased cancer risk.

TEST NAME: Urinary Hormone Metabolites Estrogen Essential

TEST REPORT | Comments *continued*

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 low levels of COMT, or lack of precursors of methylation (i.e. vitamins B6, B12, folate, betaine), the 2- and 4-hydroxyl estrogens can oxidize to 4-estrogen quinones that bind to DNA, forming adducts that can lead to permanent mutations, and eventually to cancer.

Many studies have shown that high urinary levels of these 4-hydroxyestrogens (4-OH-E2 and 4-OH-E1) are associated with increased breast cancer risk if they are not inactivated by methylation, or the more toxic down-stream oxidized 4-quinone estrogens are not inactivated by glutathione sulfation. If glutathione is low the 4-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). Maintaining adequate glutathione is key to preventing buildup of toxic/mutagenic 4-quinone estrogens, should they form due to poor methylation pathways. If 4-OH-estrogens are high and not well methylated consider avoiding trans-hydrogenated fats and eliminate heavy metals that cause the formation of Reactive Oxygen Species (ROS) that oxidize lipids. Supplementation with essential elements such as selenium and iodine will also help reduce formation of oxidized lipids, which co-oxidize 4-OH-estrogens to 4-quinone estrogens.