



Order: 999999-9999



Test: X999999-9999-1

Client #: 999999

Doctors Data Inc  
123 Main St.  
St. Charles, IL 60174 USA

Patient: Sample Patient

Id: 999999

Age: 61 DOB: 01/01/1960

Sex: Female

Body Mass Index (BMI): 25

Menopausal Status: Post-menopausal

Sample Collection Date/Time

Dinnertime 12/30/2022 19:20

Bedtime 12/30/2022 22:30

Waking 12/31/2022 07:00

2 Hr. Post Waking 12/31/2022 09:30

Collection Period Multipoint daily

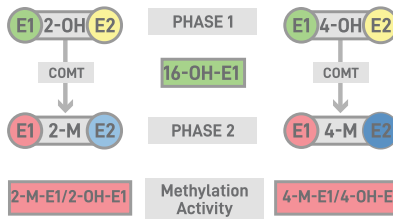
Date Received 01/01/2023

Date Reported 01/02/2023

### ESTROGENS

The bar graph represents the relationship of the catechol estrogens (2-OH-E1, 4-OH-E1, 16-OH-E1) to each other. The expected percentage for each is represented by the shaded area.

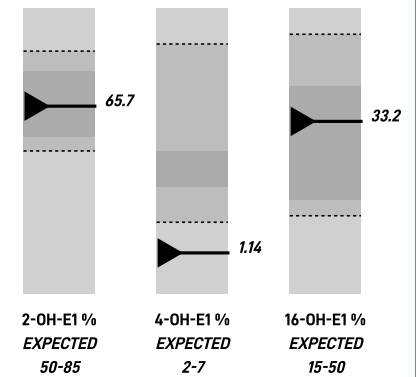
The pathway illustrates phase 1 and phase 2 metabolism of both E1 and E2. Phase 1 metabolites, also known as catechol estrogens, are active and can induce estrogenic actions. Phase 2 metabolism gives insight into a patient's ability to methylate, or potentially inactivate harmful metabolites.



2-OH: generally considered safest

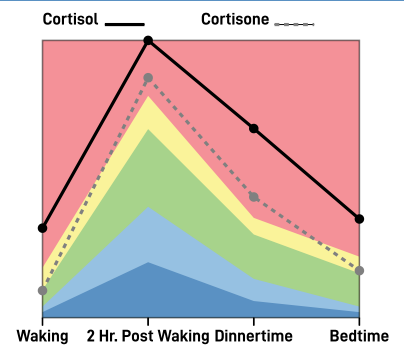
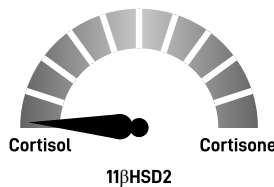
4-OH: potential for DNA damage

16-OH: considered highly estrogenic



### CORTICOIDS

11 $\beta$ HSD2 is responsible for the conversion of cortisol to cortisone. Inhibition of this enzyme may lead to the amount of cortisol being greater than cortisone, while increased enzyme activity can lead to higher levels of cortisone in comparison to cortisol.



### KEY RELATIONSHIPS

The graphs to the right represent metabolism preference by key enzymes, indicated by the arrow.

Metabolites in the 5-alpha pathway are more androgenic than their 5-beta counterparts and can be responsible for androgenic symptoms even when hormone levels appear normal.

Aromatase is an enzyme found in the greatest amounts in peripheral fat tissue which can increase estrogens in both males and females.

4-OH-E1 is considered unfavorable due to its carcinogenic potential within breast and prostatic tissue as a reactive metabolite. When methylated by COMT, this reactive metabolite becomes stable and can be removed from the body.

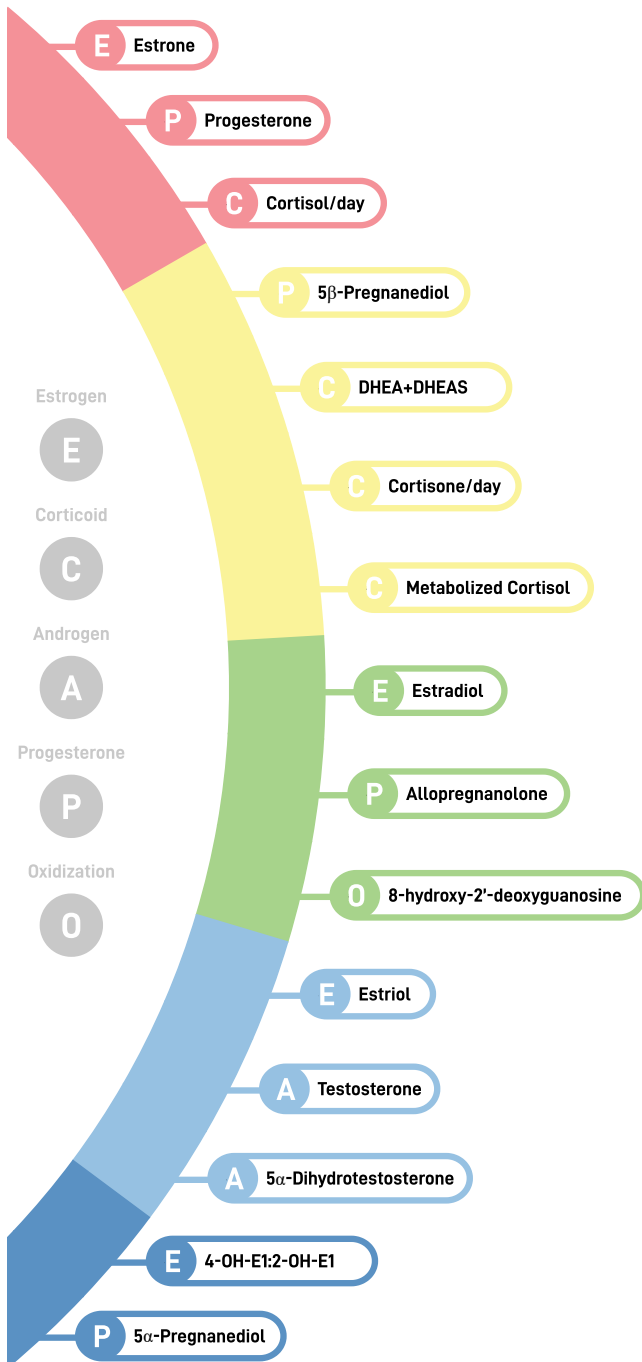
#### 5-A REDUCTASE ACTIVITY

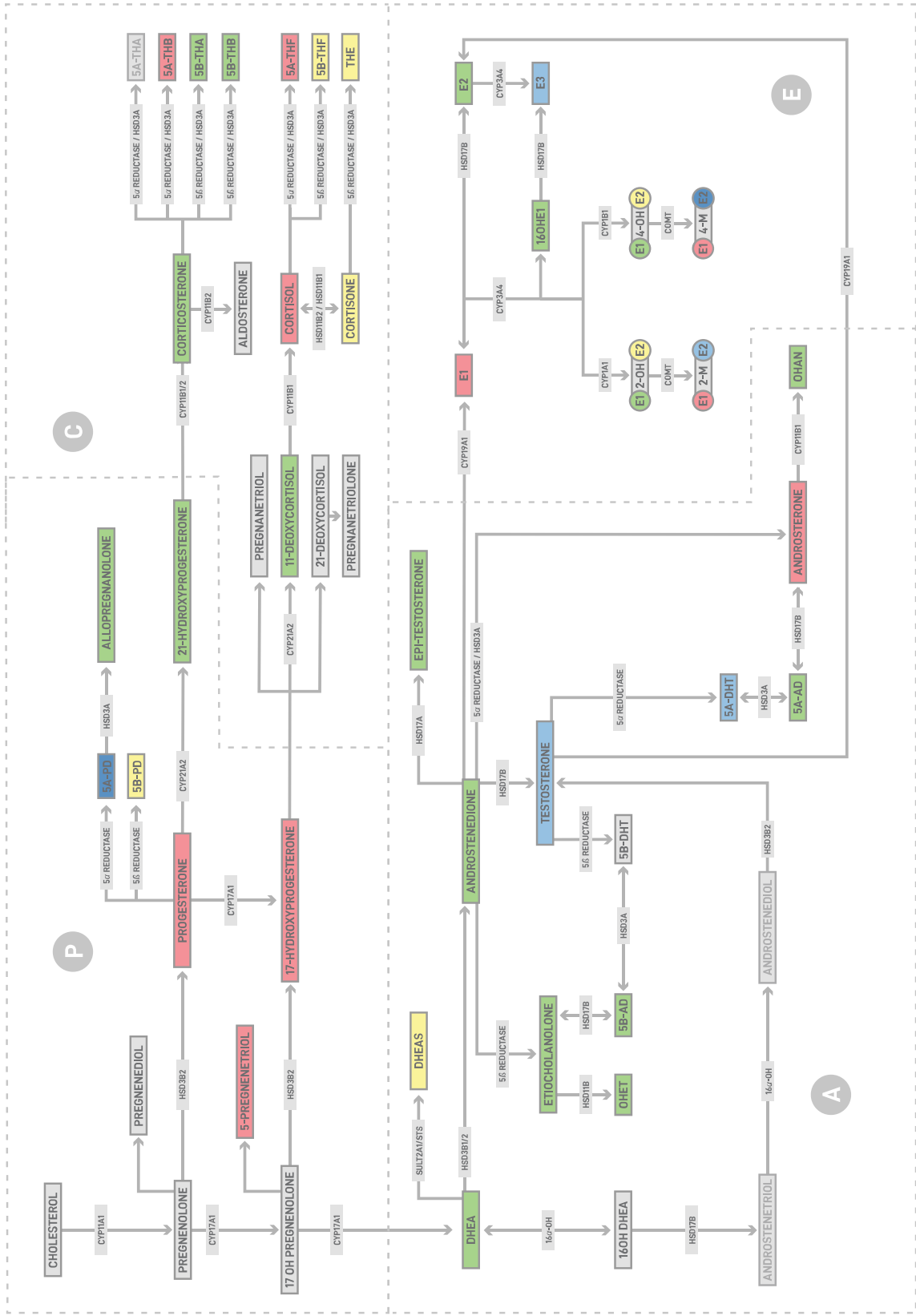


#### AROMATASE ACTIVITY



#### COMT/METHYLATION ACTIVITY







# Progesterone Metabolites; urine



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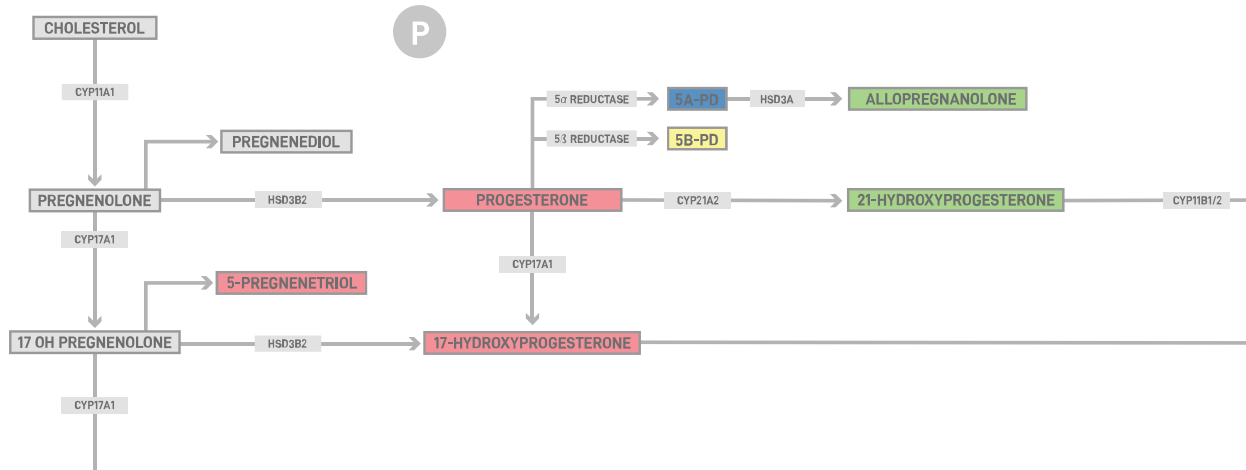
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Progesterones	Result	Unit	L	WRI	H	Reference Interval
Progesterone	(P4) 0.464	ng/mg Creat/Day				0 – 0.22
5α-Pregnanediol	(5A-PD) 18.6	ng/mg Creat/Day				21 – 50
5β-Pregnanediol	(5B-PD) 255	ng/mg Creat/Day				79 – 280
Allopregnanolone	(ALLOP) 2.74	ng/mg Creat/Day				1.4 – 4.8
21-Hydroxyprogesterone	(21-OHP) 0.837	ng/mg Creat/Day				0.3 – 1.4
17-Hydroxyprogesterone	(17-OHP) 0.629	ng/mg Creat/Day				0.17 – 0.55
5-pregnenetriol	(5-PT) 204	ng/mg Creat/Day				35 – 120
Ratios and Calculations	Result	Unit	L	WRI	H	Reference Interval
5A-PD:5B-PD (alpha vs beta metabolism)	0.073					0.1 – 0.5



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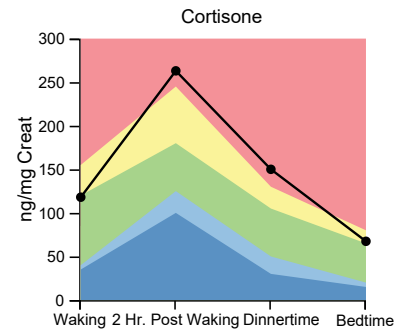
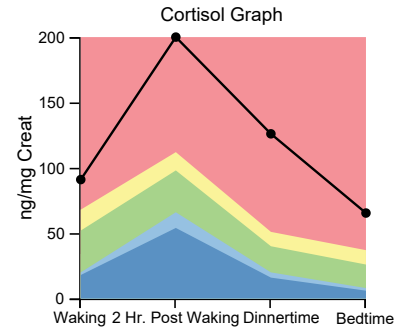
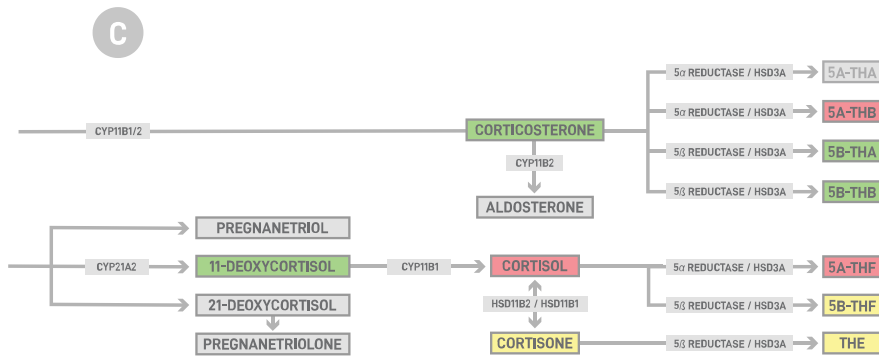
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Free Cortisol and Cortisone	Result	Unit	L	WRI			H	Reference Interval
				Green	Yellow	Red		
Cortisol Waking	91.0	ng/mg Creat	Blue	Green	Yellow	Red	18 – 68	
Cortisol Waking+2hrs	265	ng/mg Creat	Blue	Green	Yellow	Red	54 – 112	
Cortisol Dinnertime	126	ng/mg Creat	Blue	Green	Yellow	Red	16 – 51	
Cortisol Bedtime	65.4	ng/mg Creat	Blue	Green	Yellow	Red	6 – 37	
Cortisol/day (F)	130	ng/mg Creat/Day	Blue	Green	Yellow	Red	30 – 90	
Cortisone Waking	118	ng/mg Creat	Blue	Green	Yellow	Red	35 – 155	
Cortisone Waking+2hrs	263	ng/mg Creat	Blue	Green	Yellow	Red	100 – 245	
Cortisone Dinnertime	150	ng/mg Creat	Blue	Green	Yellow	Red	30 – 130	
Cortisone Bedtime	67.4	ng/mg Creat	Blue	Green	Yellow	Red	15 – 80	
Cortisone/day (E)	145	ng/mg Creat/Day	Blue	Green	Yellow	Red	60 – 165	
Creatinine Waking	68.5	mg/dL	Blue	Green	Yellow	Red	30 – 225	
Creatinine Waking+2hrs	115	mg/dL	Blue	Green	Yellow	Red	30 – 225	
Creatinine Dinnertime	93.4	mg/dL	Blue	Green	Yellow	Red	30 – 225	
Creatinine Bedtime	116	mg/dL	Blue	Green	Yellow	Red	30 – 225	
Creatinine/day	104	mg/dL/Day	Blue	Green	Yellow	Red	30 – 225	



# Adrenal Corticoid Metabolites; urine



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Corticoid Metabolites and DHEA				L	WRI	H	Reference Interval
Corticosterone	(B)	27.7	ng/mg Creat/Day		▲		10 – 47
Tetrahydrodehydrocorticosterone	(5B-THA)	111	ng/mg Creat/Day		▲		46 – 220
5β-Tetrahydrocorticosterone	(5B-THB)	202	ng/mg Creat/Day		▲		65 – 240
5α-Tetrahydrocorticosterone	(5A-THB)	515	ng/mg Creat/Day			▲	160 – 430
11-Deoxycortisol	(11-DOC)	0.949	ng/mg Creat/Day		▲		0.35 – 1.8
5α-Tetrahydrocortisol	(5A-THF)	1320	ng/mg Creat/Day			▲	200 – 1300
5β-Tetrahydrocortisol	(5B-THF)	2470	ng/mg Creat/Day			▲	900 – 2600
Tetrahydrocortisone	(THE)	3210	ng/mg Creat/Day			▲	1180 – 4000
Dehydroepiandrosterone	(DHEA)	33.9	ng/mg Creat/Day		▲		10 – 120
Dehydroepiandrosterone Sulfate	(DHEAS)	173	ng/mg Creat/Day			▲	35 – 300
Ratios and Calculations				L	WRI	H	Reference Interval
DHEA+DHEAS		207	ng/mg Creat/Day			▲	62 – 283
THE+5A-THF+5B-THF	(Metabolized Cortisol)	7000	ng/mg Creat/Day			▲	2500 – 7900
5A-THF+5B-THF/THE	(Cortisol/Cortisone Metabolites)	1.17			▲		0.7 – 1.4
Cortisol/Cortisone	(11B HSD activity)	0.891				▲	0.4 – 0.8
5A-THF/5B-THF ratio	(alpha vs beta metabolism)	0.537			▲		0.4 – 1.4



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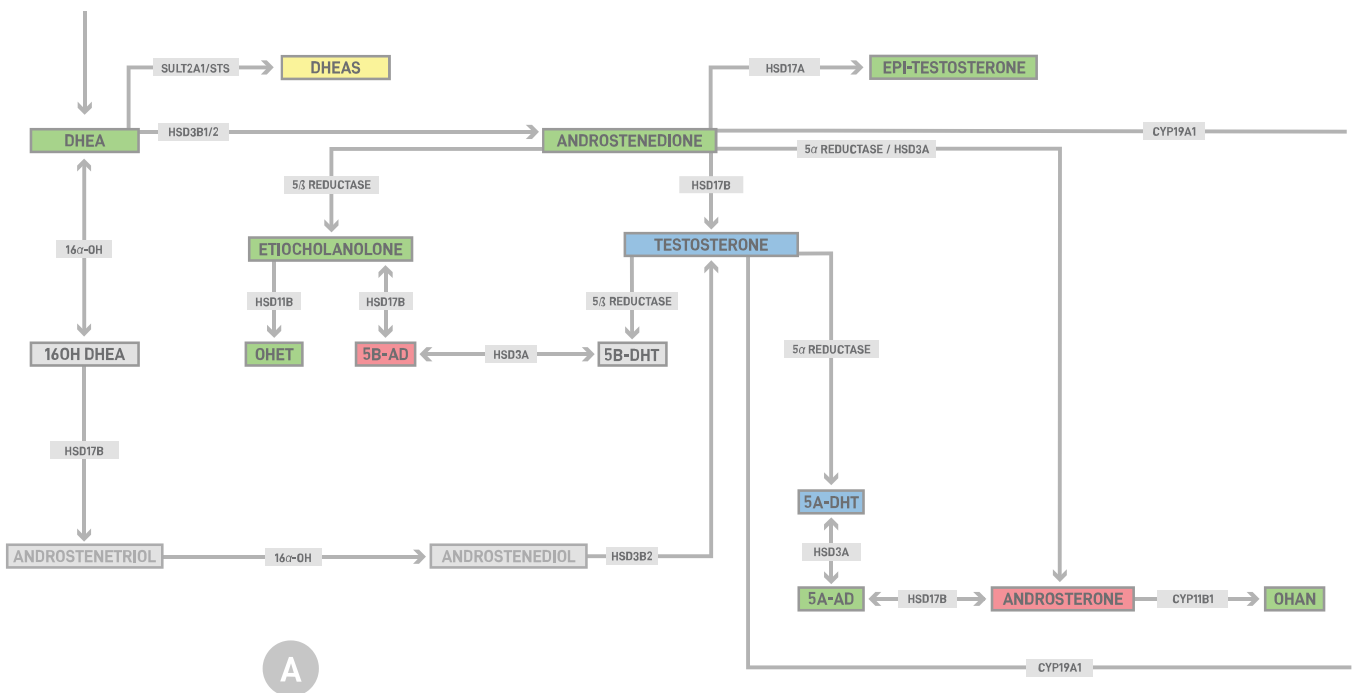
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A

Androgens	Result	Unit	L	WRI	H	Reference Interval
Androstenedione	(A4) 1.15	ng/mg Creat/Day		▲		0.2 – 5.3
EPI-Testosterone	(EPI-T) 1.38	ng/mg Creat/Day		▲		0 – 5
Testosterone	(T) 1.91	ng/mg Creat/Day	▲			0.25 – 10.9
Androsterone	(AN) 928	ng/mg Creat/Day			▲	170 – 850
11-hydroxy-Androsterone	(OHAN) 762	ng/mg Creat/Day		▲		250 – 1000
5α-Androstenediol	(5A-AD) 8.63	ng/mg Creat/Day		▲		4.8 – 16
5α-Dihydrotestosterone	(5A-DHT) 0.391	ng/mg Creat/Day	▲			0.2 – 6
Etiocholanolone	(ET) 1070	ng/mg Creat/Day		▲		240 – 1410
11-hydroxy-Etiocholanolone	(OHET) 83.0	ng/mg Creat/Day		▲		20 – 710
5β-Androstenediol	(5B-AD) 65.4	ng/mg Creat/Day			▲	14 – 62
Dehydroepiandrosterone	(DHEA) 33.9	ng/mg Creat/Day		▲		10 – 120



# Androgen Metabolites; urine



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Androgens	Result	Unit	L	WRI	H	Reference Interval
Dehydroepiandrosterone Sulfate (DHEAS)	173	ng/mg Creat/Day				35 – 300
Ratios and Calculations	Result	Unit	L	WRI	H	Reference Interval
DHEA+DHEAS	207	ng/mg Creat/Day				62 – 283
Androsterone (5 $\alpha$ ) / Etiocholanolone (5 $\beta$ ) (5 $\alpha$ Reductase Activity)	0.864					0.8 – 2.6
Testosterone / EPI-Testosterone	1.38					0.7 – 3



# Estrogen Metabolites; urine



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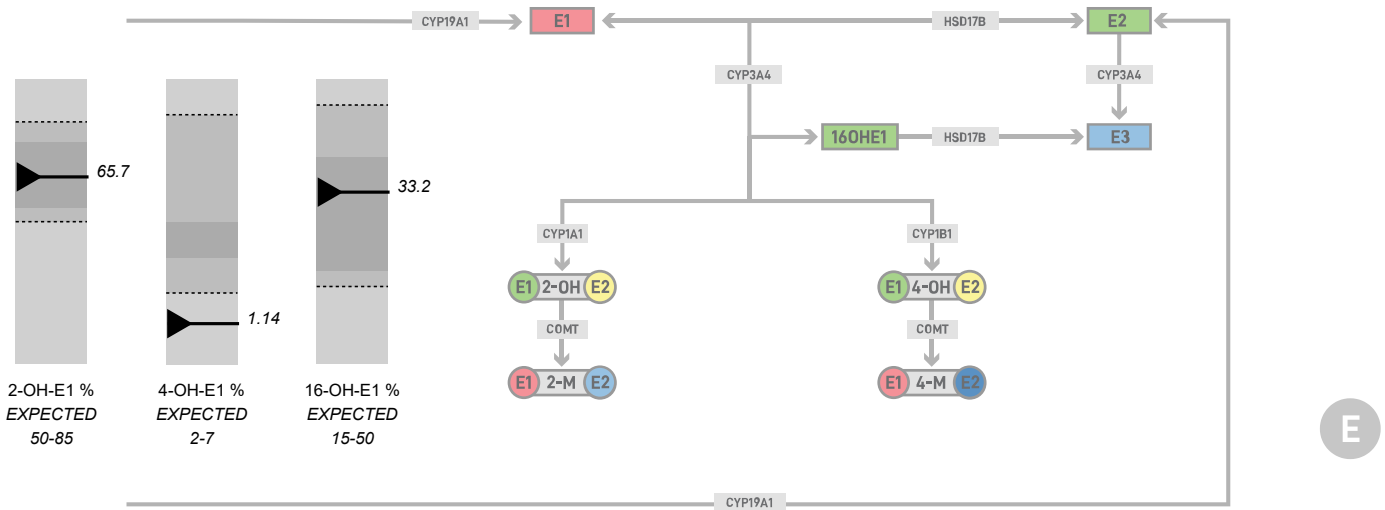
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Estrogens	Result	Unit	L	WRI	H	Reference Interval
Estrone (E1)	5.62	ng/mg Creat/Day			▲	1.75 – 5.12
2-Hydroxyestrone (2-OH-E1)	3.97	ng/mg Creat/Day		▲		1.62 – 6.5
4-Hydroxyestrone (4-OH-E1)	0.069	ng/mg Creat/Day		▲		0 – 0.3
16α-Hydroxyestrone (16-OH-E1)	2.00	ng/mg Creat/Day		▲		1.05 – 5.3
2-Methoxyestrone (2-M-E1)	2.36	ng/mg Creat/Day			▲	0.41 – 1.34
4-Methoxyestrone (4-M-E1)	0.099	ng/mg Creat/Day			▲	0.007 – 0.05
Estradiol (E2)	1.02	ng/mg Creat/Day		▲		0.2 – 1.6
2-Hydroxyestradiol (2-OH-E2)	0.288	ng/mg Creat/Day			▲	0.033 – 0.29
4-Hydroxyestradiol (4-OH-E2)	0.231	ng/mg Creat/Day			▲	0.052 – 0.26
2-Methoxyestradiol (2-M-E2)	0.018	ng/mg Creat/Day		▲		0.012 – 0.039
4-Methoxyestradiol (4-M-E2)	0.004	ng/mg Creat/Day	▲			0.009 – 0.024
Estriol (E3)	3.27	ng/mg Creat/Day		▲		1.61 – 5.6
Ratios and Calculations	Result	Unit	L	WRI	H	Reference Interval
2-OH-E1 %	65.7	%		▲		50 – 85
4-OH-E1 %	1.14	%	▲			2 – 7





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Ratios and Calculations	Result	Unit	L	WRI	H	Reference Interval
16-OH-E1 % (16-OH-E1 %)	33.2	%		▲		15 – 50
2-M-E1:2-OH-E1 (COMT/Methylation activity)	0.568				▲	0.1 – 0.36
2-M-E2:2-OH-E2 (COMT/Methylation activity)	0.061		▲			0.07 – 0.37
4-M-E1:4-OH-E1 (COMT/Methylation activity)	1.37				▲	0.09 – 0.54
4-M-E2:4-OH-E2 (COMT/Methylation activity)	0.015		▲			0.04 – 0.54
2-OH-E1:16-OH-E1	1.98			▲		1.6 – 5.1
4-OH-E1:2-OH-E1	0.017		▲			0.02 – 0.07
Oxidative Stress Metabolite	Result	Unit	L	WRI	H	Reference Interval
8-hydroxy-2'-deoxyguanosine (8-OHdG)	2.67	ng/mg Creat/Day		▲		0 – 7.5



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## Progesterones

### ↑ Progesterone (P4)

In cycling females, progesterone is primarily produced in the corpus luteum of the ovaries, and to a lesser degree in the adrenal glands. Menopausal females continue to produce small amounts of progesterone in the adrenal glands. Elevated levels of progesterone may be due to high dose pregnenolone supplementation, progesterone supplementation, exogenous progesterone exposure, pregnancy, disorders of luteinization, increased HSD3A activity, reduced activity of CYP21A or CYP17A, and rarely thecal cell tumors. In addition, elevations of both progesterone and pregnenediol, progesterone's major metabolite, have been reported in 21 hydroxylase deficiency.

### ↓ 5A-PD

Lower levels of pregnenediol have been associated with amenorrhea, decreased ovarian function, PCOS, ovarian cancer, and certain complications of pregnancy.

### ↑ 17-Hydroxyprogesterone (17-OHP)

17-Hydroxyprogesterone is the product of progesterone hydroxylation. Elevations are associated with PCOS, idiopathic hirsutism, congenital adrenal hyperplasia, 11-beta-hydroxylase deficiency, and adult onset virilizing adrenal hyperplasia. Additionally, hyperinsulinemia and hyperglycemia (metabolic syndrome) push 17-hydroxylation of progesterone.

### ↑ Pregnenetriol (5-PT)

5-pregnenetriol is a metabolite of 17 $\alpha$ -pregnenolone, an intermediary resulting from the hydroxylation of pregnenolone by CYP 17A1 enzyme. Elevations in urine may be seen in cases of PCOS, Cushing's Syndrome, congenital adrenal hyperplasia, and adrenocortical carcinoma.

### ↓ 5A-PD : 5B-PD

The metabolic prioritization for alpha or beta reductase activity within the progesterone pathway may be confirmatory of a general preference of metabolism. Comparing these results with the metabolic preference of androgens and corticoids may provide additional insight.

## Androgens

### ↑ Androsterone (AN)

Androsterone is the product of androgens metabolized by 5-alpha reductase. It acts as a neurosteroid and a weak potentiator of GABA-A receptor activity. Androsterone may also be converted to DHT via backdoor pathway using HSD3 $\beta$  and HSD17 $\beta$  making it a metabolic intermediate. Potential causes of AN elevation may include PCOS, over supplementation of DHEA or pregnenolone, androgen producing gonadal tumors, congenital adrenal hyperplasia, adult-onset adrenal hyperplasia, serious illness, shock, and burns.

### ↑ 5 $\beta$ -Androstanediol (5B-AD)

5B-AD is the result of the 5-beta reduction of DHT and is a metabolite of etiocholanolone. Elevated levels may be due to an increased conversion via 5-beta reductase, or from DHEA or testosterone supplementation.

## Corticoids

### ↑ 5 $\alpha$ -Tetrahydrocorticosterone (5A-THB)

5A-THB is a terminal metabolite of corticosterone. This metabolite along with the other terminal metabolites can be used to determine metabolism of corticosterone. While research in elevations of single terminal metabolites is limited, assessment of metabolism may provide more information regarding enzyme activity.



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### Corticoids

**↑ Cortisol (F)**

Cortisol is the main glucocorticoid released from the adrenal gland in response to stress. Elevated levels of cortisol have been reported in cases of Cushing's disease, malnutrition, early life stress, hypothyroidism, depression, alcoholism, PCOS, obesity, and critical illness. Additionally, exogenous exposure to glucocorticoids prior to testing may be a source of cortisol elevations.

**↑ 5a-Tetrahydrocortisol (5A-THF)**

5A- THF is a terminal metabolite of cortisol metabolized via 5 alpha reductase. Combining all the terminal metabolites can be used to estimate metabolized cortisol. While research into single terminal metabolite elevations is limited, it may have more clinical relevance when assessed in combination with the daily output of free cortisol.

**↑ Cortisol/Cortisone (11B HSD activity)**

Cortisol / cortisone ratio measures activity of HSD11B2 activity and assessment of tissue specific concentration of cortisol, which normally cannot be measured without a biopsy. An elevated ratio indicates suppressed enzyme activity or a low conversion rate of cortisol to cortisone. This can be seen in stress, hypertension, metabolic syndrome, insulin resistance, PCOS, depression, with cortisol supplementation, or high licorice doses.

### Estrogens

**↑ Estrone (E1)**

A component of the estrone level may be due to aromatization of androstenedione and testosterone by CYP19 (aromatase) enzyme in adipose tissue and/or conversion from estradiol due to HSD17β activity. Elevated estrone has been associated with increased risk of breast cancer in postmenopausal women, particularly when accompanied by elevated testosterone. CYP19 enzyme is induced during times of stress, exposure to xeno-estrogens, high glycemic diet, excessive adipose tissue, and alcohol consumption.

**↑ 2-Methoxyestrone (2-M-E1)**

2-M-E1 is considered a non-reactive metabolite. Higher levels correlated with antiproliferative and antiangiogenic effects as well as cardioprotective properties. Depending on other metabolite values, and if excretion from the GI tract is functioning properly, elevations in 2-M-E1 may be considered healthy.

**↑ 4-Methoxyestrone (4-M-E1)**

Methyl metabolites are considered inactive and are correlated with protective and antiproliferative effects. Proper elimination of 4-M-E1 requires optimal excretion via the GI tract; optimizing GI health is an option. To fully understand this value, it may be beneficial to examine the 4-M-E1 / 4-OH-E1 ratio.

**↓ 4-Methoxyestradiol (4-M-E2)**

Lower levels of 4-M-E2 is associated with a higher risk of certain cancers and other negative markers for breast health. Low levels of 4-M-E2 may indicate that 4-OH metabolites are favoring the quinone/semi quinone pathway which can lead to DNA damage. Supporting the COMT enzyme (methylation) is a consideration.

**↑ 2-M-E1:2-OH-E1 (COMT/Methylation activity)**

The relationship of 2-M-E1 / 2-OH-E1 represents the activity of COMT (methylation). While 2-OH-E1 is considered a safe metabolite, it is still considered a reactive metabolite until methylated and inactivated. Elevated COMT activity shows more of 2-OH-E1 is being methylated, which is considered favorable. Over time, COMT enzyme may need additional support to keep up with demand. Comparing additional areas of COMT activity (i.e., 4-M-E1/ 4-OH-E1) may give more insight into the function of this enzyme.



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### Estrogens

#### ↓ 2-M-E2:2-OH-E2 (COMT/Methylation activity)

The relationship of 2-M-E2 / 2-OH-E2 represents the activity of COMT (methylation) enzyme. A low ratio indicates slower COMT activity. While 2-OH-E2 is considered a safe metabolite, it is still considered a reactive metabolite until methylated and inactivated. Comparing additional areas of COMT activity (i.e., 4-M-E1/ 4-OH-E1) may give more insight into the function of this enzyme.

#### ↑ 4-M-E1:4-OH-E1 (COMT/Methylation activity)

The relationship of 4-M-E1 / 4-OH-E1 represents the activity of COMT (methylation). 4-OH-E1 is considered unfavorable due to its carcinogenic potential within breast and prostatic tissue. Elevated COMT activity shows more of 4-OH-E1 is being methylated, which is considered favorable. Over time, COMT enzyme may need additional support to keep up with demand. Comparing additional areas of COMT activity (i.e., 2-M-E1/ 2-OH-E1) may give more insight into the function of this enzyme.

#### ↓ 4-M-E2:4-OH-E2 (COMT/Methylation activity)

The relationship of 4-M-E2 / 4-OH-E2 represents the activity of COMT (methylation) enzyme. A low ratio indicates slower COMT activity, which may mean a higher potential for the creation of quinones, semi-quinones, and depurinating adducts. Increasing COMT enzyme activity is a consideration.

#### ↓ 4-OH-E1:2-OH-E1

A low ratio can indicate a metabolic preference for the less favorable 4-OH-E1 pathway. Optimizing methylation to support the COMT enzyme can potentiate the more protective 2-OH-E1 pathway. Increasing the activity of CYP1A1 to increase 2-OH-E1 is a consideration.