



# Androgen Interpretation

Mastering the Science Using the DUTCH Advanced Insights

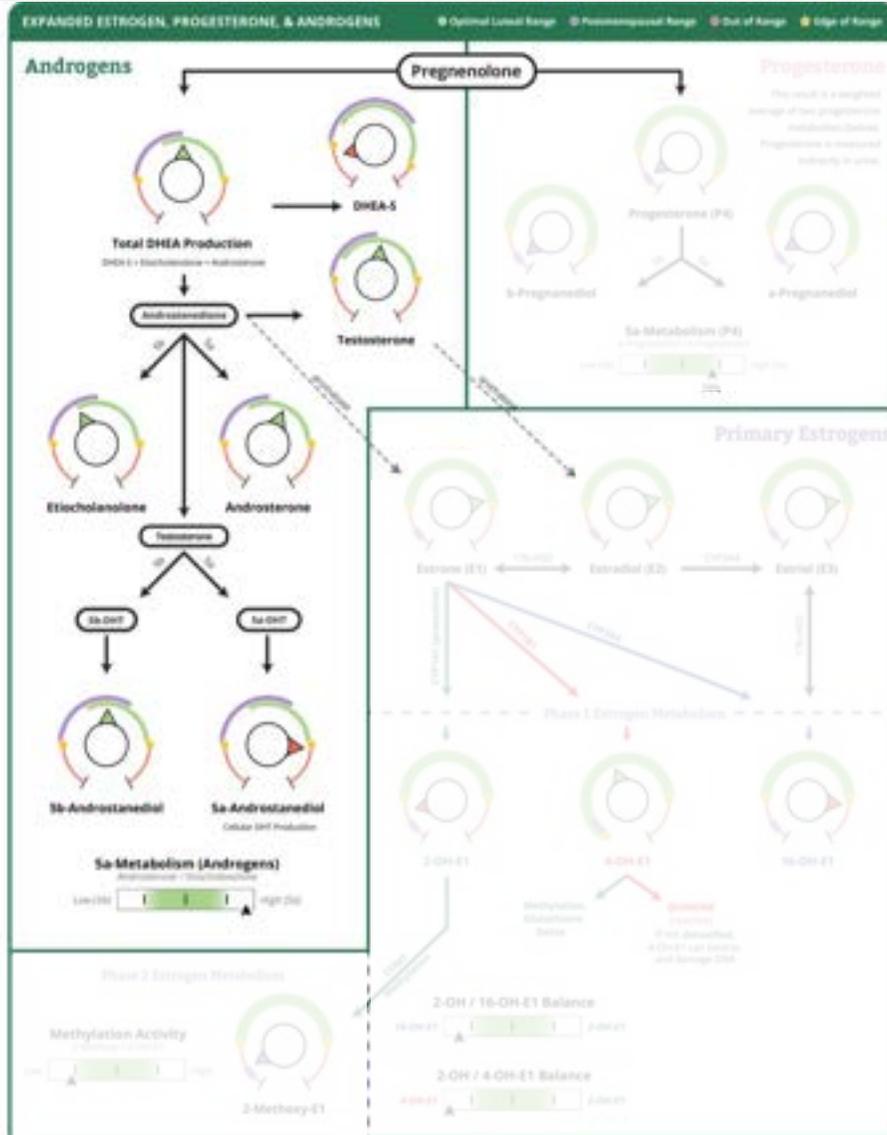
Carrie Jones, ND, FABNE, MPH, MSCP



## Carrie Jones, ND, MPH

Carrie Jones, ND, FABNE, MPH, MSCP is an internationally recognized speaker, consultant, author and educator on the topic of women's health and hormones with over 20 years in the industry. Dubbed the "Queen of Hormones," Dr. Jones is a Naturopathic Physician who did her 2-year residency focused on women's health and endocrinology. She went on to get her Master of Public Health (MPH), was one of the first to become board certified through the American Board of Naturopathic Endocrinology (FABNE), and is a Menopause Society Certified Practitioner (MSCP). She was the first Medical Director for Precision Analytical (the DUTCH Test), the first Head of Medical Education at Rupa Health (a Fullscript Company) and was on Under Armour's Human Performance Council. She serves as a consultant and educator for several women's health and lab-focused companies. Dr. Jones co-hosted the highly popular show, the Root Cause Medicine Podcast that has over 10 million downloads and now hosts her own, Hello Hormones podcast. She is the Chief Medical Officer at NuEthix Formulations.

# A DUTCH Androgen Advanced Insights: Digging Deeper with Pages 2, 3



Page 2

## DUTCH Dozen (page 1)

- Page 1 – Total DHEA Production, Testosterone, 5a-Androstanediol, 5a-Metabolism Slider

## DUTCH Androgen Advanced Insights (pages 2 & 3)

- Page 2 – Detailed DHEA & Testosterone Metabolism
- Page 3 – Individual listings, including 5a-DHT, Epi-T

## DUTCH Androgen-Related OATs (page 6)

### Sex Hormones & Metabolites

TEST	RESULT	UNITS	Range
<b>Androgens and Metabolites (Urine)</b>			
DHEA-S	Within range	193.2	ng/mg 20 - 750
Androsterone	Within range	607.5	ng/mg 200 - 1650
Etiocholanolone	Within range	634.9	ng/mg 200 - 1000
Testosterone	Within range	5.56	ng/mg 2.3 - 14
5a-DHT	Within range	3.3	ng/mg 0 - 6.6
5a-Androstanediol	Within range	17.0	ng/mg 6 - 30
5b-Androstanediol	Above range	106.9	ng/mg 12 - 75
Epi-Testosterone	Within range	5.6	ng/mg 2.3 - 14

Page 3

# Learning Objectives

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- Understand the purpose and clinical application of the four **androgen-related** DUTCH Advanced Insights.
- Evaluate the balance between **DHEA-S** and the **Total DHEA Production** and its association with inflammation.
- Assess whether urine testosterone accurately reflects systemic levels, considering the impact of the **UGT2B17 deletion**.
- Assess whether **5a-DHT** levels confirm cellular androgen activity represented by 5a-androstanediol.
- Identify abnormalities in **androgen-related organic acids** and understand their relevance to androgen imbalances.



## Estrogen Progesterone

- 1 Assess estrogen levels given the patient's reproductive status
- 2 Assess progesterone levels given the patient's reproductive status
- 3 Assess 2-OH preference in phase 1 estrogen metabolism
- 4 Assess methylation of 2-OH estrogens

## Androgens

- 5 Assess adrenal androgen levels (Total DHEA)
- 6 Assess testosterone levels
- 7 Assess cellular production of 5a-DHT via 5a-androstenediol
- 8 Assess if there is a preference for the more potent alpha metabolism of the androgens

## Cortisol

- 9 Assess the daily free cortisol pattern
- 10 Assess the daily total of free cortisol in circulation (24hr Free Cortisol)
- 11 Assess the total cortisol produced by the adrenal glands (Metabolized Cortisol)
- 12 Assess the rate of cortisol clearance from the body

Dutch Advanced Insights

## Estrogen Progesterone

- 1 Assess whether E1, E3, or 16-OH-E1 add more insight into overall estrogenic activity
- 2 Assess if there is a preference for alpha metabolism of progesterone
- 3 Assess estrogen clearance through phase 1 and 2
- 4 Assess whether any of the estrogen-related organic acids are out of range

## Androgens

- 5 Assess if the DHEA-S is relatively lower than the Total DHEA
- 6 Assess the androgen pattern to determine if urine testosterone may not accurately reflect systemic levels (UGT2B17)
- 7 While 5a-androstanediol best represents **cellular** 5a-DHT production, assess if 5a-DHT offers additional insight into androgenic activity
- 8 Assess whether any of the androgen-related organic acids are out of range

## Cortisol

- 9 Assess if cortisone (inactive) adds more insight to the free cortisol assessment
- 10 Assess if there is a whole-body preference for (inactive) cortisone or (active) cortisol
- 11 Assess for anabolic-catabolic balance
- 12 Assess whether any of the cortisol-related organic acids are out of range

## DUTCH Dozen Androgens

- 5 Assess adrenal androgen levels (Total DHEA)
- 6 Assess testosterone levels
- 7 Assess cellular production of 5a-DHT via 5a-androstanediol
- 8 Assess if there is a preference for the more potent alpha metabolism of the androgens

## Advanced Insights Androgens

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- 6 Assess the androgen pattern to determine if urine testosterone may not accurately reflect systemic levels (UGT2B17)
- 7 While 5a-androstanediol best represents **cellular** 5a-DHT production, assess if 5a-DHT offers additional insight into androgenic activity
- 8 Assess whether any of the androgen-related organic acids are out of range

May change your DUTCH Dozen based conclusions

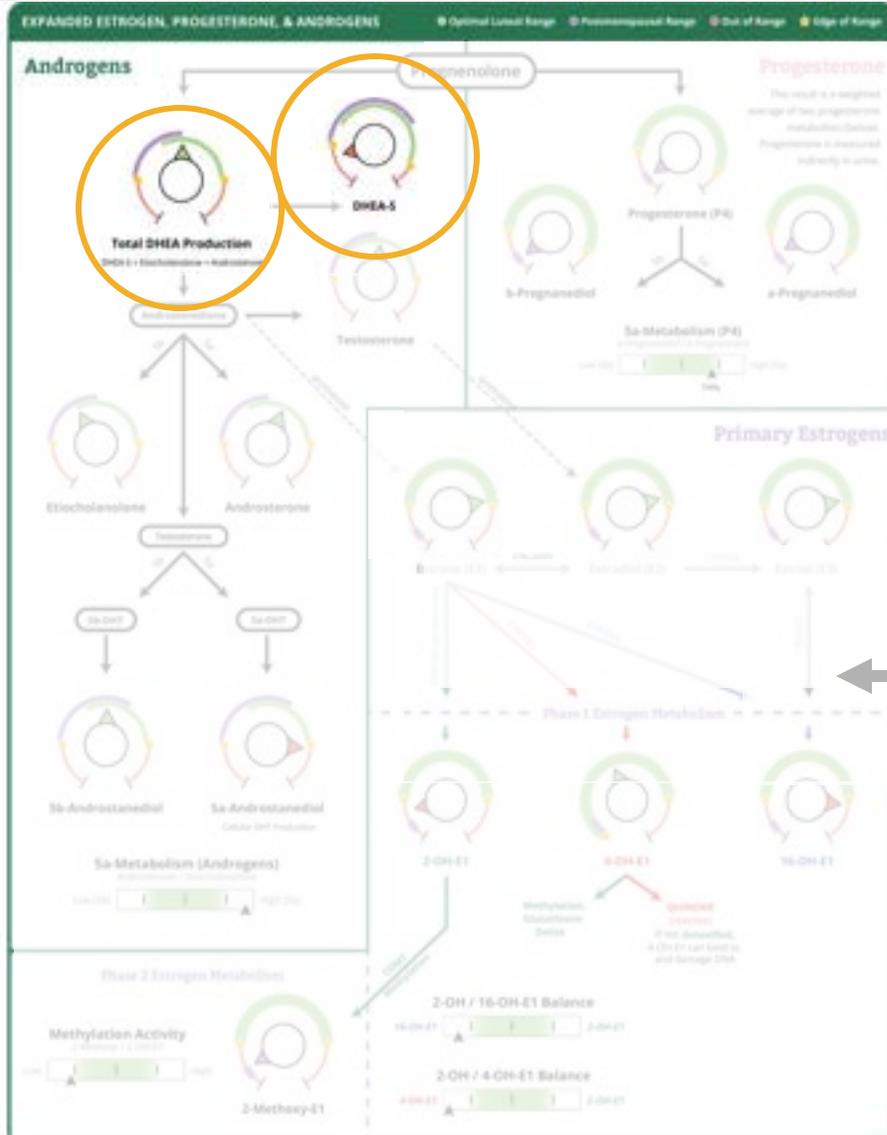
Provide additional information that will add to (but likely won't change) your DUTCH Dozen based conclusions

# DUTCH Advanced Insights

## DHEA-S vs. Total DHEA



# A DUTCH Advanced Insights: 5 DHEA-S vs Total DHEA



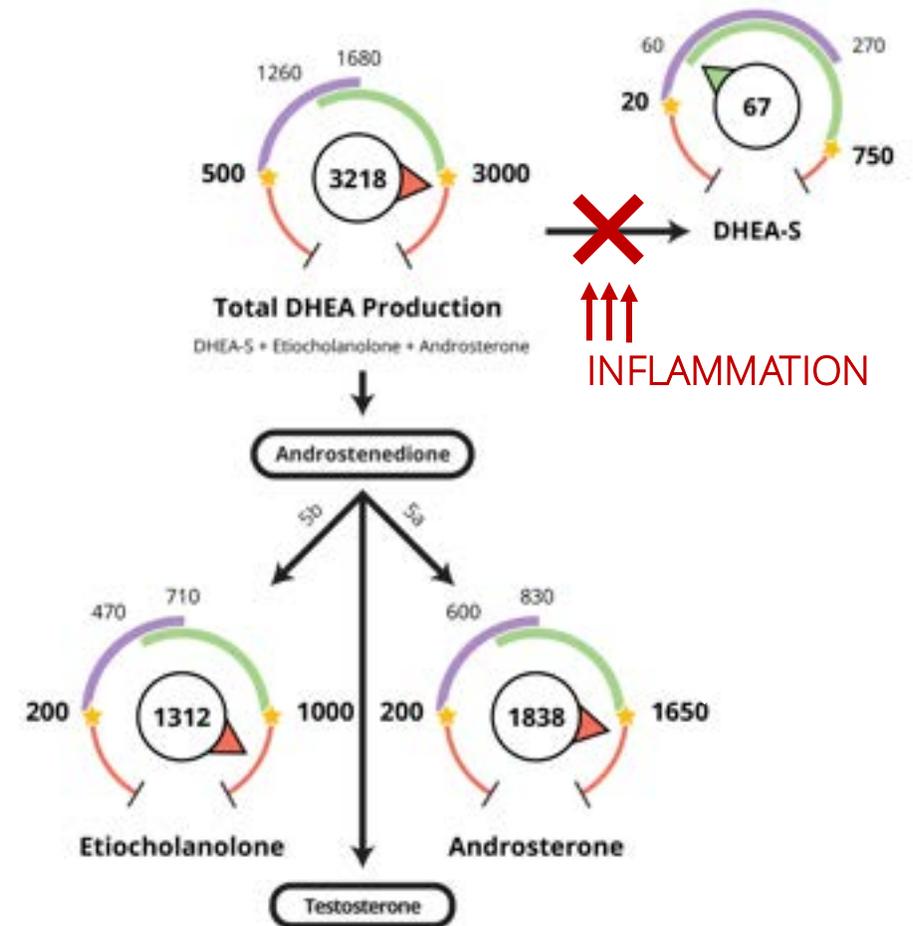
## Androgens

- 5 Assess if the DHEA-S is relatively lower than the Total DHEA

Page 2

# A DUTCH Advanced Insights: 5 DHEA-S vs Total DHEA

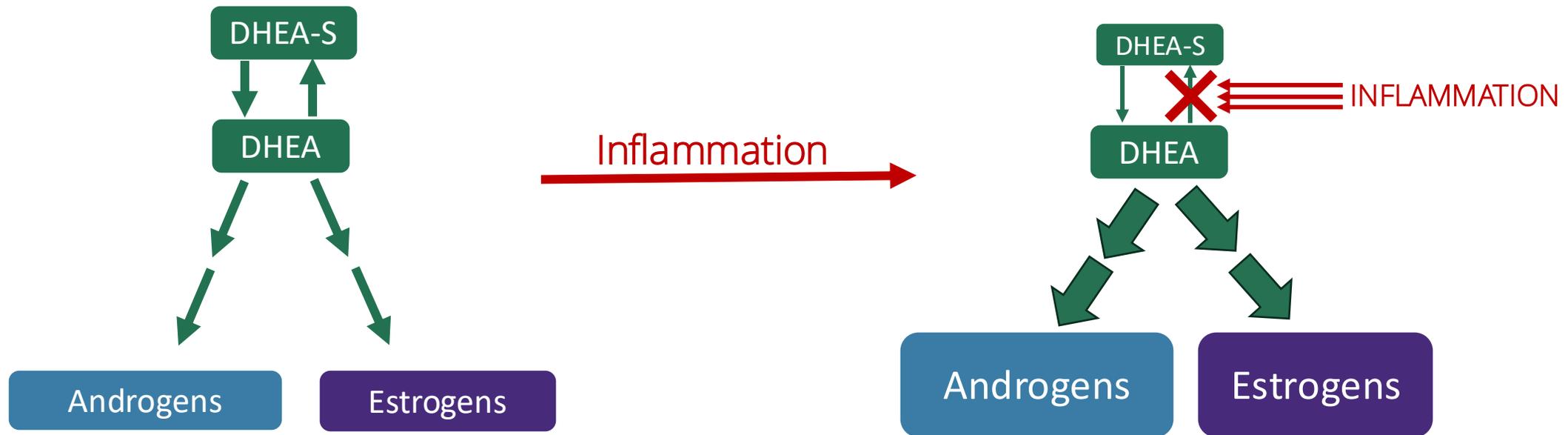
- **Research suggests that serum DHEA-S lowers relative to DHEA with acute inflammatory stress.**
- This inflammatory stress may be impairing the sulfation process.
- Therefore, if DHEA-S is relatively lower than the Total DHEA Production, inflammation may be:
  - Inhibiting the sulfation of DHEA to DHEA-S
  - Resulting in **more** downstream DHEA conversion into Etiocholanolone and Androsterone.



Straub RH, et al. Eur J Endocrinol. 2002 Mar;146(3):365-74.

## Why is this important?

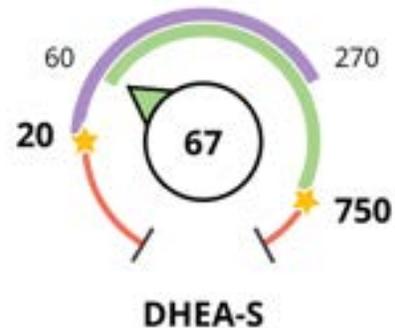
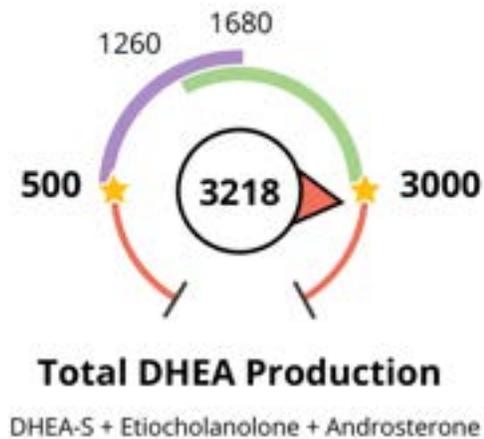
- When less DHEA is sulfated into DHEA-S, then more of it is available to be converted downstream into **active androgens and estrogens**.
- This can increase the androgenic and estrogenic activity in the body that may or may not be desirable!



# A DUTCH Advanced Insights: 5 DHEA-S vs Total DHEA

## How do we assess this?

- Visually, compare the DHEA-S level to the Total DHEA Production.
- **Evaluate each against its respective reference range.**



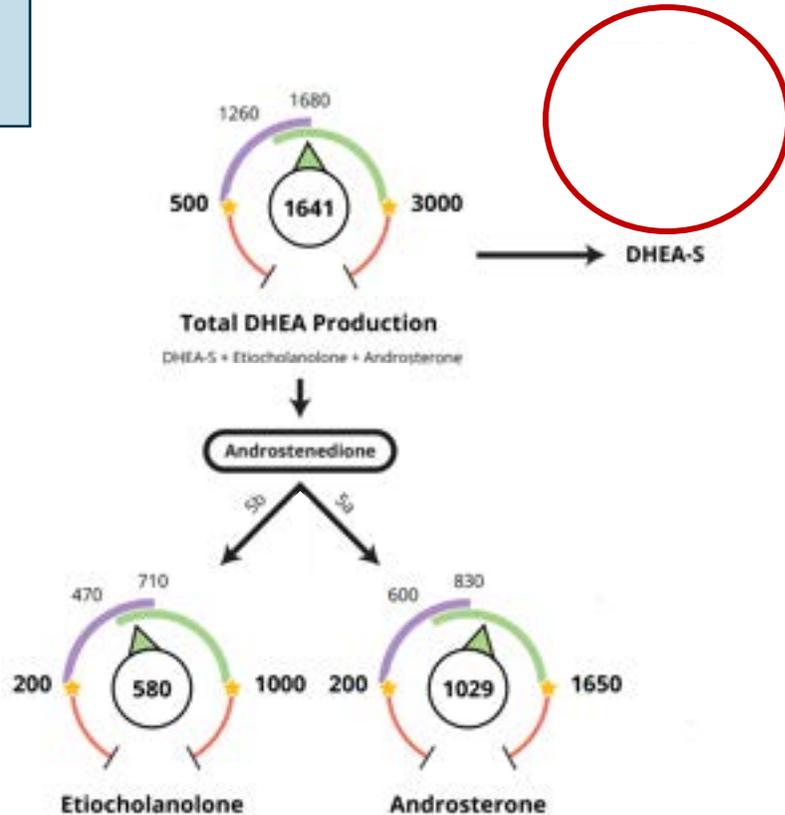
## Example:

- DHEA-S is 67 (RR 20-750)
- Total DHEA is 3,218 (RR 500 – 3,000)
- Therefore, **DHEA-S is relatively lower than total DHEA Production** when each is evaluated against its respective reference range.

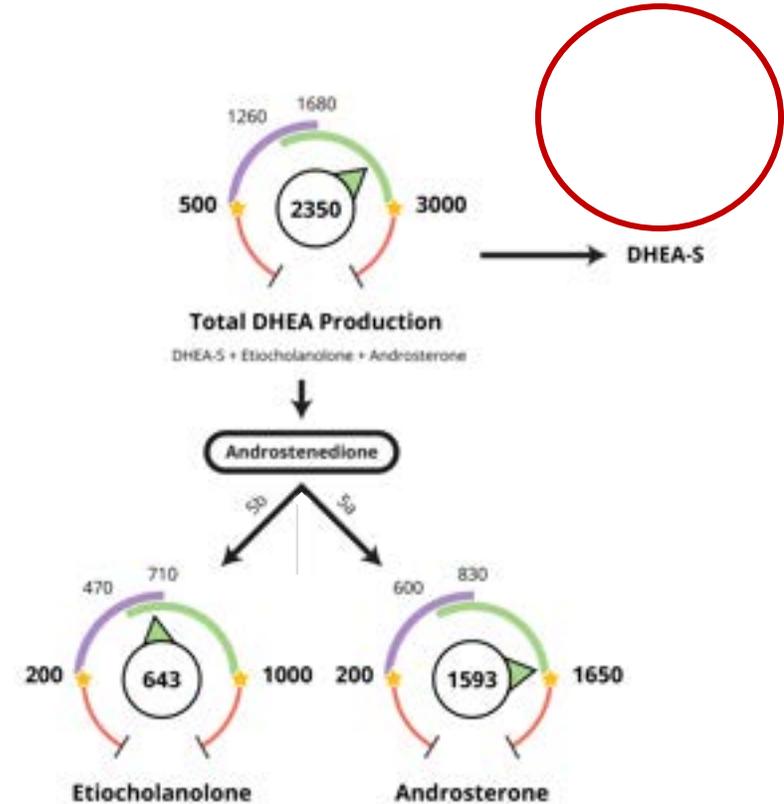
# A DUTCH Advanced Insights: 5 DHEA-S vs Total DHEA

Think about it!

**Game time!** Would you expect these patients' DHEA-S to be relatively **lower** or **higher** than their Total DHEA Production?



37-year-old female  
CRP-hs 9.0, Obesity (BMI 34.9), Fatty liver



17-year-old female  
CRP-hs 11.4, Obesity (BMI 36.3),  
Headaches 4x weekly; Menorrhagia

What are other patterns of inflammation on the DUTCH Test?

High inflammation is associated with the following results observed on the DUTCH Test:

- 5 $\alpha$ -Reductase upregulated
- Aromatase upregulated (testosterone and androstenedione to E2 and E1, respectively)
- DHEA-S lower compared to metabolites etiocholanolone and androsterone
- Estrogen clearance favoring 4-OH and/or 16-OH
- Elevated cortisol metabolism rate
- Elevated free cortisol
- Cortisol metabolism favoring THF when acute, and THE when chronic
- Elevated kynurenate
- Low or elevated pyroglutamate
- Elevated indican
- Elevated quinolinate
- Elevated 8-OHdG

Page 190 of the DUTCH Interpretive Guide

## Low DHEA-S Relative to Total DHEA Treatments

The treatment you choose depends on the cause, but also the symptoms, treatment goals, and patient preferences.

# The DUTCH Treatment Guide: **Low DHEA-S Relative to Total DHEA**

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# DUTCH Advanced Insights

## UGT Deletion



6

## Sex Hormones & Metabolites

TEST	RESULT	UNITS	LUTEAL*	POSTMENOPAUSAL
<b>Progesterone Metabolites (Urine)</b>				
b-Pregnanediol	Below luteal range	140.0	ng/mg	600 - 2000 60 - 200
a-Pregnanediol	Below luteal range	19.4	ng/mg	200 - 740 15 - 50
<b>Estrogens and Metabolites (Urine)</b>				
Estrone (E1)	Below luteal range	5.00	ng/mg	12 - 26 1.0 - 7.0
Estradiol (E2)	Below luteal range	0.90	ng/mg	1.8 - 4.5 0.2 - 0.7
Estriol (E3)	Below luteal range	4.7	ng/mg	5 - 18 0.6 - 4.0
2-OH-E1	Below luteal range	3.58	ng/mg	5.1 - 13.1 0.3 - 2.0
4-OH-E1	Within luteal range	0.25	ng/mg	0 - 1.8 0 - 0.3
16-OH-E1	Below luteal range	0.53	ng/mg	0.7 - 2.6 0.2 - 0.6
2-Methoxy-E1	Below luteal range	1.35	ng/mg	2.5 - 6.5 0.3 - 1.4
2-OH-E2	Low end of luteal range	0.35	ng/mg	0 - 3.1 0 - 0.52
4-OH-E2	Within luteal range	0.26	ng/mg	0 - 0.52 0 - 0.12
Total Estrogen	Below range	16.9	ng/mg	35 - 70 3.5 - 15
<b>Metabolite Ratios (Urine)</b>				
2-OH / 16-OH-E1 Balance	Within range	6.75	ratio	2.69 - 11.83
2-OH / 4-OH-E1 Balance	Above range	14.32	ratio	5.4 - 12.62
2-Methoxy / 2-OH Balance	Below range	0.38	ratio	0.39 - 0.67
<b>Androgens and Metabolites (Urine)</b>				
				<b>Range</b>
DHEA-S	Low end of range	23.4	ng/mg	20 - 750
Androsterone	Within range	795.0	ng/mg	200 - 1650
Etiocholanolone	Within range	675.0	ng/mg	200 - 1000
Testosterone	Low end of range	3.60	ng/mg	2.3 - 14
5a-DHT	Within range	2.5	ng/mg	0 - 6.6
5a-Androstenediol	High end of range	26.1	ng/mg	6 - 30
5b-Androstenediol	Within range	42.6	ng/mg	12 - 75
Epi-Testosterone	Low end of range	2.7	ng/mg	2.3 - 14

## Androgens

- 6 Assess the androgen pattern to determine if urine testosterone may not accurately reflect systemic levels (UGT2B17)

## **DUTCH urine testing parallels serum in *most cases*.**

- However, some people are born with a genetic deletion that causes their:
  - **Testosterone**
  - **5a-DHT**
  - **5b-androstanediol**
  - **to be falsely low in the urine (*but still accurate in the serum*).**
- This genetic difference is known as the **UGT2B17 deletion**.

## **How does this genetic deletion cause testosterone, 5a-DHT, and 5b-androstanediol to be falsely low in the urine?**

- Testosterone, in the liver, is primarily glucuronidated by the **UGT2B17 enzyme**, which also produces 5a-DHT and 5b-androstanediol glucuronides.
- A genetic deletion in this enzyme reduce these urinary hormone levels without affecting serum levels.

Martin-Escudero P, et al. Physiol Rep. 2015;3(12).

## Who is affected?

- The genetic UGT2B17 deletion frequency varies among populations, with a higher incidence seen in individuals of East Asian descent.

## Is there a difference between homozygous vs heterozygous?

- Yes: The **homozygous** (double deletion) polymorphism shows almost **no urinary excretion of testosterone**, regardless of the patient's circulating testosterone levels.
- **Heterozygous** (single deletion) individuals show **milder reductions in urinary testosterone**, 5a-DHT, and 5b-Androstanediol levels than homozygous individuals.

## Conclusion:

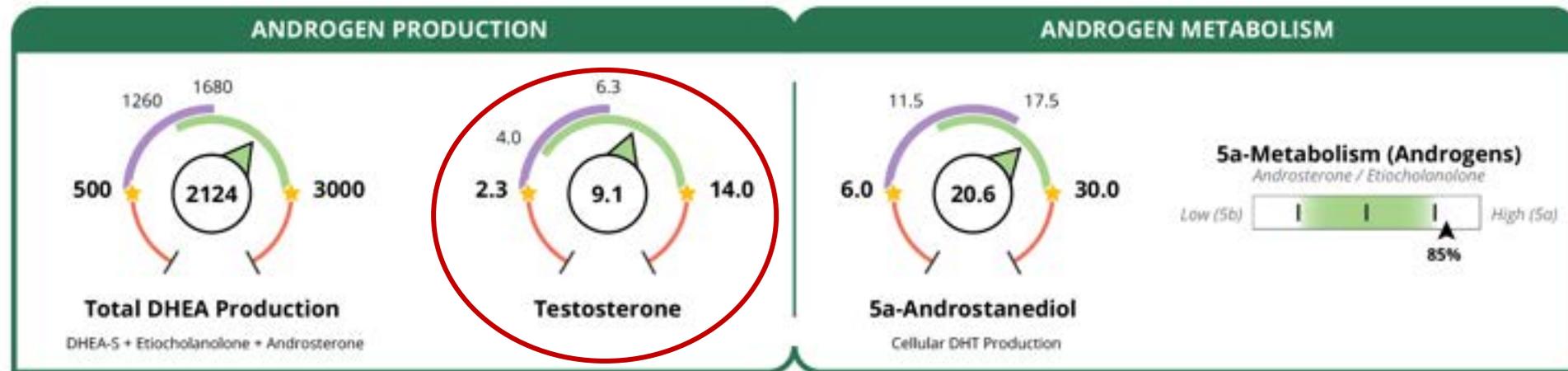
- **Low or very low testosterone on the DUTCH test suggest confirming it in serum.**

Martin-Escudero P, et al. Physiol Rep. 2015;3(12).

# A DUTCH Advanced Insights: 6 UGT Deletion

## How do I identify if there is a UGT pattern?

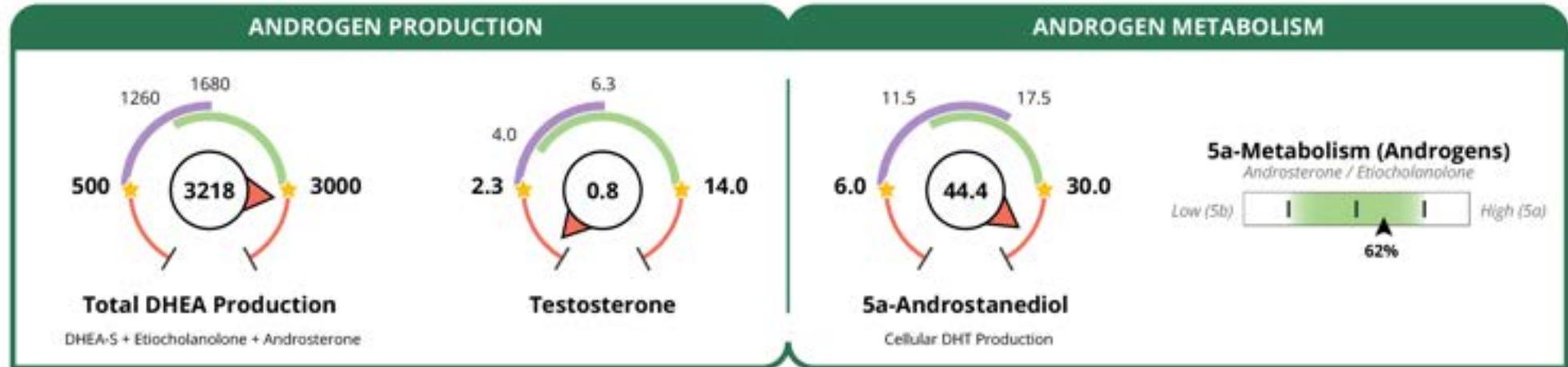
- First, compare the **Testosterone** to the **Total DHEA Production** and **5a-Androstanediol** dials on page #1.
- Is testosterone lower than these other two markers?



- If not (as seen in this example), then the patient **likely does not** have the UGT deletion and urine testosterone levels are **accurate**.

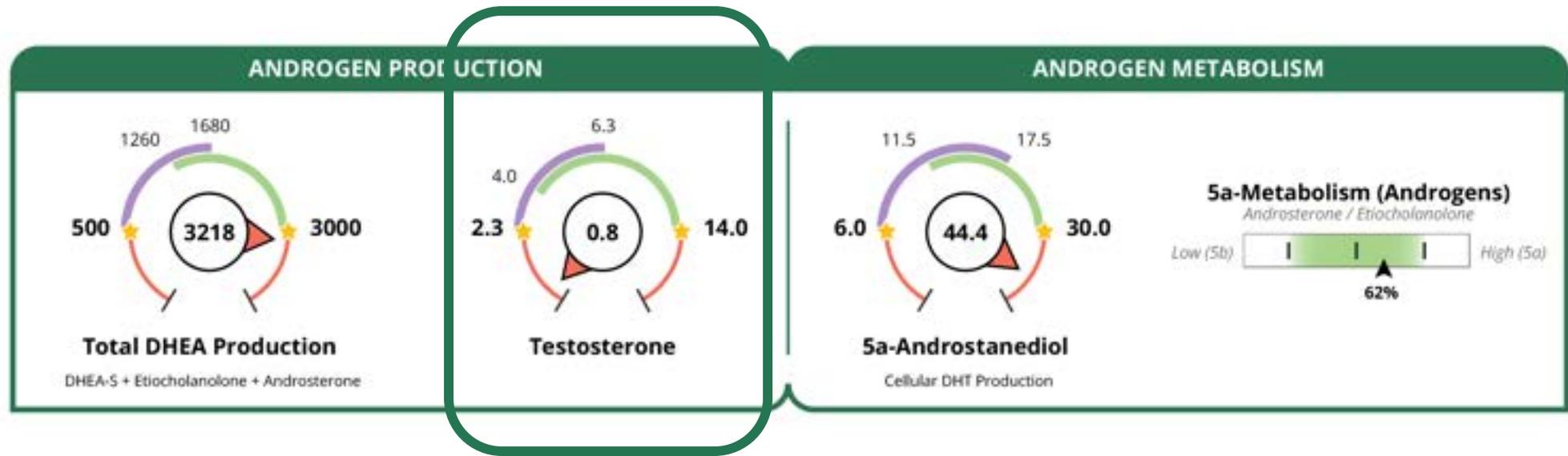
# A DUTCH Advanced Insights: 6 UGT Deletion

- If testosterone **is** generally lower than the total DHEA and 5a-androstanediol, then the patient may have the UGT deletion.
- This patient's urinary (**but not serum**) testosterone levels are likely falsely low.



# A DUTCH Advanced Insights: 6 UGT Deletion

- If testosterone **is** generally lower than the total DHEA and 5a-androstanediol, then the patient may have the UGT deletion.
- This patient's urinary (**but not serum**) testosterone levels are likely falsely low.



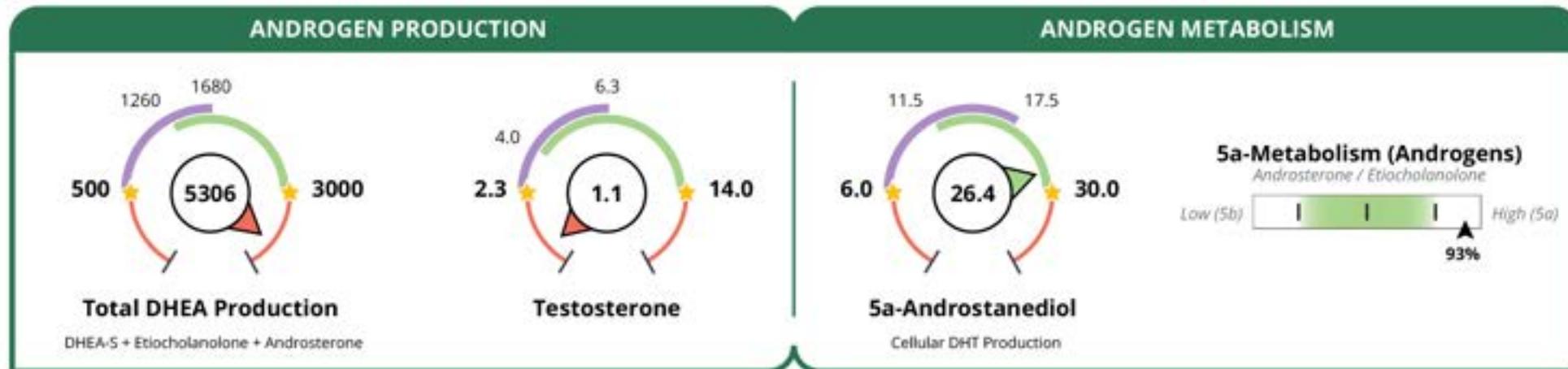
Think about it!

## Game time!

What is more likely?

- A. This patient has much higher DHEA and 5a-DHT (5a-Androstanediol) production compared to testosterone production.
- B. The urine testosterone is inaccurate.

To REALLY know the answer, let's look at the UGT deletion *pattern*!



## UGT Deletion Pattern

- **Epi-Testosterone may help to identify the UGT Deletion Pattern.**
- In males and females, it is made in the gonads in about the same concentration as testosterone, however, unlike testosterone, it's is not androgenic.
- Epi-Testosterone is NOT affected by the UGT deletion. Thus, if epi-testosterone is much higher than testosterone, the UGT deletion may be present, and testosterone should be measured in serum.

→	Testosterone	Below range	<b>Low</b> 1.14	ng/mg	2.3 - 14
	5a-DHT	Within range	3.1	ng/mg	0 - 6.6
	5a-Androstanediol	Within range	26.4	ng/mg	6 - 30
	5b-Androstanediol	Within range	16.9	ng/mg	12 - 75
→	Epi-Testosterone	Within range	<b>Normal</b> 9.2	ng/mg	2.3 - 14

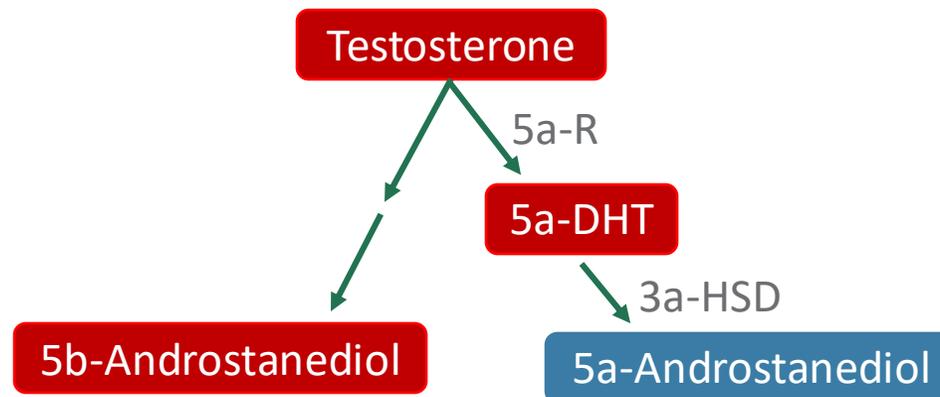
**UGT Pattern Detected!!!**

- *Note: Epi-Testosterone is a less reliable marker of testosterone production in women who are taking oral contraceptives and in women after menopause.*

# A DUTCH Advanced Insights: 6 UGT Deletion

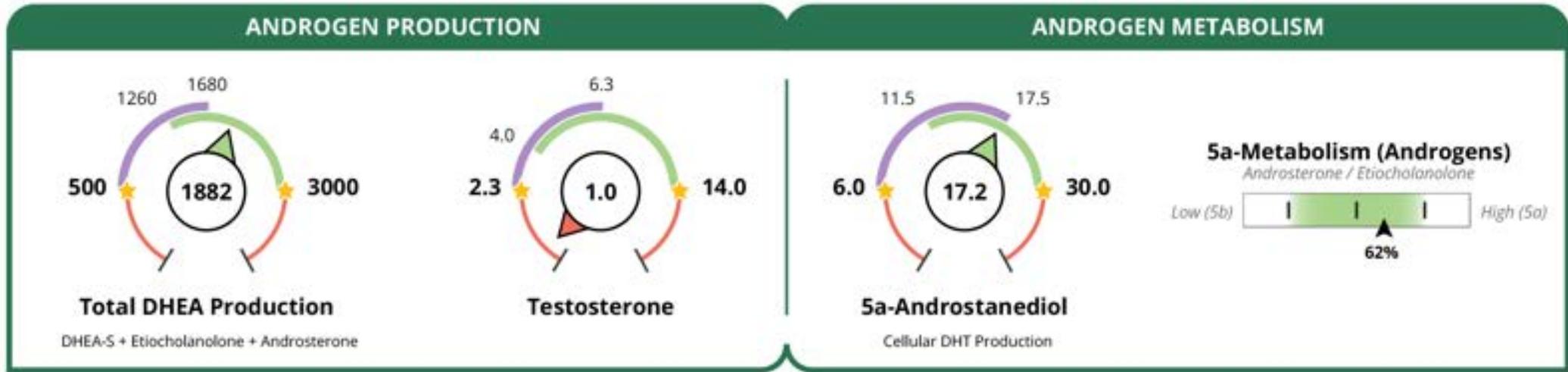
## Let's Recap:

- The UGT2B17 deletion causes ***three*** testosterone-related markers to be falsely low:
  - **Testosterone**
  - **5a-DHT**
  - **5b-Androstanediol**
- It does NOT affect ***two*** of the testosterone-related makers (these are true values):
  - **Epi-testosterone (*not androgenic*)**
  - **5a-Androstanediol**



# A DUTCH Advanced Insights: 6 UGT Deletion

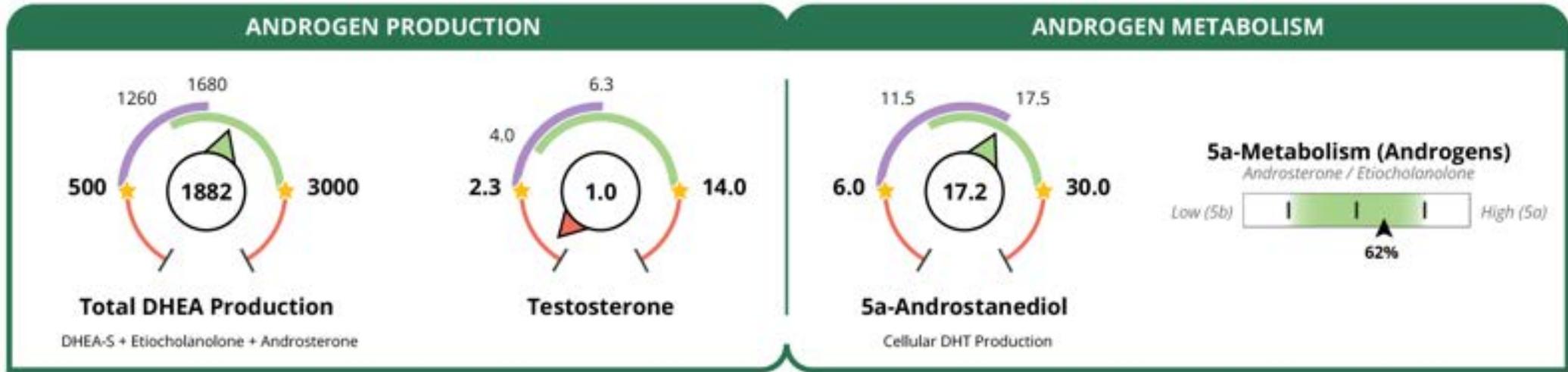
**EXAMPLE:** Suspected **UGT2B17** deletion polymorphism in a 27-year-old female:



<b>Falsely low</b> →	Testosterone	Below range	0.97	ng/mg	2.3 - 14
<b>Falsely low</b> →	5a-DHT	Within range	1.7	ng/mg	0 - 6.6
	5a-Androstanediol	Within range	17.2	ng/mg	6 - 30
<b>Falsely low</b> →	5b-Androstanediol	Within range	20.0	ng/mg	12 - 75
	Epi-Testosterone	Above range	15.7	ng/mg	2.3 - 14

# A DUTCH Advanced Insights: 6 UGT Deletion

**EXAMPLE:** Suspected **UGT2B17** deletion polymorphism in a 27-year-old female:



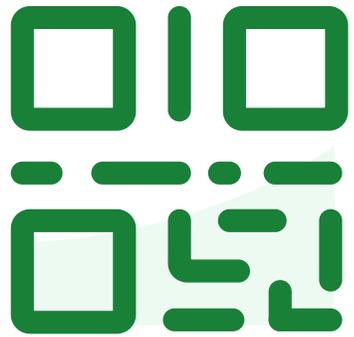
	Testosterone	Below range	0.97	ng/mg	2.3 - 14
	5a-DHT	Within range	1.7	ng/mg	0 - 6.6
<b>True result</b> →	5a-Androstanediol	Within range	17.2	ng/mg	6 - 30
	5b-Androstanediol	Within range	20.0	ng/mg	12 - 75
<b>True result</b> →	Epi-Testosterone	Above range	15.7	ng/mg	2.3 - 14

## EXAMPLE: Suspected **UGT2B17 deletion polymorphism**

 **Hooray!** Even if you suspect the patient has the UGT deletion, **you can still assess their 5a-Androstanediol levels**, which may be a better indicator of 5a-DHT activity in the tissues than 5a-DHT itself.

- In this example, the 27-year-old female patient's 5a-Androstanediol is within range, signifying normal tissue androgen activity.

	Testosterone	Below range	0.97	ng/mg	2.3 - 14
	5a-DHT	Within range	1.7	ng/mg	0 - 6.6
<b>True result</b> →	5a-Androstanediol	Within range	17.2	ng/mg	6 - 30
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<b>True result</b> →	Epi-Testosterone	Above range	15.7	ng/mg	2.3 - 14



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#DUTCHFEST5**

# A DUTCH Advanced Insights: 6 UGT Deletion

## Polling Question

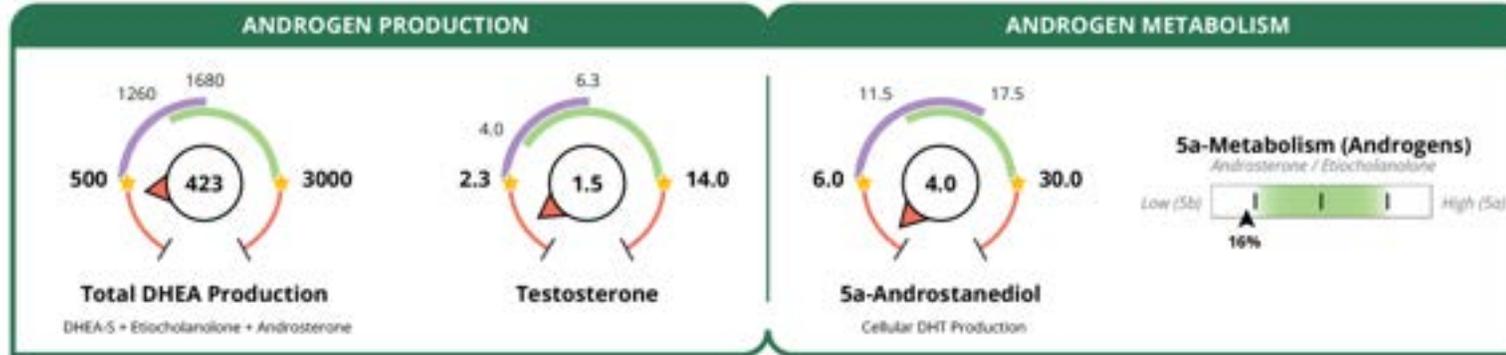


## Game time!

Is this 55-year-old female's testosterone really this low or do you suspect the UGT deletion?



**slido.com**  
**#DUTCHFEST5**



Testosterone	Below range	1.51	ng/mg	2.3 - 14
5a-DHT	Within range	0.8	ng/mg	0 - 6.6
5a-Androstanediol	Below range	4.0	ng/mg	6 - 30
5b-Androstanediol	Within range	13.4	ng/mg	12 - 75
Epi-Testosterone	Below range	0.5	ng/mg	2.3 - 14



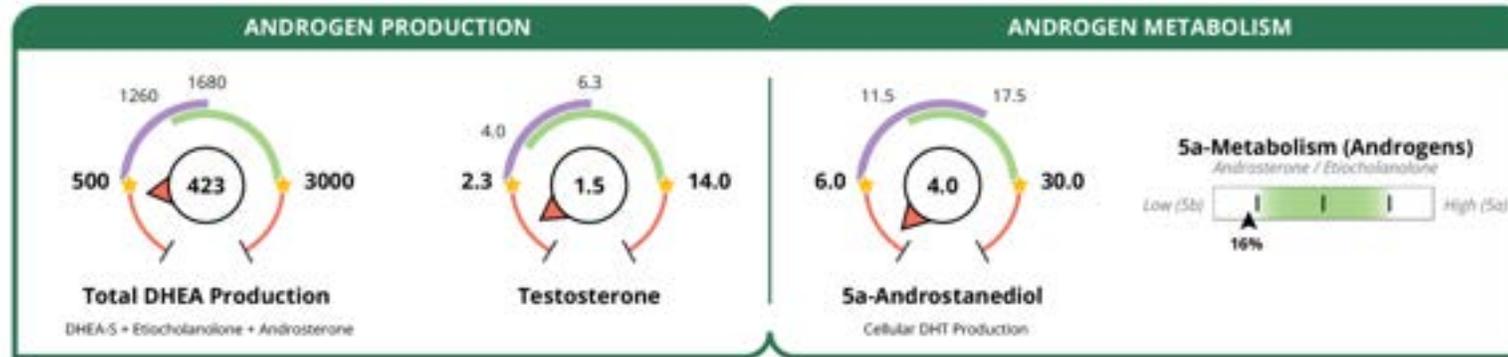
**Question 1: Is this 55-year-old female's testosterone really this low or do you suspect the UGT deletion? Choose the best answer.**

# A DUTCH Advanced Insights: 6 UGT Deletion

## Polling Question



**Game time!** Is this 55-year-old female's testosterone really this low??



<b>Low</b> →	Testosterone	Below range	1.51	ng/mg	2.3 - 14
<b>Low</b> →	5a-DHT	Within range	0.8	ng/mg	0 - 6.6
<b>Low</b> →	5a-Androstanediol	Below range	4.0	ng/mg	6 - 30
<b>Low</b> →	5b-Androstanediol	Within range	13.4	ng/mg	12 - 75
<b>Low</b> →	Epi-Testosterone	Below range	0.5	ng/mg	2.3 - 14

### Yes, it is likely low!

- ALL androgens are low or low-end, therefore there is no indication from downstream metabolites that there is much testosterone in the system.
- Serum labs reveal **total testosterone 3 ng/dL** (RR 15-70) and **free T 0.4 pg/mL** (RR 0.00-4.2).

# DUTCH Advanced Insights

## 5a-DHT



## Sex Hormones & Metabolites

TEST		RESULT	UNITS	LUTEAL*	POSTMENOPAUSAL
<b>Progesterone Metabolites (Urine)</b>					
b-Pregnanediol	Below luteal range	140.0	ng/mg	600 - 2000	60 - 200
a-Pregnanediol	Below luteal range	19.4	ng/mg	200 - 740	15 - 50
<b>Estrogens and Metabolites (Urine)</b>					
Estrone (E1)	Below luteal range	5.00	ng/mg	12 - 26	1.0 - 7.0
Estradiol (E2)	Below luteal range	0.90	ng/mg	1.8 - 4.5	0.2 - 0.7
Estriol (E3)	Below luteal range	4.7	ng/mg	5 - 18	0.6 - 4.0
2-OH-E1	Below luteal range	3.58	ng/mg	5.1 - 13.1	0.3 - 2.0
4-OH-E1	Within luteal range	0.25	ng/mg	0 - 1.8	0 - 0.3
16-OH-E1	Below luteal range	0.53	ng/mg	0.7 - 2.6	0.2 - 0.6
2-Methoxy-E1	Below luteal range	1.35	ng/mg	2.5 - 6.5	0.3 - 1.4
2-OH-E2	Low end of luteal range	0.35	ng/mg	0 - 3.1	0 - 0.52
4-OH-E2	Within luteal range	0.26	ng/mg	0 - 0.52	0 - 0.12
Total Estrogen	Below range	16.9	ng/mg	35 - 70	3.5 - 15
<b>Metabolite Ratios (Urine)</b>					
2-OH / 16-OH-E1 Balance	Within range	6.75	ratio	2.69 - 11.83	
2-OH / 4-OH-E1 Balance	Above range	14.32	ratio	5.4 - 12.62	
2-Methoxy / 2-OH Balance	Below range	0.38	ratio	0.39 - 0.67	
<b>Androgens and Metabolites (Urine)</b>				<b>Range</b>	
DHEA-S	Low end of range	23.4	ng/mg	20 - 750	
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Etiocholanolone	Within range	675.0	ng/mg	200 - 1000	
Testosterone	Low end of range	3.60	ng/mg	2.3 - 14	
<b>5a-DHT</b>	<b>Within range</b>	<b>2.5</b>	<b>ng/mg</b>	<b>0 - 6.6</b>	
5a-Androstanediol	High end of range	26.1	ng/mg	6 - 30	
5b-Androstanediol	Within range	42.6	ng/mg	12 - 75	
Epi-Testosterone	Low end of range	2.7	ng/mg	2.3 - 14	



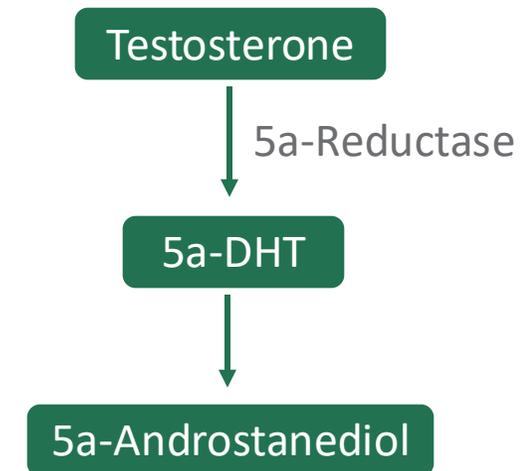
## Androgens

7 While 5a-androstanediol best represents **cellular** 5a-DHT production, assess if 5a-DHT offers additional insight into androgenic activity

# A DUTCH Advanced Insights: 7 5a-DHT

- **Although 5a-Androstanediol may be a better indicator of 5a-DHT activity in the tissues than 5a-DHT itself, we still recommend evaluating 5a-DHT levels on the DUTCH test.**
  - 5a-DHT is listed on page 3 of a female or male DUTCH Complete or Plus.

Androgens and Metabolites (Urine)				Range
DHEA-S	Within range	60.0	ng/mg	20 - 750
Androsterone	Within range	546.8	ng/mg	200 - 1650
Etiocholanolone	Within range	962.8	ng/mg	200 - 1000
Testosterone	Above range	17.88	ng/mg	2.3 - 14
5a-DHT	Within range	6.2	ng/mg	0 - 6.6
5a-Androstanediol	Within range	14.6	ng/mg	6 - 30
5b-Androstanediol	Within range	39.0	ng/mg	12 - 75
Epi-Testosterone	Above range	15.9	ng/mg	2.3 - 14



**Remember, 5a-DHT is our most potent androgen!  
It has 4x the androgenic activity as testosterone!**

## Comparing 5a-DHT and 5a-Androstanediol:

- If 5a-DHT and 5a-Androstanediol are **BOTH** high, this indicates high tissue androgen activity.

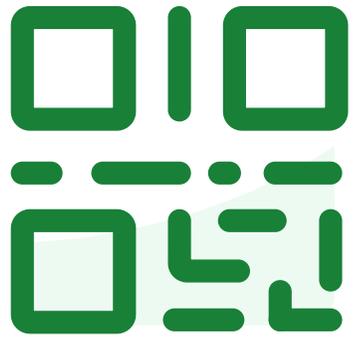
Testosterone	Within range	13.37	ng/mg	2.3 - 14
5a-DHT	Above range	10.5	ng/mg	0 - 6.6
5a-Androstanediol	Above range	51.5	ng/mg	6 - 30
5b-Androstanediol	Above range	150.6	ng/mg	12 - 75
Epi-Testosterone	Within range	11.1	ng/mg	2.3 - 14

Think  
about  
it!

## Game time!

What if one is high and the other is not?

Testosterone	Above range	18.18	ng/mg	2.3 - 14
5a-DHT	Above range	7.3	ng/mg	0 - 6.6
5a-Androstanediol	Within range	21.4	ng/mg	6 - 30
5b-Androstanediol	Within range	58.5	ng/mg	12 - 75
Epi-Testosterone	Within range	10.0	ng/mg	2.3 - 14



**Join at [slido.com](https://slido.com)  
#DUTCHFEST5**

**Polling  
Question**



# Game time!

Would you expect lower or higher 5a-DHT in PCOS? With Finasteride?



**slido.com**  
**#DUTCHFEST5**



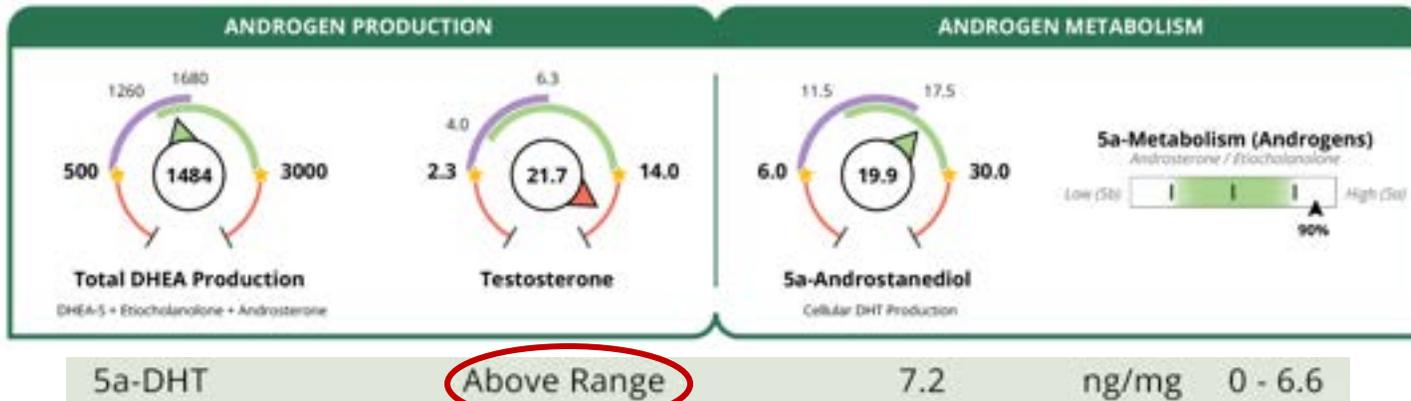
**Question 2: Would you expect lower or higher 5 $\alpha$ -DHT in PCOS? With Finasteride?**

## Polling Question



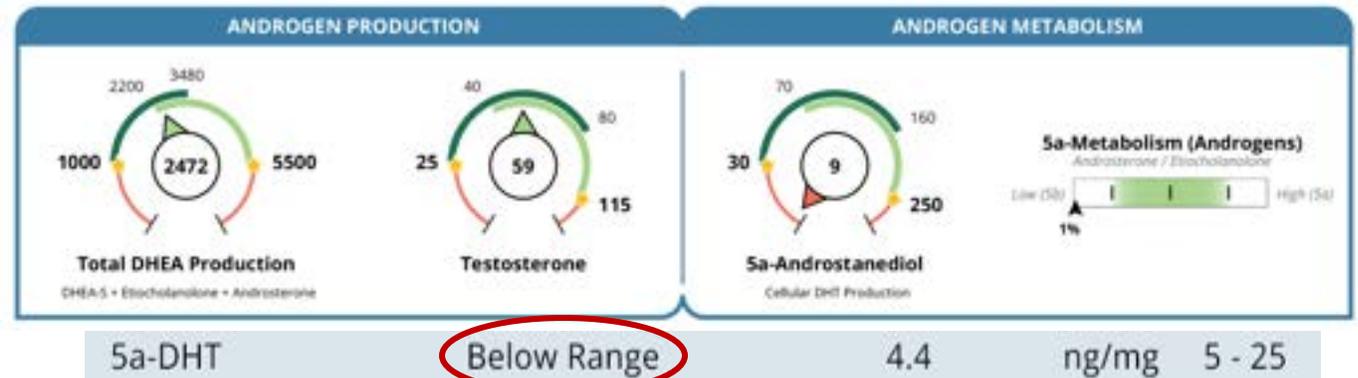
# Game time!

Would you expect lower or higher 5a-DHT in PCOS? With Spironolactone?



31-year-old female with PCOS  
**Higher 5a-R and higher 5a-DHT**

58-year-old male on Finasteride  
**Lower 5a-R and lower 5a-DHT**



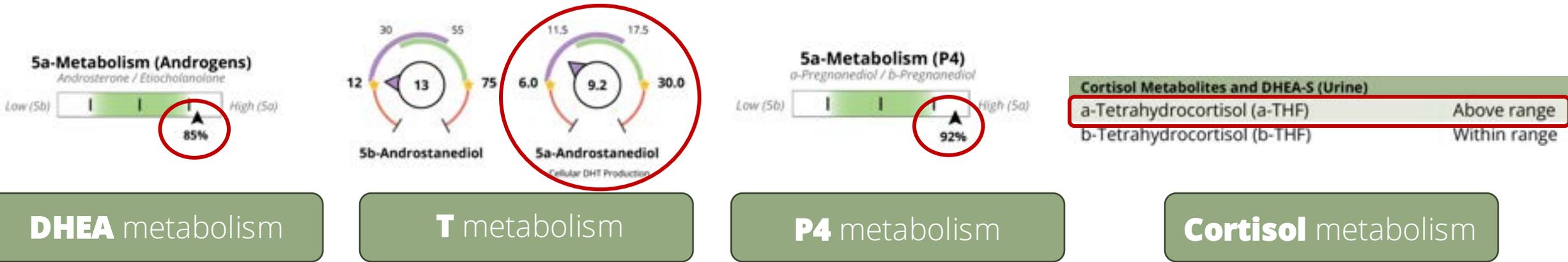
# Advanced Concepts

How to determine if the patient has a strong overall 5-alpha preference

# Advanced Concept

Sometimes it's helpful to know if all the tissues are preferring the alpha (or beta) pathway.

- A **strong** overall 5a-Preference **across the tissues** can be confirmed by looking at:

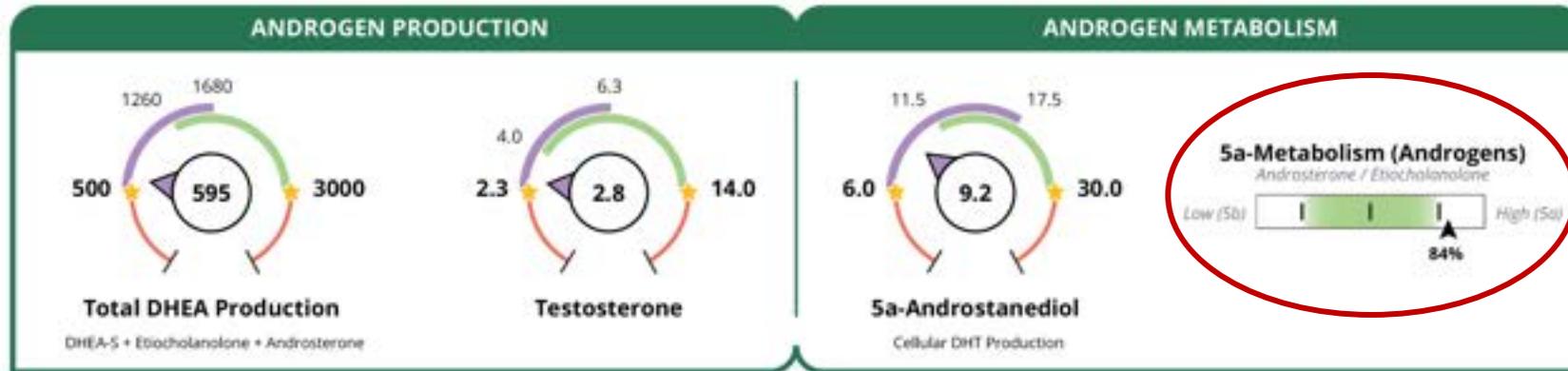


- Being a **strong** “alpha pusher” could be due to **obesity, insulin resistance, or inflammation.**

# Advanced Concept – 5a-Metabolism

## Example: Androgen Therapy Dosing

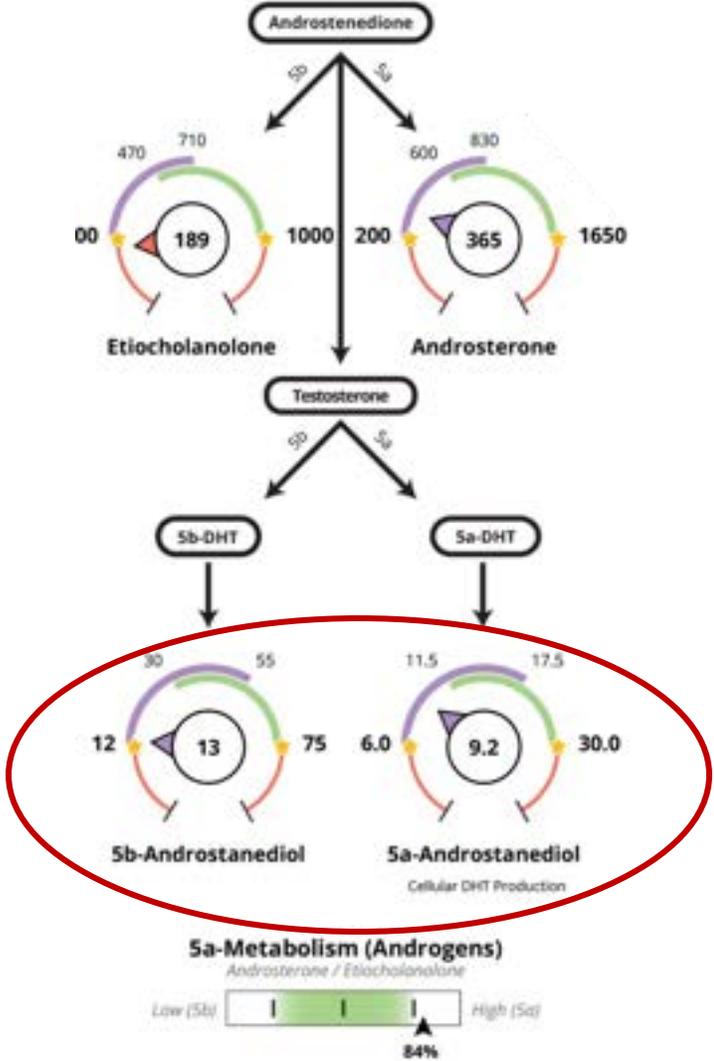
- **What if we want to increase androgen levels in this 32-year-old woman with oral DHEA but the patient is preferring the more androgenic alpha pathway?**
- Will most of the DHEA be converted into alpha metabolites and cause **acne**???
- To most thoroughly answer this question, we should **confirm** her strong alpha preference by looking at **testosterone, progesterone and cortisol metabolism**.



# Advanced Concept – 5a-Metabolism

## Testosterone Metabolism

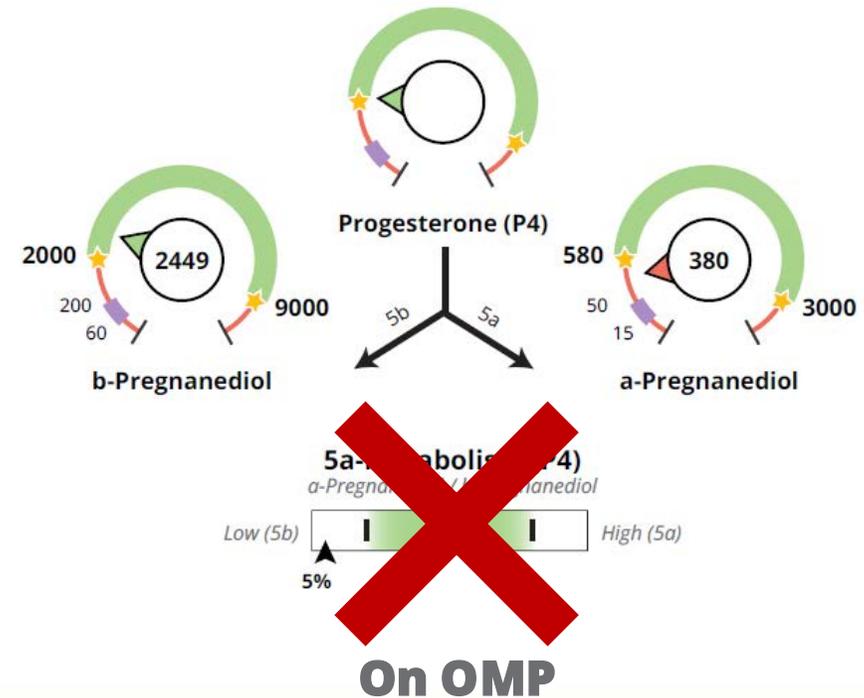
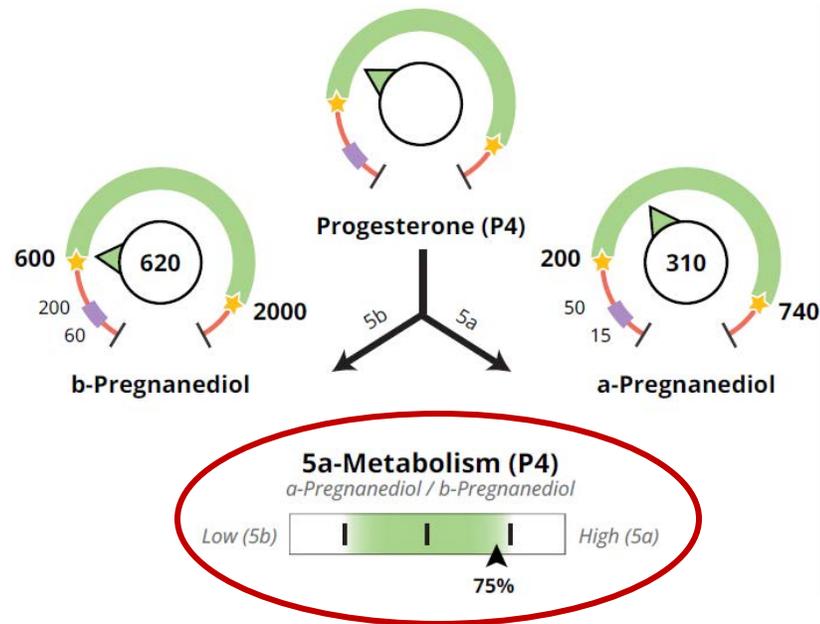
- Her testosterone metabolites **confirm** the alpha preference.



# Advanced Concept – 5a-Metabolism

## Progesterone Metabolism

- Her progesterone metabolism also **confirms** the alpha preference.
- **Note that progesterone metabolism on OMP reflects gut/liver preference (not tissue/body preference) so cannot be used when assessing overall tissue alpha/beta preference.**



# Advanced Concept – 5a-Metabolism

## Cortisol Metabolism

- a-THF is relatively higher than b-THF, which **confirms** her alpha preference.

Cortisol Metabolites and DHEA-S (Urine)				
a-Tetrahydrocortisol (a-THF)	Above range	414.8	ng/mg	75 - 370
b-Tetrahydrocortisol (b-THF)	Low end of range	1123.3	ng/mg	1050 - 2500

### Therefore, for this 37-year-old woman:

- We may want to use more caution with androgen therapy due to the patient's strong overall alpha preference across the tissues.
- Some providers may choose to start with a relatively **lower** DHEA dose and slowly increase as tolerated by the patient to avoid androgen excess symptoms (acne, hair loss, etc.) and consider using 5a-blocking agents.

# DUTCH Advanced Insights

## Androgen-Related OATs



8

## Organic Acid Tests (OATs)

TEST	RESULT	UNITS	NORMAL RANGE	
<b>Nutritional Organic Acids (Urine)</b>				
Vitamin B12 Marker - May be deficient if high				
Methylmalonate (MMA)	Above range	4.9	ug/mg	0 - 2.5
Vitamin B6 Markers - May be deficient if high				
Xanthurenate	Above range	1.23	ug/mg	0.12 - 1.2
Kynurenate	Above range	5.3	ug/mg	0.8 - 4.5
Biotin Marker - May be deficient if high				
b-Hydroxyisovalerate	Within range	7.9	ug/mg	0 - 12.5
Glutathione Marker - May be deficient if low or high				
Pyroglutamate	Below range	0.0	ug/mg	28 - 58
Gut Marker - Potential gut putrefaction or dysbiosis if high				
Indican	High end of range	90.4	ug/mg	0 - 100
<b>Neuro-Related Markers (Urine)</b>				
Dopamine Metabolite				
Homovanillate (HVA)	Within range	4.4	ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite				
Vanilmandelate (VMA)	Above range	7.3	ug/mg	2.2 - 5.5
Neuroinflammation Marker				
Quinolate	Above range	13.2	ug/mg	0 - 9.6
<b>Additional Markers (Urine)</b>				
Melatonin - Waking				
6-OH-Melatonin-Sulfate	Below range	1.3	ng/mg	10 - 85
Oxidative Stress / DNA Damage				
8-Hydroxy-2-deoxyguanosine (8-OHdG)	Within range	3.8	ng/mg	0 - 5.2

## Androgens

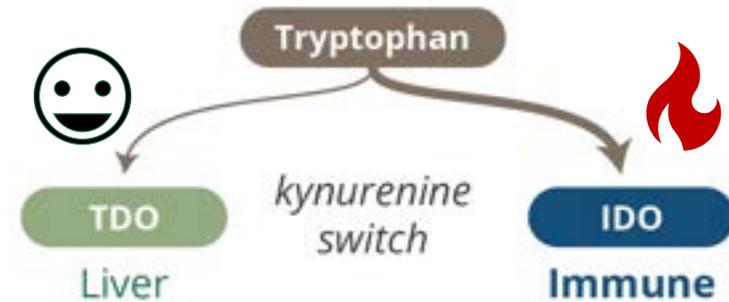
The androgen OATs include:

1. Xanthurenate
2. Kynurenate
3. b-Hydroxyisovalerate
4. Quinolate

8 Assess whether any of the androgen-related organic acids are out of range

## Xanthurenate, Kynurenate, Quinolate

- High Xanthurenate, Kynurenate, and/or Quinolate **may indicate abnormalities in tryptophan metabolism.**
- Abnormalities in tryptophan metabolism have been linked to **inflammation, high androgen production**, and **PCOS** in cycling women.
- Remember, high Xanthurenate and/or Kynurenate can also indicate a vitamin B6 deficiency!



***With inflammation, tryptophan metabolism switches from the normal metabolic TDO pathway to the inflammatory immune dedicated IDO pathway.***

***Therefore, when Xan, Kyn, and Quin are elevated we may want to assess for inflammation.***

## b-Hydroxyisovalerate

- When elevated can indicate a **biotin** deficiency.
- Biotin deficiency can contribute to hair loss.
- If one of the patient's high androgen complaints includes hair loss, check for elevated levels.
- **DUTCH-related contributors to hair loss:** Assess for high (alpha) 5a-Metabolism, high 5a-DHT, high 5a-Androstenediol, high cortisol, and/or high b-Hydroxyisovalerate.

Biotin Marker - May be deficient if high

b-Hydroxyisovalerate

Above range

13.0

ug/mg

0 - 12.5

49-year-old female  
Severe scalp hair loss

## Quinolate

- Again, high quinolate is a sign of abnormal tryptophan metabolism, and it has also been linked to **inflammation, high androgen production**, and **PCOS** in cycling women.

### Neuroinflammation Marker

Quinolate

Above range

10.5

ug/mg

0 - 9.6

36-year-old female  
PCOS and hair loss  
"excess facial and body hair"  
BMI 37.9

## Quinolate

- Quinolate is a **neurotoxin**.
- Elevated quinolate may be associated with neuroinflammation, general inflammation, obesity, infection, phthalate exposure, low serotonin, low niacin (vitamin B3), and oral tryptophan use.

### Quinolate - Neuroinflammation Marker

In addition to treating the underlying cause (see the DUTCH Interpretive Guide), other potential support considerations for a high quinolate in females and males include:

#### If Inflammation is Contributing

- Lower systemic inflammation. See [page 53](#).
- Support glutathione. See "Pyroglutamate" on [page 45](#).

#### Other

- Supplement with niacin (vitamin B3), if appropriate.
- Support serotonin, if appropriate
  - Adequate dietary protein
  - Tryptophan<sup>1</sup>
  - 5-HTP<sup>2</sup>
  - Vitamin B6
- See "Serotonin Support" under "Mood Supportive" in the "Herbal Support Overview" on [page 37](#) for herbal serotonin support.
- If infection is contributing, treat the infection.

### Support Glutathione

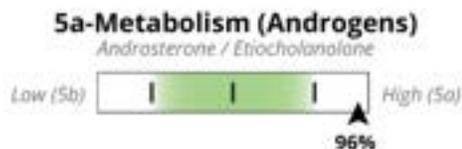
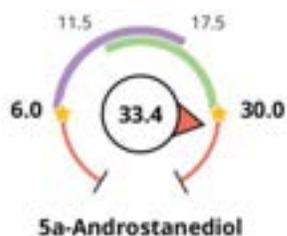
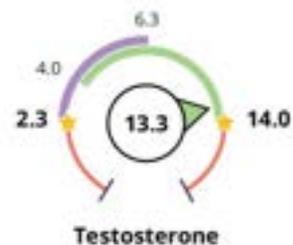
- Adequate dietary protein
- Alpha lipoic acid (ALA)
- B vitamins (B2, B6)
- Brassica and allium vegetables
- Curcumin
- Fruit and vegetable juices
- Glycine
- Green tea
- Liposomal/Intravenous glutathione
- NAC
- Salmon
- Selenium
- Vitamin C
- Vitamin E
- Whey protein
- Zinc (balance copper)

Pages 46 (left) and 45 (right) of the DUTCH Treatment Guide

# A DUTCH Advanced Insights: Androgen-Related OATs

## Example: 12-year-old female with acne and hair loss

- PCOS suspected, fasting insulin 100; glucose 96; HbA1c 5.3



### Organic Acid Tests (OATs)

TEST	RESULT	UNITS	NORMAL RANGE	
<b>Nutritional Organic Acids (Urine)</b>				
Vitamin B12 Marker - May be deficient if high				
Methylmalonate (MMA)	Above range	3.0	ug/mg	0 - 2.5
Vitamin B6 Markers - May be deficient if high				
Xanthurenate	Above range	1.29	ug/mg	0.12 - 1.2
Kynurenate	High end of range	4.5	ug/mg	0.8 - 4.5
Biotin Marker - May be deficient if high				
b-Hydroxyisovalerate	Above range	29.0	ug/mg	0 - 12.5
Glutathione Marker - May be deficient if high				
Pyroglutamate	Within range	46.8	ug/mg	28 - 58
Gut Marker - Potential gut putrefaction or dysbiosis if high				
Indican	Within range	59.8	ug/mg	0 - 100
<b>Neuro-Related Markers (Urine)</b>				
Dopamine Metabolite				
Homovanillate (HVA)	Within range	5.3	ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite				
Vanilmandelate (VMA)	Within range	4.4	ug/mg	2.2 - 5.5
Neuroinflammation Marker				
Quinolinatate	Above range	12.9	ug/mg	0 - 9.6
<b>Additional Markers (Urine)</b>				
Melatonin - Waking				
6-OH-Melatonin-Sulfate	High end of range	84.2	ng/mg	10 - 85
Oxidative Stress / DNA Damage				
8-Hydroxy-2-deoxyguanosine (8-OHdG)	Within range	3.0	ng/mg	0 - 5.2

Abnormalities in tryptophan metabolism have been linked to inflammation, high androgen production, and PCOS in cycling women.

Along with high androgens, biotin deficiency can also contribute to hair loss.

# Androgen-Related OATs Treatments

The treatment you choose depends on the cause, but also the symptoms, treatment goals, and patient preferences.

# The DUTCH Treatment Guide: **Androgen-Related OATs**

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Xanthurenate  
Kynurenate  
*Page 44*

**b-Hydroxyisovalerate**  
*Page 44*

Quinolinate  
*Page 46*

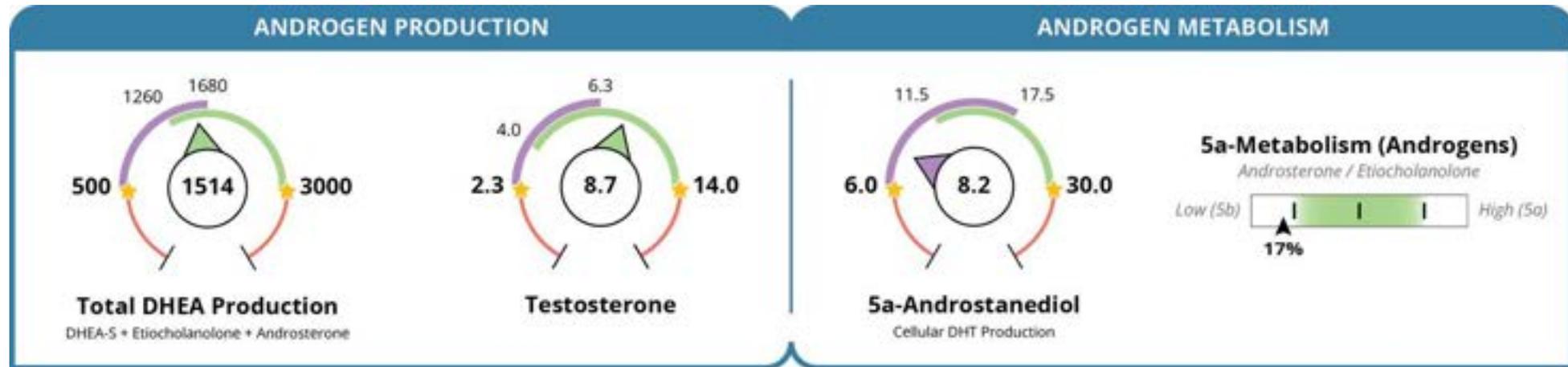
 OATs Support



Putting it All Together!

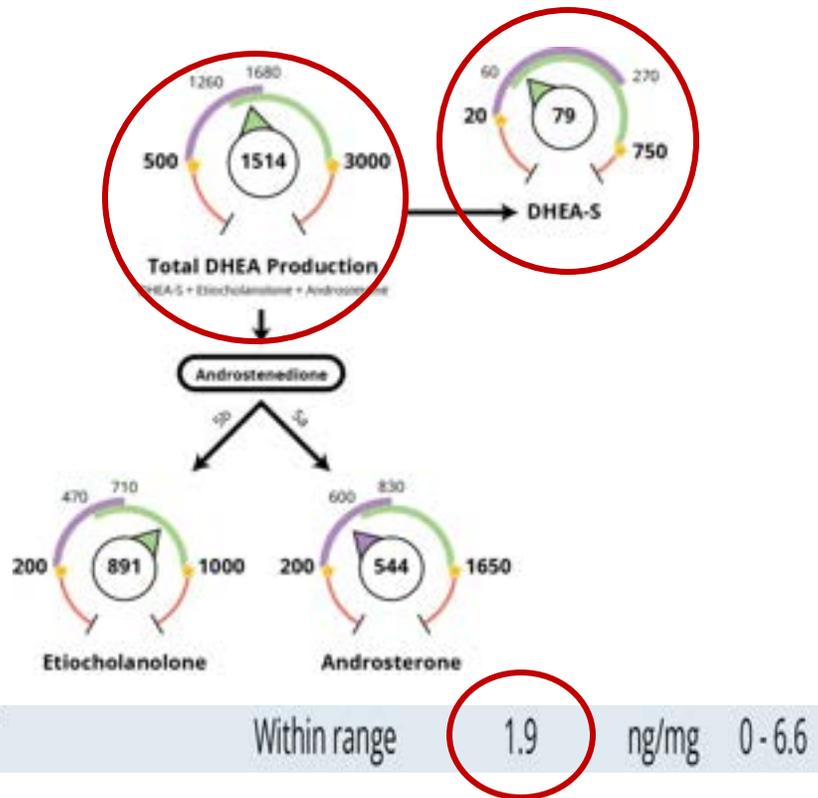
# A DUTCH Advanced Insights: Putting it all together!

- 24-year-old female diagnosed with Premature Ovarian Insufficiency (POI). Complains of fatigue, low libido, and stressful roommate situation (doesn't like to be home). BMI 21.3.



# A DUTCH Advanced Insights: Putting it all together!

- 24-year-old female diagnosed with Premature Ovarian Insufficiency (POI). Complains of fatigue, low libido, and stressful roommate situation (doesn't like to be home). BMI 21.3.
- Looking at the Advanced Insights, what might be contributing to her diagnosis and complaints?



## Organic Acid Tests (OATs)

TEST	RESULT	UNITS	NORMAL RANGE
<b>Nutritional Organic Acids (Urine)</b>			
Vitamin B12 Marker - May be deficient if high			
Methylmalonate (MMA)	Above range	3.2	ug/mg 0 - 2.5
Vitamin B6 Markers - May be deficient if high			
Xanthurenate	Within range	0.26	ug/mg 0.12 - 1.2
Kynurenate	Above range	5.4	ug/mg 0.8 - 4.5
Biotin Marker - May be deficient if high			
b-Hydroxyisovalerate	Within range	4.8	ug/mg 0 - 12.5
Glutathione Marker - May be deficient if low or high			
Pyroglutamate	Within range	35.5	ug/mg 28 - 58
Gut Marker - Potential gut putrefaction or dysbiosis if high			
Indican	Within range	58.7	ug/mg 0 - 100
<b>Neuro-Related Markers (Urine)</b>			
Dopamine Metabolite			
Homovanillate (HVA)	Within range	5.0	ug/mg 3 - 11
Norepinephrine/Epinephrine Metabolite			
Vanilmandelate (VMA)	Within range	3.2	ug/mg 2.2 - 5.5
Neuroinflammation Marker			
Quinolinatate	High end of range	9.1	ug/mg 0 - 9.6
<b>Additional Markers (Urine)</b>			
Melatonin - Waking			
6-OH-Melatonin-Sulfate	Within range	40.1	ng/mg 10 - 85
Oxidative Stress / DNA Damage			
8-Hydroxy-2-deoxyguanosine (8-OHdG)	Within range	2.1	ng/mg 0 - 5.2

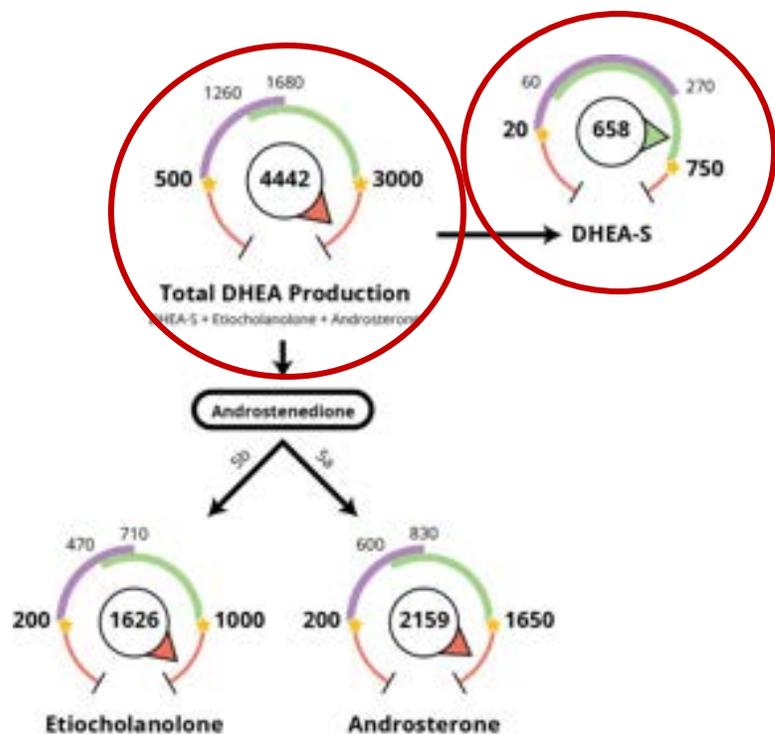
# A DUTCH Advanced Insights: Putting it all together!

- 29-year-old female diagnosed with PCOS. Complains of irregular cycles, high stress, facial hair, and breast tenderness. BMI 29.3.



# A DUTCH Advanced Insights: Putting it all together!

- 29-year-old female diagnosed with PCOS. Complains of irregular cycles, high stress, facial hair, and breast tenderness. BMI 29.3.
- Her 5 $\alpha$ -Androstenediol is above range at 43 ng/mg, but her 5 $\alpha$ -DHT is within range at 4.7 (RR 0-6.6). Does this change your conclusion about androgenic activity in her body?



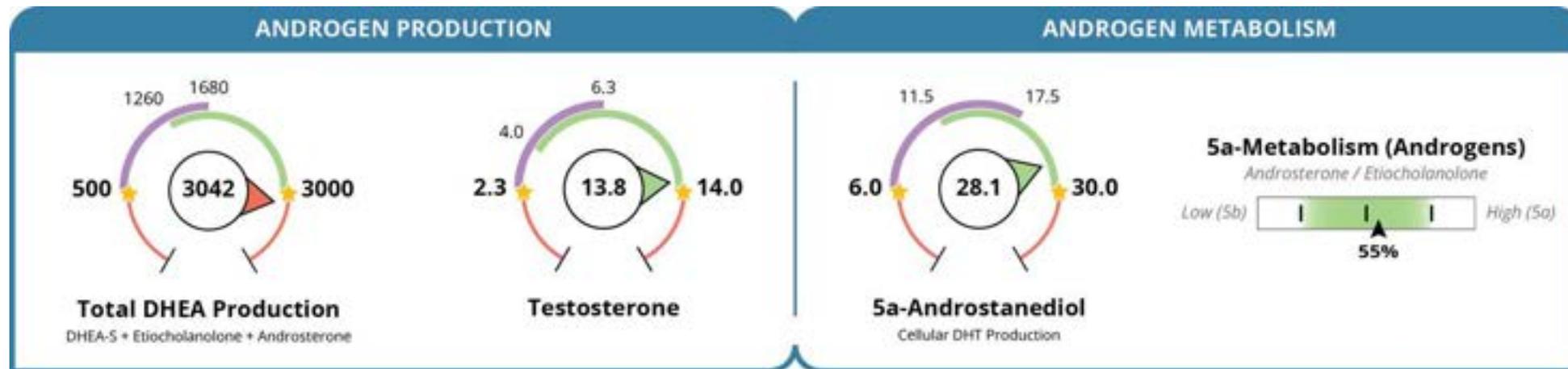
## Organic Acid Tests (OATs)

TEST	RESULT	UNITS	NORMAL RANGE
<b>Nutritional Organic Acids (Urine)</b>			
Vitamin B12 Marker - May be deficient if high			
Methylmalonate (MMA)	Within range	1.3 ug/mg	0 - 2.5
Vitamin B6 Markers - May be deficient if high			
Xanthurenate	Within range	0.37 ug/mg	0.12 - 1.2
Kynurenate	Within range	2.0 ug/mg	0.8 - 4.5
Biotin Marker - May be deficient if high			
b-Hydroxyisovalerate	Within range	8.3 ug/mg	0 - 12.5
Glutathione Marker - May be deficient if low or high			
Pyroglutamate	Above range	67.2 ug/mg	28 - 58
Gut Marker - Potential gut putrefaction or dysbiosis if high			
Indican	Above range	102.3 ug/mg	0 - 100
<b>Neuro-Related Markers (Urine)</b>			
Dopamine Metabolite			
Homovanillate (HVA)	Within range	4.0 ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite			
Vanilmandelate (VMA)	Within range	3.9 ug/mg	2.2 - 5.5
Neuroinflammation Marker			
Quinolinatate	Above range	15.1 ug/mg	0 - 9.6
<b>Additional Markers (Urine)</b>			
Melatonin - Waking			
6-OH-Melatonin-Sulfate	Within range	62.9 ng/mg	10 - 85
Oxidative Stress / DNA Damage			
8-Hydroxy-2-deoxyguanosine (8-OHdG)	Within range	2.1 ng/mg	0 - 5.2

Abnormalities in tryptophan metabolism have been linked to inflammation, high androgen production, and PCOS in cycling women.

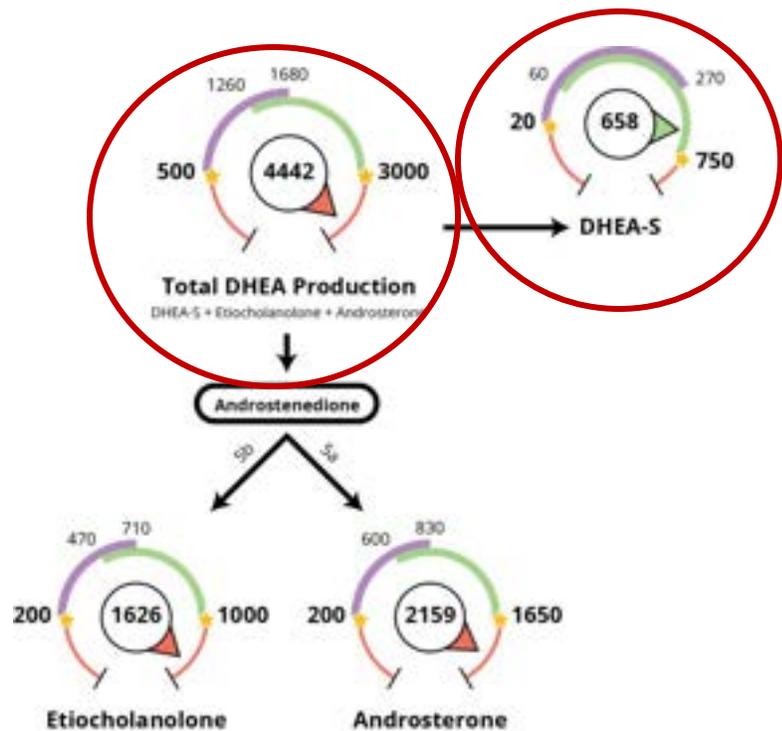
# A DUTCH Advanced Insights: Putting it all together!

- 39-year-old female with suspected endometriosis. Complains of dysmenorrhea, heavy bleeding, and frequent night wakings. BMI 26.6.



# A DUTCH Advanced Insights: Putting it all together!

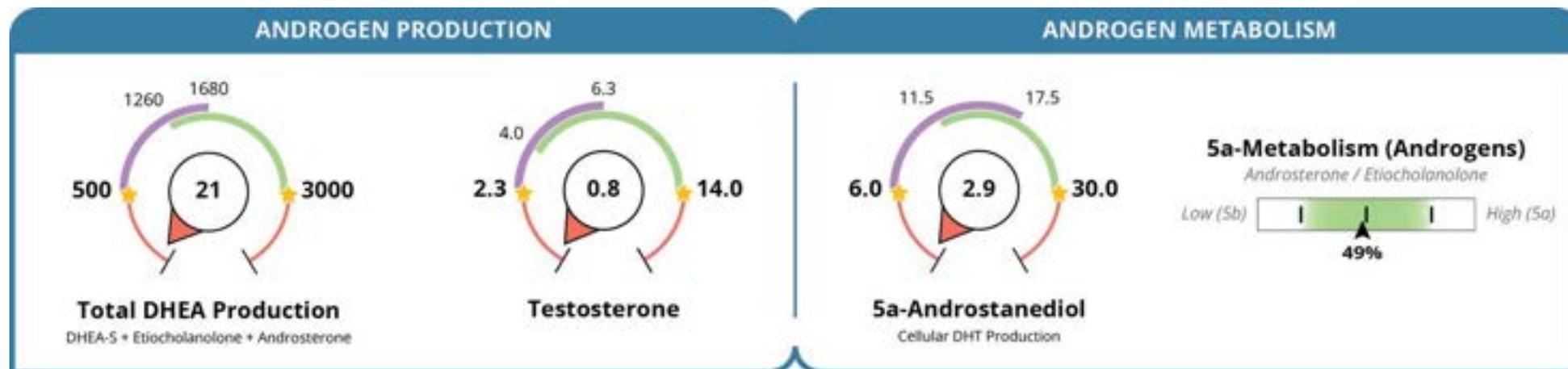
- 39-year-old female with suspected endometriosis. Complains of dysmenorrhea, heavy bleeding, and frequent night wakings. BMI 26.6.
- Her testosterone and 5 $\alpha$ -Androstanediol are within range (13.8 & 28.1, respectively), however, why might you prioritize testosterone-lowering treatments after looking at the Advanced Insights?



5 $\alpha$ -DHT High end of range 6.3 ng/mg 0 - 6.6

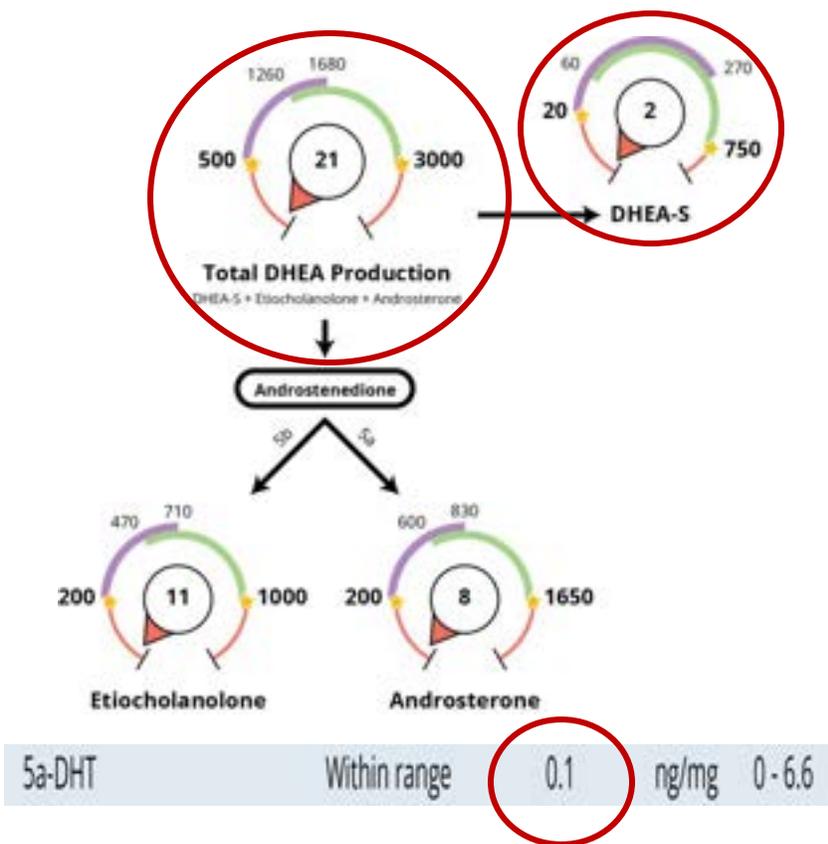
# A DUTCH Advanced Insights: Putting it all together!

- 55-year-old PMP female on 15 mg prednisone for the past month. She has not been able to taper below 15 mg without her ulcerative colitis flaring up. Complains of hair loss, hot flashes, irritability, and sleep issues. BMI 28.1.



# A DUTCH Advanced Insights: Putting it all together!

- 55-year-old PMP female on 15 mg prednisone for the past month. She has not been able to taper below 15 mg without her ulcerative colitis flaring up. Complains of hair loss, hot flashes, irritability, and sleep issues. BMI 28.1.



- Her testosterone and 5a-Androstanediol are very low (0.8 & 2.9, respectively). Her Epi-T is also very low at 0.3 ng/mg.
- Is her testosterone likely falsely low due to the UGT2B17 mutation?

# A DUTCH Advanced Insights: Putting it all together!

- 55-year-old PMP female on 15 mg prednisone for the past month. She has not been able to taper below 15 mg without her ulcerative colitis flaring up. Complains of hair loss, hot flashes, irritability, and sleep issues. BMI 28.1.

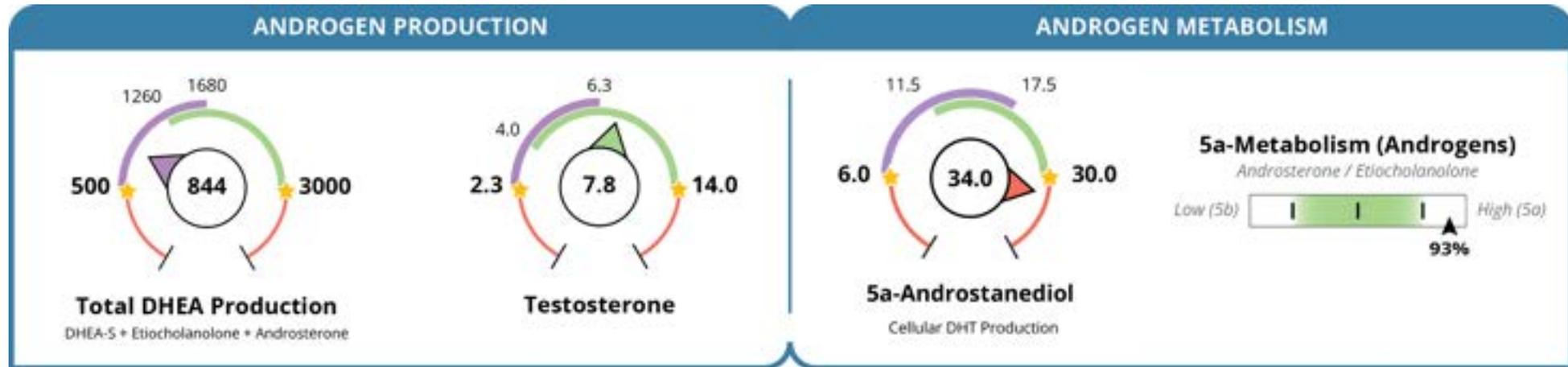
- What else besides the prednisone could be contributing to her hair loss?

## Organic Acid Tests (OATs)

TEST		RESULT	UNITS	NORMAL RANGE
<b>Nutritional Organic Acids (Urine)</b>				
Vitamin B12 Marker - May be deficient if high				
Methylmalonate (MMA)	Within range	1.6	ug/mg	0 - 2.5
Vitamin B6 Markers - May be deficient if high				
Xanthurenate	Within range	0.60	ug/mg	0.12 - 1.2
Kynurenate	Within range	1.5	ug/mg	0.8 - 4.5
Biotin Marker - May be deficient if high				
b-Hydroxyisovalerate	Above range	16.5	ug/mg	0 - 12.5
Glutathione Marker - May be deficient if low or high				
Pyroglutamate	Within range	50.3	ug/mg	28 - 58
Gut Marker - Potential gut putrefaction or dysbiosis if high				
Indican	Within range	58.0	ug/mg	0 - 100
<b>Neuro-Related Markers (Urine)</b>				
Dopamine Metabolite				
Homovanillate (HVA)	Within range	5.9	ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite				
Vanilmandelate (VMA)	Within range	4.7	ug/mg	2.2 - 5.5
Neuroinflammation Marker				
Quinolinat	Within range	3.0	ug/mg	0 - 9.6
<b>Additional Markers (Urine)</b>				
Melatonin - Waking				
6-OH-Melatonin-Sulfate	Below range	9.3	ng/mg	10 - 85
Oxidative Stress / DNA Damage				
8-Hydroxy-2-deoxyguanosine (8-OHdG)	Above range	6.5	ng/mg	0 - 5.2

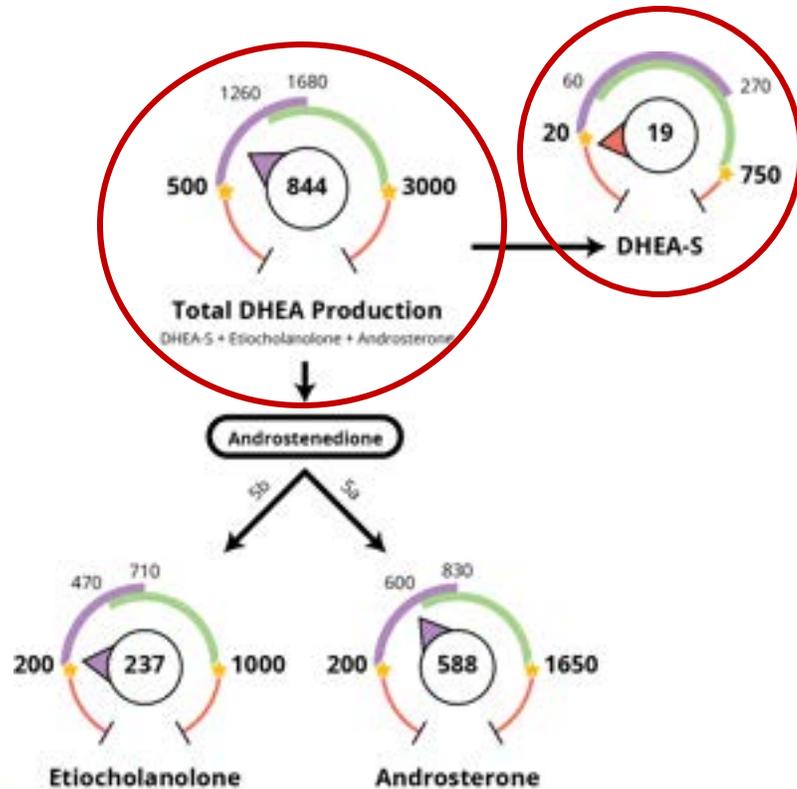
# A DUTCH Advanced Insights: Putting it all together!

- **58-year-old PMP female** on 100 mg OMP, 0.075 E2 patch, 5 mg transdermal T cream, and 1.0 mg vaginal E3. Complains of acne, occasional bothersome hot flashes, and weight loss resistance. BMI 30.1.



# A DUTCH Advanced Insights: Putting it all together!

- **58-year-old PMP female** on 100 mg OMP, 0.075 E2 patch, 5 mg transdermal T cream, and 1.0 mg vaginal E3. Complains of acne, occasional bothersome hot flashes, and weight loss resistance. BMI 30.1.
- Looking at the Advanced Insights, what could be promoting her alpha androgen metabolism that is likely contributing to her acne?



## Organic Acid Tests (OATs)

TEST	RESULT	UNITS	NORMAL RANGE
<b>Nutritional Organic Acids (Urine)</b>			
Vitamin B12 Marker - May be deficient if high			
Methylmalonate (MMA)	Within range	1.4 ug/mg	0 - 2.5
Vitamin B6 Markers - May be deficient if high			
Xanthurenate	Within range	0.54 ug/mg	0.12 - 1.2
Kynurenate	Above range	5.2 ug/mg	0.8 - 4.5
Biotin Marker - May be deficient if high			
b-Hydroxyisovalerate	Within range	4.8 ug/mg	0 - 12.5
Glutathione Marker - May be deficient if low or high			
Pyroglutamate	High end of range	57.7 ug/mg	28 - 58
Gut Marker - Potential gut putrefaction or dysbiosis if high			
Indican	Within range	65.6 ug/mg	0 - 100
<b>Neuro-Related Markers (Urine)</b>			
Dopamine Metabolite			
Homovanillate (HVA)	Within range	5.0 ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite			
Vanilmandelate (VMA)	Within range	5.1 ug/mg	2.2 - 5.5
<b>Neuroinflammation Marker</b>			
Quinolinatate	Above range	9.9 ug/mg	0 - 9.6
<b>Additional Markers (Urine)</b>			
Melatonin - Waking			
6-OH-Melatonin-Sulfate	Within range	43.5 ng/mg	10 - 85
<b>Oxidative Stress / DNA Damage</b>			
8-Hydroxy-2-deoxyguanosine (8-OHdG)	High end of range	4.9 ng/mg	0 - 5.2

# References

# References

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# Thank You!

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