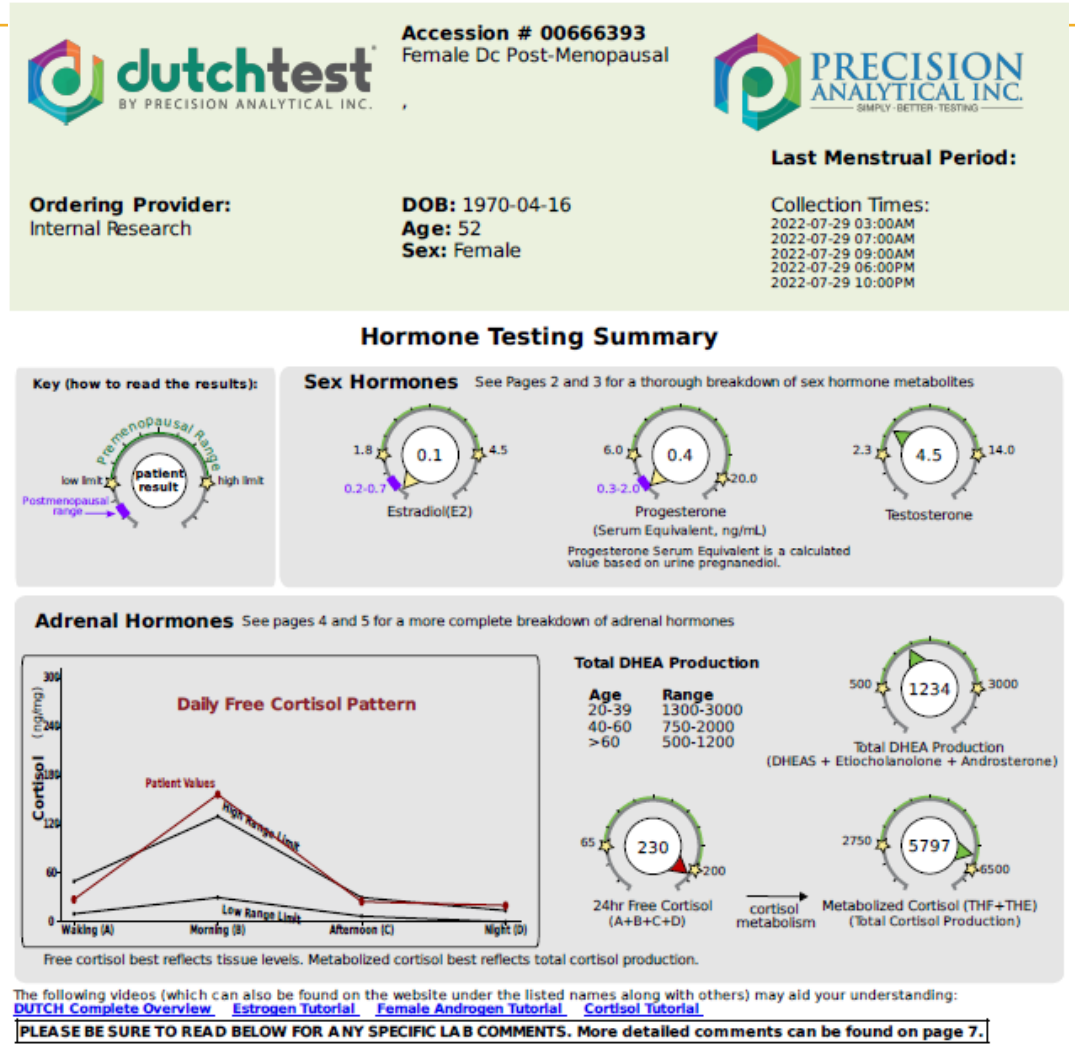
BONUS: Interpreting the DUTCH Test

In a Postmenopausal Female

dutch®

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 # 00666393
Female Dc Post-Menopausal
,

PRECISION ANALYTICAL INC. SIMPLY · BETTER · TESTING

Last Menstrual Period:

Ordering Provider:
Internal Research

DOB: 1970-04-16
Age: 52
Sex: Female

Collection Times:
2022-07-29 03:00AM
2022-07-29 07:00AM
2022-07-29 09:00AM
2022-07-29 06:00PM
2022-07-29 10:00PM

Hormone Testing Summary

Key (how to read the results):
Premenopausal Range
low limit
patient result
high limit
Postmenopausal range

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

Estradiol(E2): 1.8 | 0.1 | 4.5 (0.2-0.7)
Progesterone (Serum Equivalent, ng/mL): 6.0 | 0.4 | 20.0 (0.3-2.0)
Testosterone: 2.3 | 4.5 | 14.0

Progesterone Serum Equivalent is a calculated value based on urine pregnanediol.

Adrenal Hormones See pages 4 and 5 for a more complete breakdown of adrenal hormones

Daily Free Cortisol Pattern
Cortisol (ng/mg)
Patient Values
High Range Limit
Low Range Limit
Waking (A) | Morning (B) | Afternoon (C) | Night (D)

Total DHEA Production

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

500 | 1234 | 3000
Total DHEA Production (DHEAS + Etiocholanolone + Androsterone)

65 | 230 | 200
24hr Free Cortisol (A+B+C+D)

cortisol metabolism

2750 | 5797 | 6500
Metabolized Cortisol (THF+THE) (Total Cortisol Production)

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.

glucocorticoid use, oral progesterone use comment, etc.

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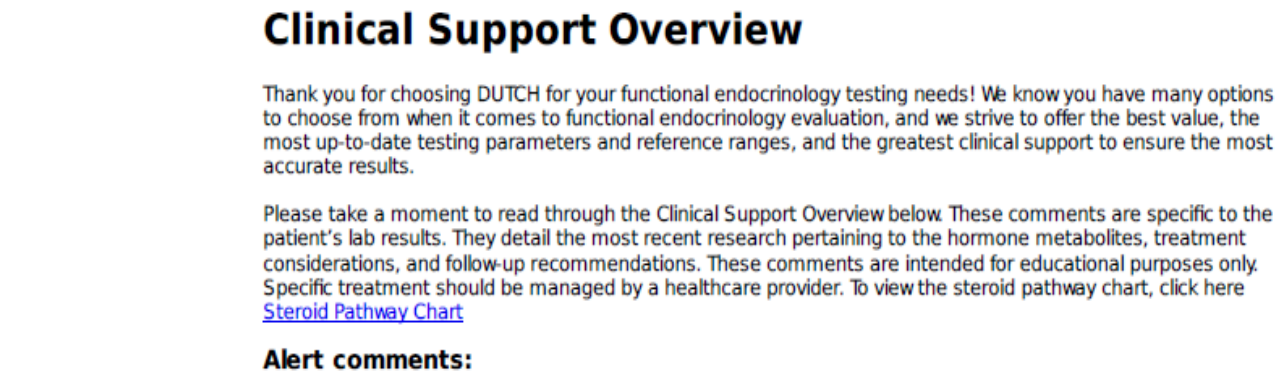
Reviewing Report

- 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.).

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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).

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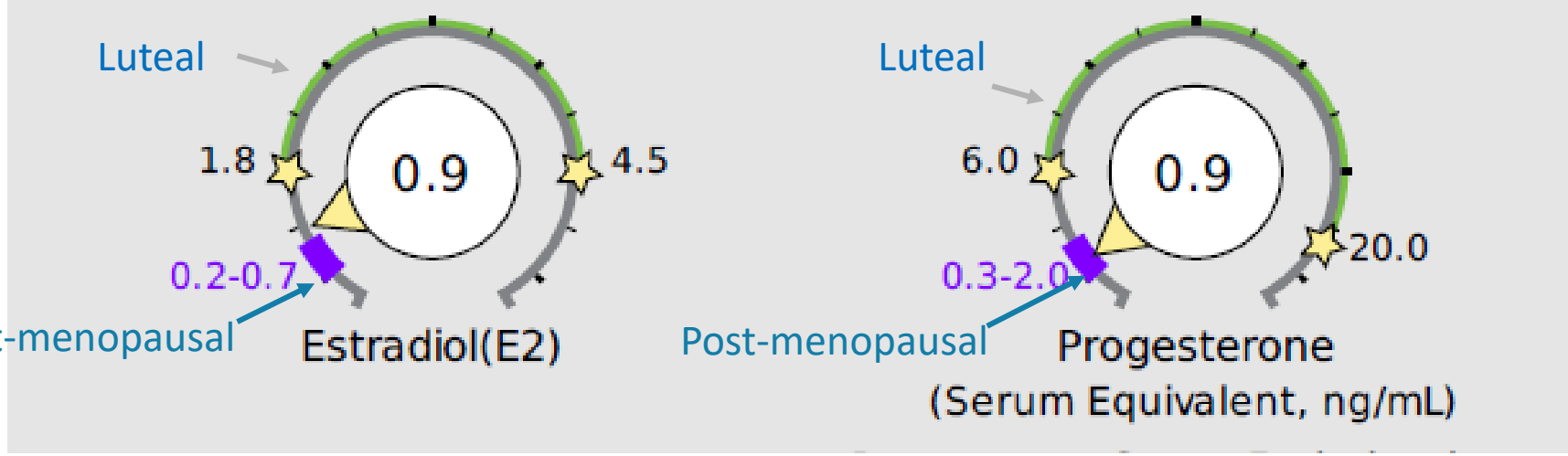
Reference Ranges



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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-Androstanediol	20%	80%	6	30					
5b-Androstanediol	20%	80%	20	75	**Calculated Values**				
Epi-Testosterone	20%	80%	2.3	14	Total DHEA Production	20%	80%	500	3000
a-THF	20%	90%	75	370	Total Estrogens	20%	80%	35	70
b-THF	20%	90%	1050	2500	Metabolized Cortisol	20%	90%	2750	6500
b-THE	20%	90%	1550	3800	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."

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Page 2

- 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-Androstanediol	Within range	12.7	ng/mg	6 - 30
5b-Androstanediol	Low end of range	24.2	ng/mg	20 - 75
Epi-Testosterone	Within range	9.3	ng/mg	2.3 - 14

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A Note About Androgens

- 5a-reductase is the enzyme responsible for metabolizing DHEA and testosterone into their active, androgenic metabolites.
  - DHEA → Androsterone (~ 7x weaker than testosterone)
  - Testosterone → DHT (4x more potent than testosterone)
  - 5a-Androstanediol = end-clearance of ALL 5a metabolites
- Increased 5a-reductase activity is associated with inflammation, elevated circulating blood sugar (insulin resistance, sudden cortisol surge, exercise), and it may be favored genetically.

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DHT

- 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.

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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.

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Page 3- Progesterone

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

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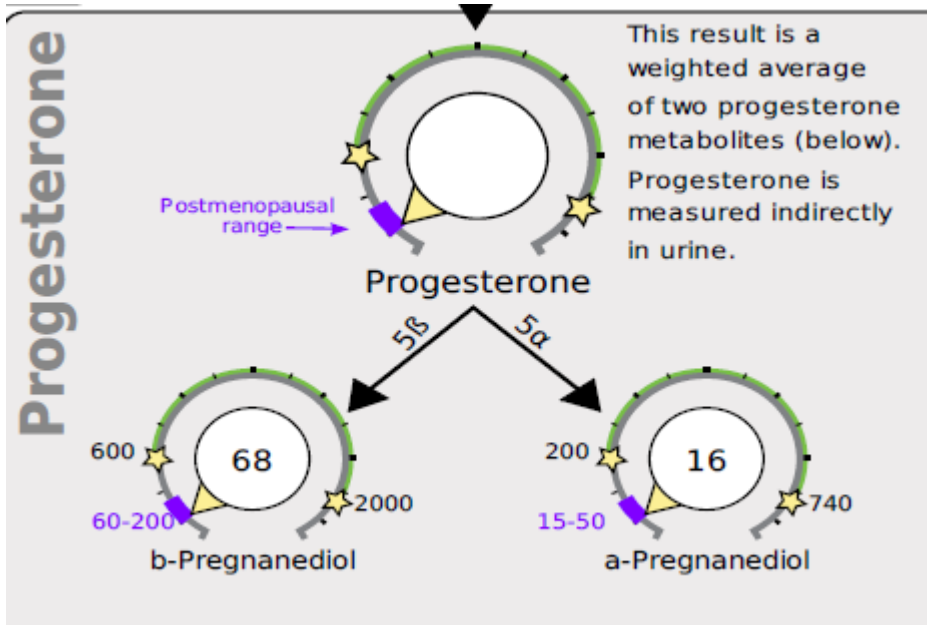

- If a <u>postmenopausal</u> female is not taking bioidentical hormones or pregnenolone, then the progesterone she produces will be sourced SOLEY from the adrenals.
  - The ovaries are not functioning and no longer contribute to estrogen and progesterone sex hormone production.
  - Pregnenolone metabolites are seen on the DUTCH test as 5-alpha- and beta-pregnanediol
- Under normal circumstances (not acute stress), adrenal production of progesterone is very minimal.
- With the loss of a-pregnanediol's effect on the brain's GABA response, it is not uncommon for postmenopausal females to struggle with insomnia and anxiety (less GABA)

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Page 3- Estrogen

- Estrone and estradiol are the primary parent estrogens in circulation.
- Produced predominately in the ovary in cycling females, although fat tissue and the adrenals will also contribute to small amounts of production.
- For a post-menopausal female, production will be SOLEY from the adrenals and fat tissue.

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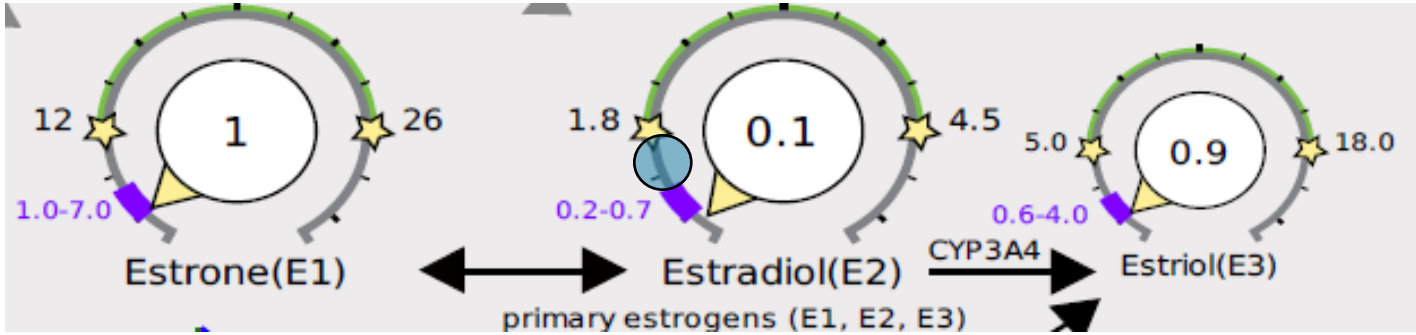
Page 3- Estrogen

- Although expected, the perimenopausal and postmenopausal sudden decline in estradiol are associated with bone loss, increased cardiovascular events, and cognitive decline.



- In serum, the E2 bone protective range established using an LC-MS/MS assay is 20-40 pg/mL
- Using DUTCH, this equates to 0.7-1.8 ng/mg, or right in the gap between the postmenopausal box and the low-end luteal star.

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Page 3 – Phase 1 Detoxification

- 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.

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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 (uterine, breast cancers, etc).

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Phase 1 Detoxification

- 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.

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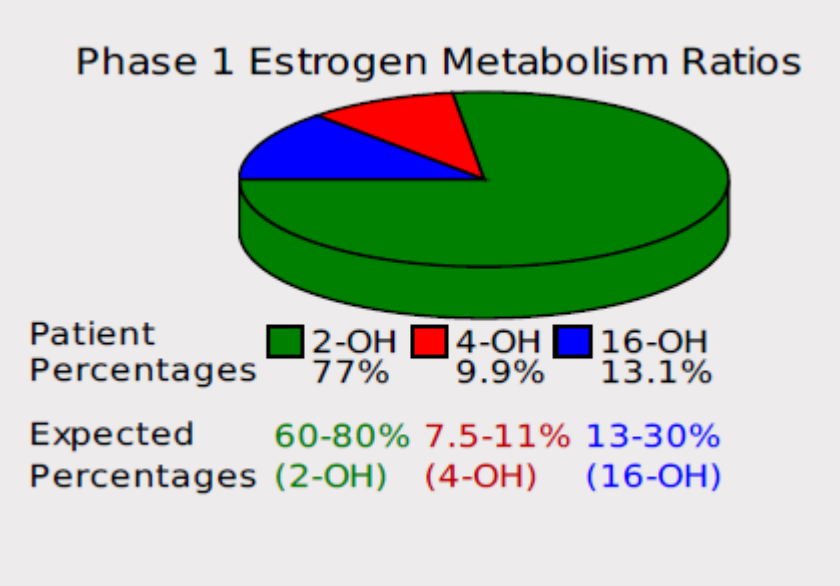
Phase 1 Detoxification

- 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



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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

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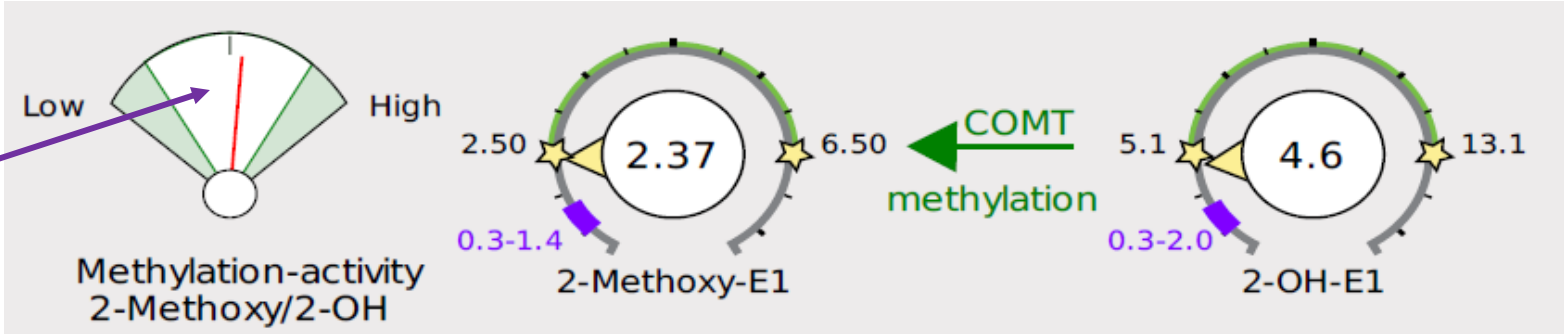
Phase 2 Detoxification

- 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



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Page 3 – Androgens

- 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.

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Page 3 – Androgens

- 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**

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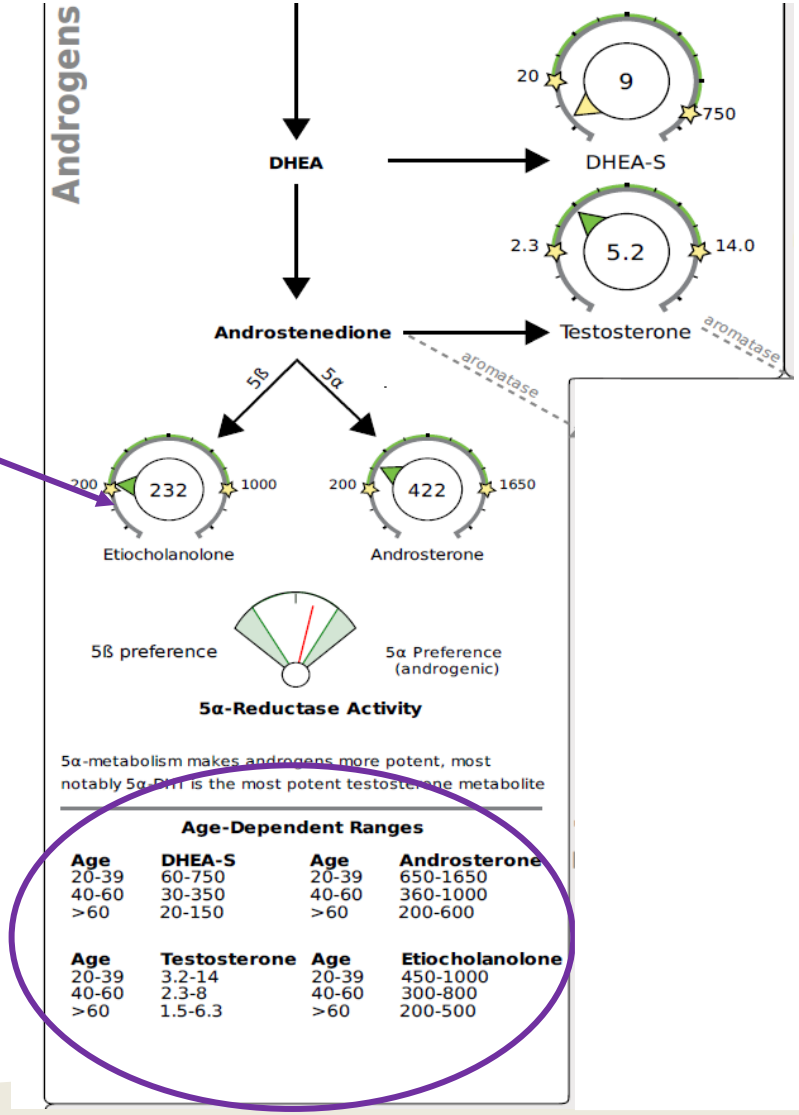
- When assessing DHEA, check:
  - DHEA-S vs. metabolites
  - 5a/5b preference
  - Age-expected range
  - Testosterone



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

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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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