

BONUS: Interpreting the DUTCH Test

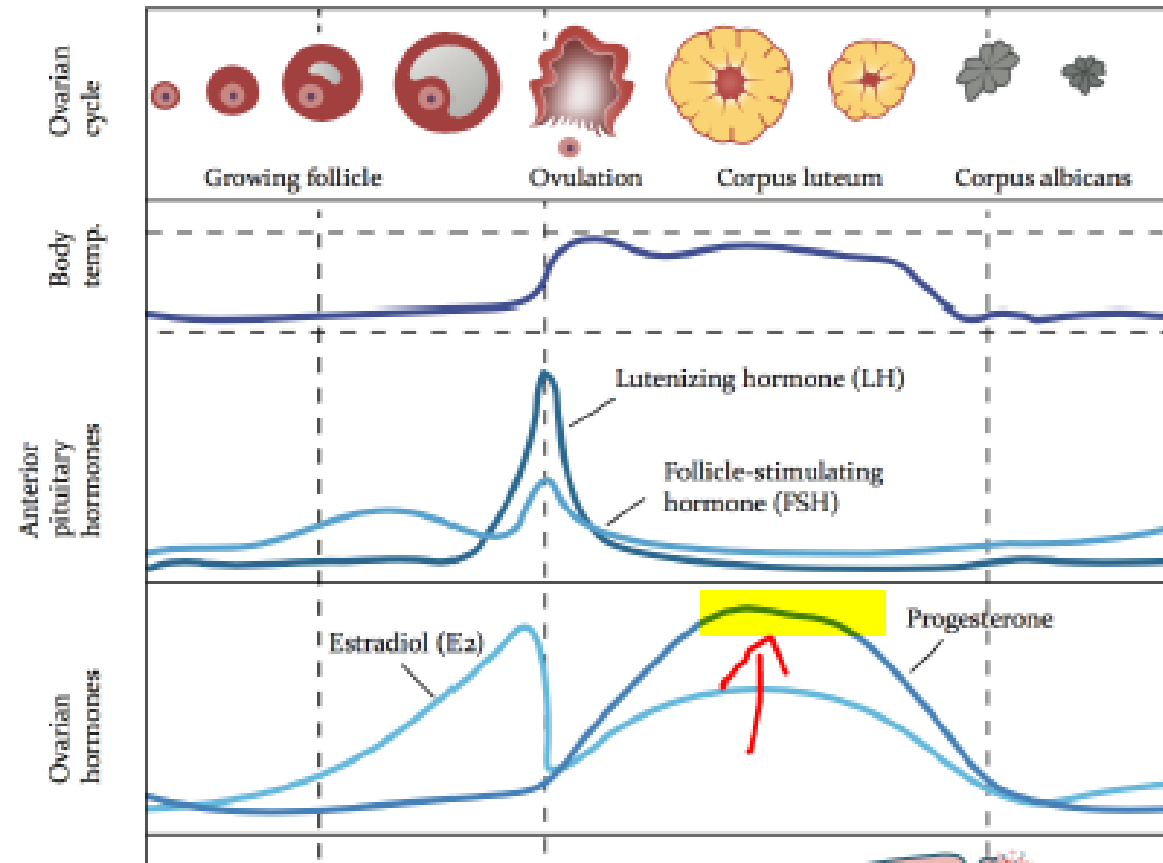
Hormones in Cycling Females

What You Can Learn from the DUTCH Test for a Cycling Female

- Relative abundance of estrogens, progesterone, and androgens
- Hormone Metabolism Patterns
 - Progesterone metabolism patterns that may affect sleep and mood.
 - Estrogen metabolism patterns that can influence breast & uterine cancer risk.
 - Androgen metabolism patterns that may help explain the person's symptoms of high androgens (hair loss, acne, etc.) or low androgens (inability to build muscle mass, weight gain, fatigue, etc.).
- Adrenal status
- Nutritional deficiencies, neurotransmitter metabolites, DNA damage marker (8OHdG), dysbiosis marker (indican), neuroinflammatory marker (quinolinate) and melatonin.
- DUTCH Testing can be used to monitor some forms of hormone replacement therapy (HRT).

Cycling Female

- Collect on days 19-22 of a 28-day cycle OR roughly 5-9 days BEFORE the next cycle is expected to start.



Tips on Collection: Irregular Cycles

- **Try to test for Ovulation using an Ovulation Predictor Kit (measures LH)**
 - LH starts to peak around 11am, so test mid-morning, not first morning void, for daily accuracy.
 - Collect 5-7 days after a positive LH.
- **Basal Body Temperature**
 - Body temp will rise (ever so slight) at ovulation.
 - Collect body temperature with special basal body thermometer. Measure first thing in the morning, while still in bed (key).
 - Track temperature daily from first day of menstrual bleed.
 - A temperature decrease followed by a rise of 0.5-1.0 F (or 0.3-0.6 C) signifies that ovulation likely took place the day before. Temperature falls at ovulation, and then will rise the next day as the corpus luteum starts generating progesterone.
 - Collect samples 5-7 days after the first temperature spike.

- **Multiple collections to determine mid-luteal phase for a DUTCH Complete or DUTCH Plus**
 - Start collection roughly 10 days before your earliest cycle has started.
 - Collect urine samples as though you're taking the full DUTCH (all 4 samples), let them dry completely, LABEL samples with the date, and FREEZE samples.
 - Collect urine samples again 2 days later, let samples dry completely, LABEL, and FREEZE.
 - Collect in this fashion every 2 days, until your period starts.
 - Go back roughly 8-9 days from your period start date, and send in JUST those samples, which likely fell right within the mid-luteal phase.

Reviewing Report

- Alerts about the report:
 - Some alerts are found on the bottom of page 1
 - Others are found at the back of the report (page #7)– see next slide.

dutchtest BY PRECISION ANALYTICAL INC. Accession # 00577274 Cycling Female Dutch Complete

PRECISION ANALYTICAL INC. SIMPLY BETTER TESTING

Ordering Provider: Precision Analytical **DOB:** 1989-06-29 **Age:** 32 **Sex:** Female

Last Menstrual Period: 2021-08-26
Collection Times: 2021-09-14 07:22AM, 2021-09-14 09:29AM, 2021-09-14 05:00PM, 2021-09-14 10:00PM

Hormone Testing Summary

Key (how to read the results):

Sex Hormones See Pages 2 and 3 for a thorough breakdown of sex hormone metabolites

Estradiol(E2) 1.80 - 4.50 Patient Result: 3.51	Progesterone (Serum Equivalent, ng/mL) 0.3-2.0 Patient Result: 17.3 <small>Progesterone Serum Equivalent is a calculated value based on urine pregnanediol.</small>	Testosterone 2.3 - 14.0 Patient Result: 9.1
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Adrenal Hormones See pages 4 and 5 for a more complete breakdown of adrenal hormones

Daily Free Cortisol Pattern

Total DHEA Production

Age	Range
20-39	1300-3000
40-60	750-2000
>60	500-1200

Age 65, Patient Result: 857

24hr Free Cortisol (A+B+C+D): 73
Metabolized Cortisol (THF+THE) (Total Cortisol Production): 3204

Free cortisol best reflects tissue levels. Metabolized cortisol best reflects total cortisol production.

The following videos (which can also be found on the website under the listed names along with others) may aid your understanding:
[DUTCH Complete Overview](#), [Estrogen Tutorial](#), [Female Androgen Tutorial](#), [Cortisol Tutorial](#)
PLEASE BE SURE TO READ BELOW FOR ANY SPECIFIC LAB COMMENTS. More detailed comments can be found on page 7.

Birth control; glucocorticoid use

Reviewing Report

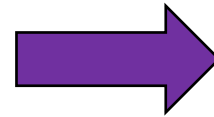
- Alerts about the report:
 - Found on page 7

Clinical Support Overview

Thank you for choosing DUTCH for your functional endocrinology testing needs! We know you have many options to choose from when it comes to functional endocrinology evaluation, and we strive to offer the best value, the most up-to-date testing parameters and reference ranges, and the greatest clinical support to ensure the most accurate results.

Please take a moment to read through the Clinical Support Overview below. These comments are specific to the patient's lab results. They detail the most recent research pertaining to the hormone metabolites, treatment considerations, and follow-up recommendations. These comments are intended for educational purposes only. Specific treatment should be managed by a healthcare provider. To view the steroid pathway chart, click here [Steroid Pathway Chart](#)

Alert comments:



Special notes, alerts about therapies, alerts about status of test (prelim, repeat, etc.).

Urine Hormones

- **Truly bio-available**

- To be a urine hormone, the hormone had to first be “seen” by your cells while passing through the bloodstream.

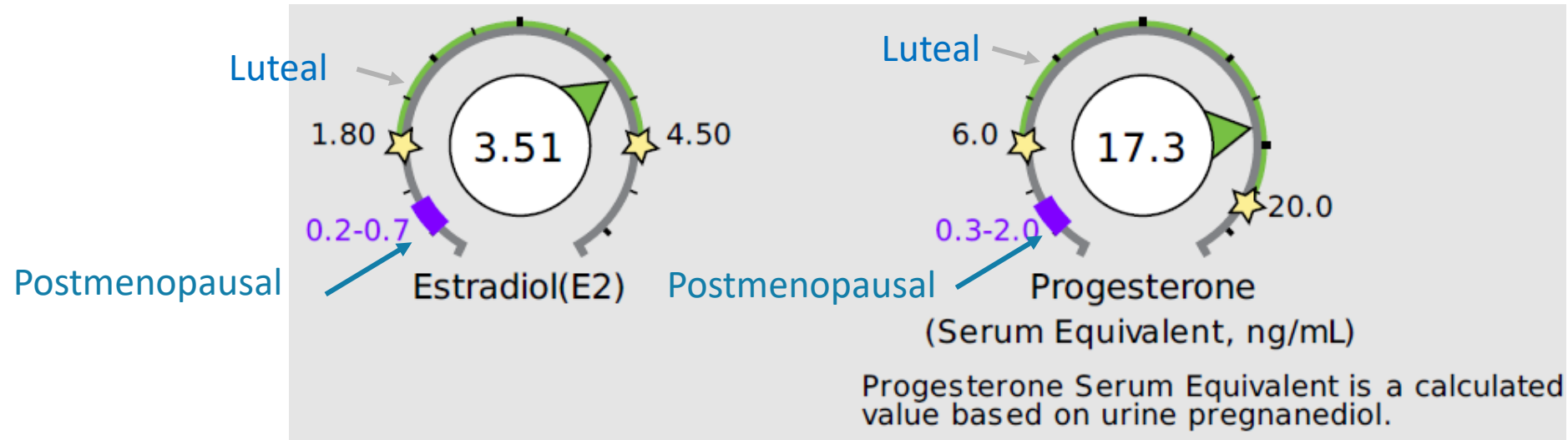
- **Waste Product**

- Urine captures the end-products of hormone clearance, helping ascertain how the cells are utilizing and metabolizing the hormones (for better or for worse).

- **Diurnal average**

- The patient is collecting samples at 4 major times over a 24-hour window.
- This captures the daily average of a given hormone or metabolite.
- Whereas blood or serum looks at a single point in time (the time the blood was drawn).

Reference Ranges



- Want to see progesterone (Pg) in an equal or higher percentile (higher up on the dial) than the estradiol (E2).
- When E2 is higher than Pg, even if E2 is not above the reference range, patient may have estrogen dominant symptoms.

Reference Ranges

Reference Range Determination (last updated 11.23.2021)

We aim to make the reference ranges for our DUTCH tests as clinically appropriate and useful as possible. This includes the testing of thousands of healthy individuals and combing through the data to exclude those that are not considered "healthy" or "normal" with respect to a particular hormone. As an example, we only use a premenopausal woman's data for estrogen range determination if the associated progesterone result is within the luteal range (days 19-21 when progesterone should be at its peak). We exclude women on birth control or with any conditions that may be related to estrogen production. Over time the database of results for reference ranges has grown quite large. This has allowed us to refine some of the ranges to optimize for clinical utility. The manner in which a metabolite's range is determined can be different depending on the nature of the metabolite. For example, it would not make clinical sense to tell a patient they are deficient in the carcinogenic estrogen metabolite, 4-OH-E1 therefore the lower range limit for this metabolite is set to zero for both men and women. Modestly elevated testosterone is associated with unwanted symptoms in women more so than in men, so the high range limit is set at the 80th percentile in women and the 90th percentile for men. Note: the 90th percentile is defined as a result higher than 90% (9 out of 10) of a healthy population.

Classic reference ranges for disease determination are usually calculated by determining the average value and adding and subtracting two standard deviations from the average, which defines 95% of the population as being "normal." When testing cortisol, for example, these types of two standard deviation ranges are effective for determining if a patient might have Addison's (very low cortisol) or Cushing's (very high cortisol) Disease. Our ranges are set more tightly to be optimally used for Functional Medicine practices.

Below you will find a description of the range for each test:

Female Reference Ranges (Updated 11.23.2021)									
	Low%	High%	Low	High		Low%	High%	Low	High
b-Pregnanediol	20%	90%	600	2000	Cortisol A (waking)	20%	90%	10	50
a-Pregnanediol	20%	90%	200	740	Cortisol B (morning)	20%	90%	30	130
Estrone (E1)	20%	80%	12	26	Cortisol C (~5pm)	20%	90%	7	30
Estradiol (E2)	20%	80%	1.8	4.5	Cortisol D (bed)	0	90%	0	14
Estriol (E3)	20%	80%	5	18	Cortisone A (waking)	20%	90%	40	120
2-OH-E1	20%	80%	5.1	13.1	Cortisone B (morning)	20%	90%	90	230
4-OH-E1	0	80%	0	1.8	Cortisone C (~5pm)	20%	90%	32	110
16-OH-E1	20%	80%	0.7	2.6	Cortisone D (bed)	0	90%	0	55
2-Methoxy-E1	20%	80%	2.5	6.5	Melatonin (6-OHMS)	20%	90%	10	85
2-OH-E2	0	80%	0	1.2	8-OHdG	0	90%	0	5.2
4-OH-E2	0	80%	0	0.5	Methylmalonate	0	90%	0	2.2
DHEA-S	20%	90%	20	750	Xanthurenate	0	90%	0	1.4
Androsterone	20%	80%	200	1650	Kynurenate	0	90%	0	7.3
Etiocholanolone	20%	80%	200	1000	Pyroglutamate	10%	90%	32	60
Testosterone	20%	80%	2.3	14	Homovanillate	10%	95%	4	13
5a-DHT	0	80%	0	6.6	Vanilmandelate	10%	95%	2.4	6.4
5a-Androstenediol	20%	80%	6	30					
5b-Androstenediol	20%	80%	20	75					
Epi-Testosterone	20%	80%	2.3	14	Calculated Values				
a-THF	20%	90%	75	370	Total DHEA Production	20%	80%	500	3000
b-THF	20%	90%	1050	2500	Total Estrogens	20%	80%	35	70
b-THE	20%	90%	1550	3800	Metabolized Cortisol	20%	90%	2750	6500
					24hr Free Cortisol	20%	90%	65	200
					24hr Free Cortisone	20%	90%	220	450

% = population percentile: Example - a high limit of 90% means results higher than 90% of the women tested for the reference range will be designated as "high."

- Some androgen metabolites are measured, but not yet plotted in visual form. They can be found on page 2 of the DUTCH Complete or DUTCH Plus reports, or page 1 of the Sex Hormone-only reports.

Androgens and Metabolites (Urine)				
DHEA-S	Below range	9.0	ng/mg	20 - 750
Androsterone	Low end of range	422.0	ng/mg	200 - 1650
Etiocholanolone	Low end of range	232.0	ng/mg	200 - 1000
Testosterone	Within range	5.2	ng/mg	2.3 - 14
5a-DHT	Low end of range	1.04	ng/mg	0 - 6.6
5a-Androstenediol	Within range	12.7	ng/mg	6 - 30
5b-Androstenediol	Low end of range	24.2	ng/mg	20 - 75
Epi-Testosterone	Within range	9.3	ng/mg	2.3 - 14

A Note About Androgens

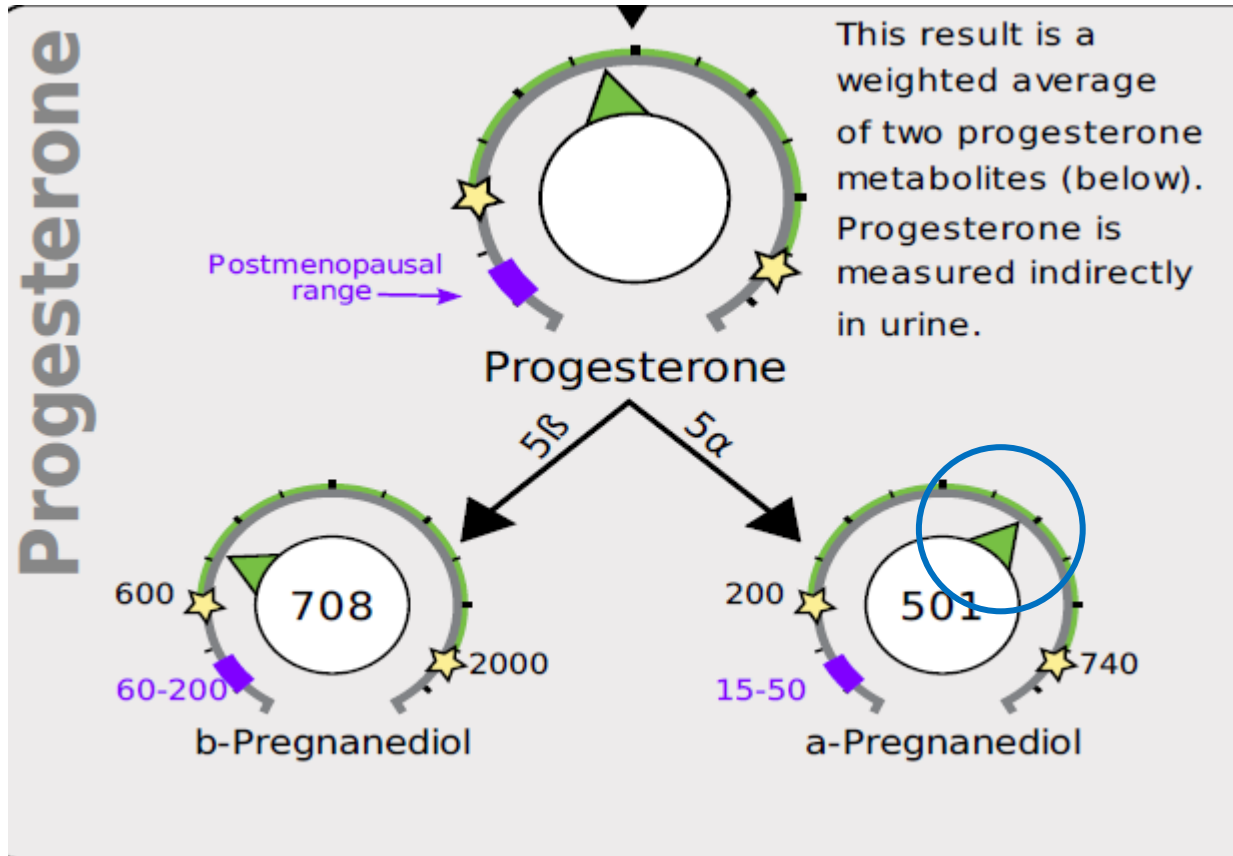
- 5 α -reductase is the enzyme responsible for metabolizing DHEA and testosterone into their active, androgenic metabolites.
 - DHEA \rightarrow Androsterone (~ 7x weaker than testosterone)
 - Testosterone \rightarrow DHT (4x more potent than testosterone)
 - 5 α -Androstane-3 α ,20-diol = end-clearance of ALL 5 α metabolites
- Increased 5 α -reductase activity is associated with inflammation, elevated circulating blood sugar (insulin resistance, sudden cortisol surge, exercise), and it may also be more common in women with PCOS.

- When DHT is high, it can help with skeletal muscle turnover, improving strength.
- DHT damages hair follicles, increasing body hair and decreasing scalp hair growth.
- DHT can cause cystic acne development.
- DHT can act as a neuro-steroid and increase agitation.

Take home from page 2

- It is important to check the 5a-DHT level, and overall 5a-reductase preference (is 5a-androstanediol high?) especially if a female is struggling with acne, scalp hair loss, or excess body hair growth.

- In the upper right corner, you will find progesterone.
- We measure progesterone's alpha- and beta-pregnenediol metabolites.
- Most of progesterone gets metabolized into pregnenediol.
- However, the small amount of a-pregnenediol that crosses the blood brain barrier improves the brain's GABA response.
- Measure alpha-pregnenediol's response, not by the absolute value, but rather by where the dial falls when compared to beta-pregnenediol.



- Here we see a higher value for the a-pregnanediol metabolite when compared to beta-pregnanediol.
- Optimally, alpha- and beta-pregnanediol should be balanced.
- Some research suggests that progesterone's 5-alpha metabolites may have proliferative effects.

- Estrone and estradiol are the primary parent estrogens in circulation.
- Produced predominately in the ovary, although fat tissue and the adrenals will also contribute to small amounts of production.

- Recall, all sex hormones are steroid-based hormones (meaning they are built from cholesterol).
- For a steroid hormone to become inert, it must bio-transform through a multi-step process, the first two steps capture urine excreted metabolites (phase 1 and phase 2 detoxification).
- Phase 1 detoxification uses the CYP450 enzyme family to convert estradiol from a fat-based hormone, to a water-soluble hormone.

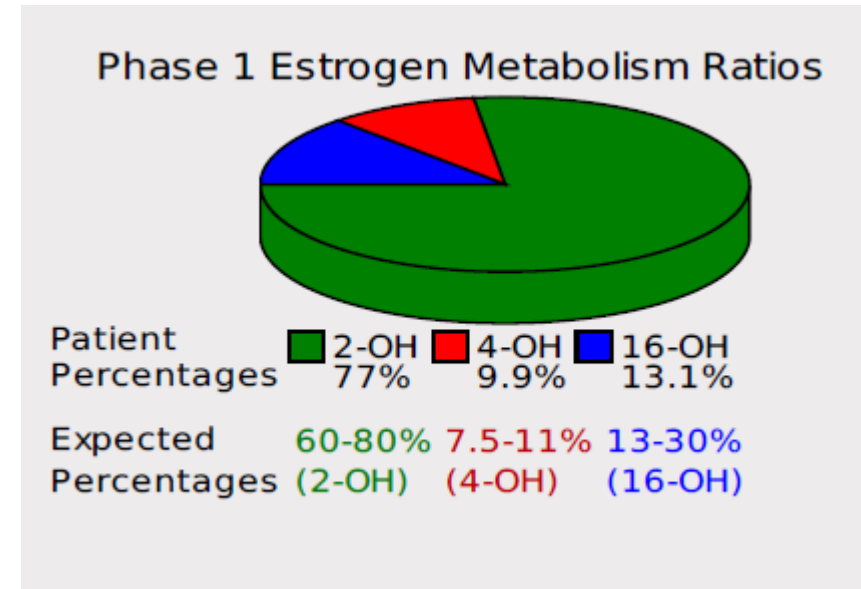
Phase 1 Detoxification

- The 3 enzymes of the CYP450 family for estrogen detoxification are:
 - CYP1A1 → 2-OH-Estrogen (E1) (good)
 - Usually considered a “better estrogen” than 16-OH E1 and 4-OH-E1. Waits patiently for methyl donors to clear out safely from tissue.
 - If not methylated, it too, may become a toxic intermediary.
 - CYP3A4 → 16-OH- Estrogen (bad)
 - A tissue proliferator. Although not associated with cancer causation, if an estrogen-sensitive tumor is present, it may cause it to grow more rapidly (also triggers growth of fibrocystic breasts, fibroids, cysts, and endometrial tissue).
 - CYP1B1 → 4-OH-Estrogen (ugly)
 - Can transform to quinones that cause unstable adducts on DNA, which can, over time, result in damage and even increase cancer risk.

- **The importance of the pie chart**
 - Besides looking at the metabolite values, it is important to know each metabolite's percentage relative to each other and the expected ranges.
 - This is the importance of the pie chart.

Phase 1 Detoxification

- This patient's phase 1 metabolites:
 - 77% are from the 2-OH pathway
 - 9.9% are from the 4-OH pathway
 - 13.1% are from the 16-OH pathway



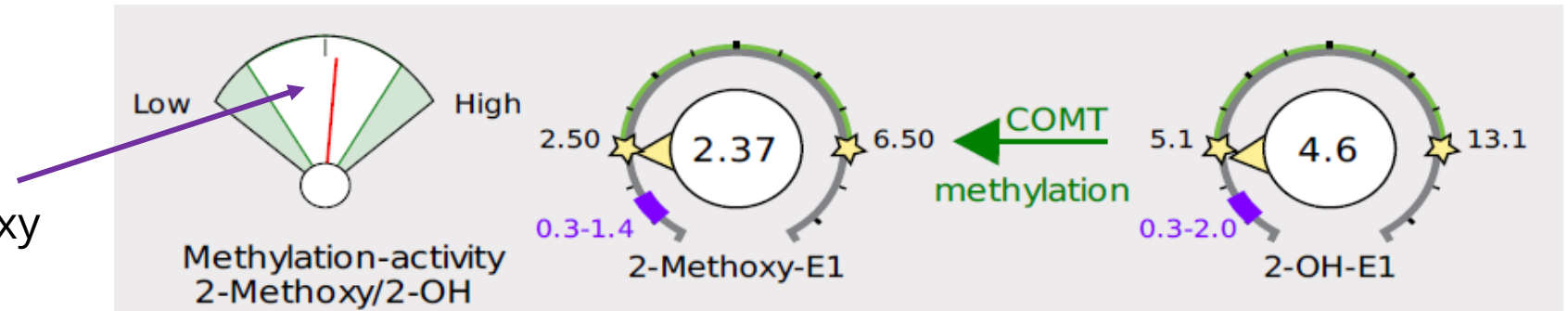
Phase 2 Detoxification

- Phase 1 is not the end
- Phase 1 intermediates must methylate to become completely inactive
- Catechol estrogen methylation is dependent on:
 - COMT activity
 - SAMe availability

Phase 2 Detoxification

- The methylation gauge reflects a ratio. If SAME is available and COMT is functioning normally, at least half of 2-OH-E1 will transform to 2-Methoxy-E1.

- If half of 2-OH-E1 is transforming to 2-Methoxy E1, then the dial will be near the middle

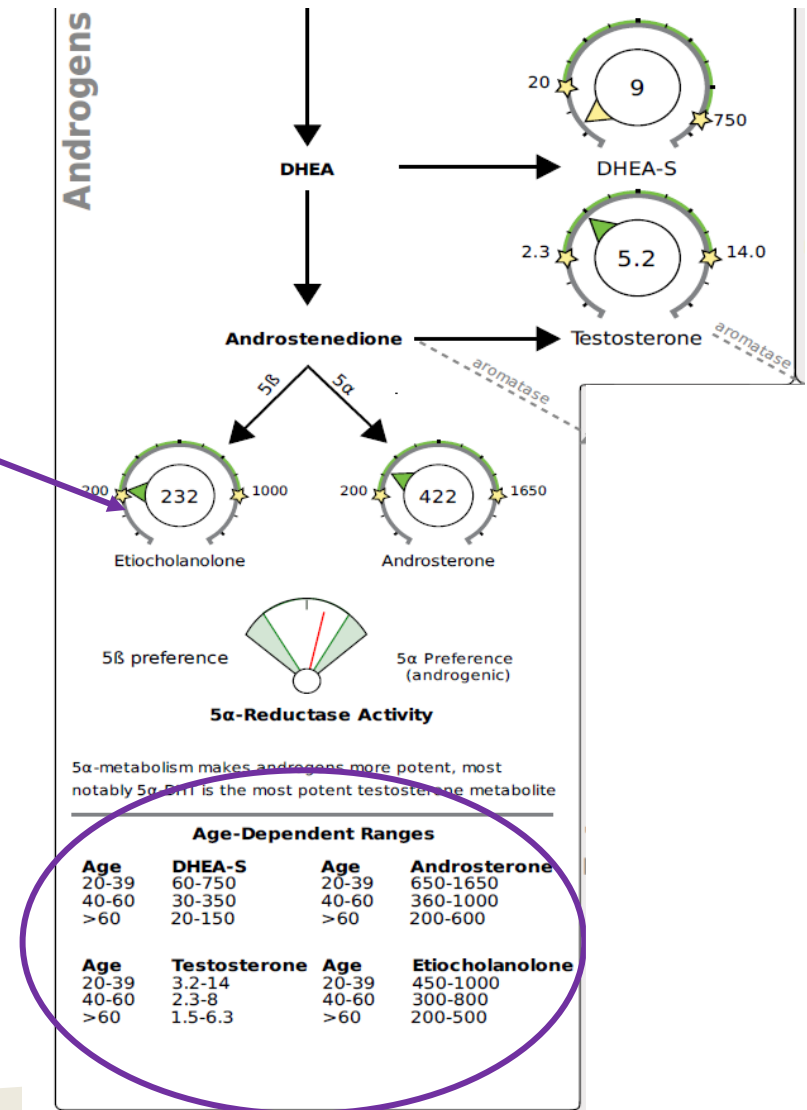


- On the left side of the hormone profile, you will see DHEA and testosterone markers.
- DHEA-S is only produced in the adrenals. The sulfur group stabilizes DHEA in the bloodstream, so that it can reach target tissues like the brain, bone, and skeletal muscles.
- When DHEA is used by the tissues, it will get metabolized to androsterone or etiocholanolone.

- To know how much DHEA is being produced, it is important consider:
 - How much remained in circulation throughout the day (DHEA-S) and
 - How much was metabolized by our body to etiocholanolone and androsterone
- **Lab note: androsterone will more closely match SERUM DHEA-S levels**

- When assessing DHEA, check:
 - DHEA-S vs. metabolites
 - 5 α /5 β preference
 - Age-expected range
 - Testosterone: refer to page 2 notes above

• **NOTE: Lower DHEA-S in the presence of HIGH DHEA metabolites can be a pattern suggesting inflammation**



Thank You!

If you are interested in learning more about hormones, each week we hold one-hour long mentorship sessions! Once you are a registered DUTCH provider, you can book these through our online scheduling link. Please call to get registered today.

For questions, contact:

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