



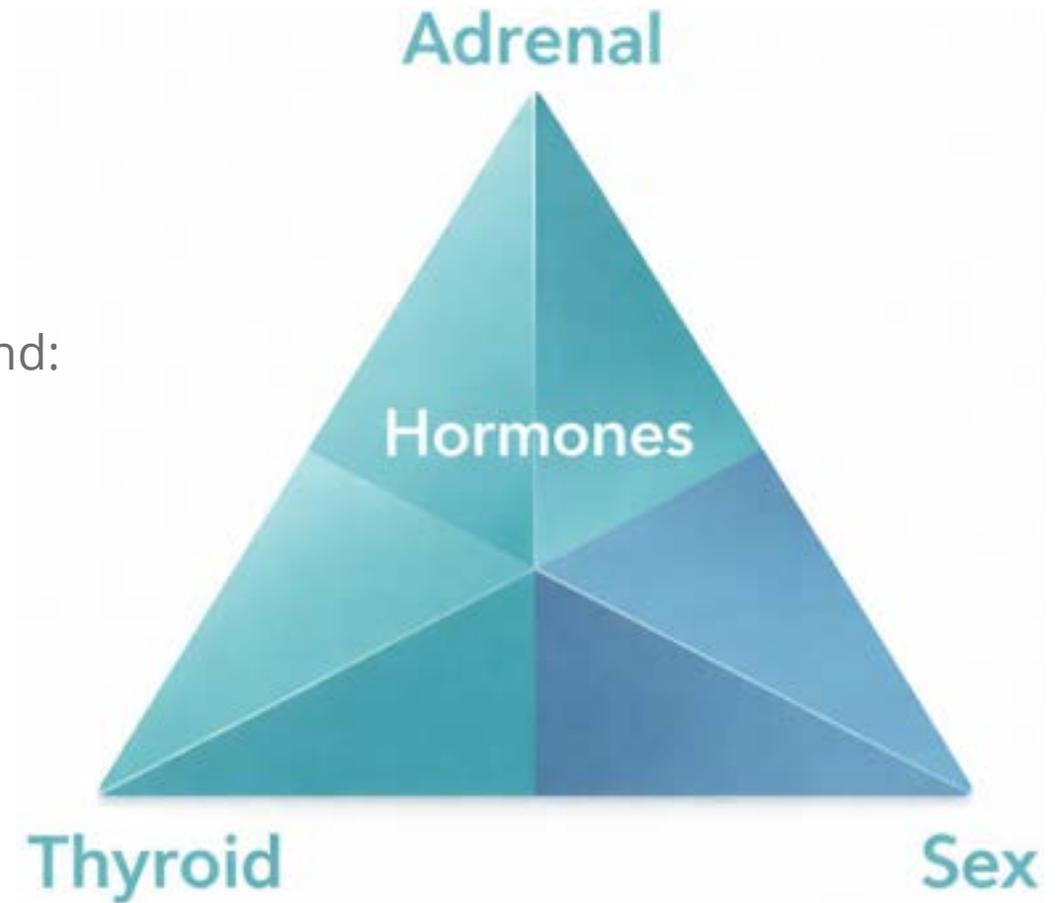
# Mastering DUTCH Test Essentials with Efficiency & Speed

Mark Newman, Precision Analytical

# Why are we here?

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- Your patients have problems and need answers
- Lab testing often has answers
- It is more likely we will find answers if we understand:
  - Adrenal Hormones
  - Sex/Reproductive Hormones
  - Thyroid Hormones

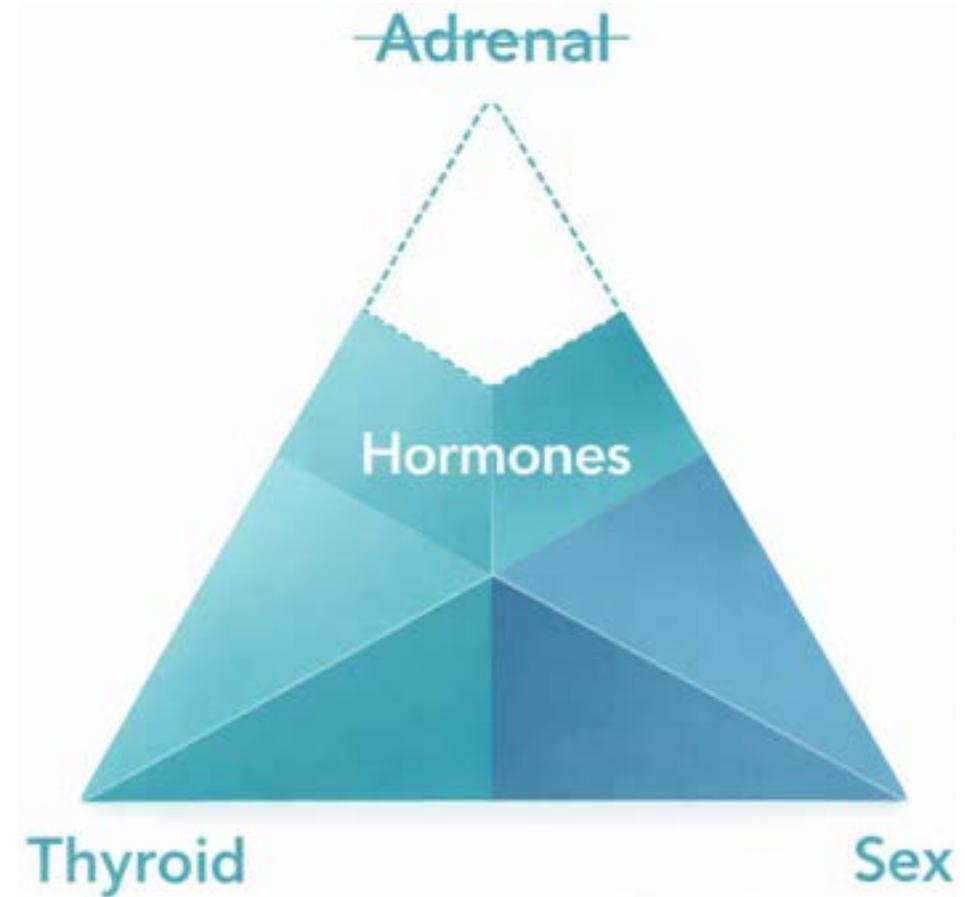


# Serum Testing – Necessary but not sufficient



Best way to test many things:

- Thyroid, Insulin, HbA1c
- SHBG, LH, FSH
- Inflammatory markers
- Standard blood tests, etc.

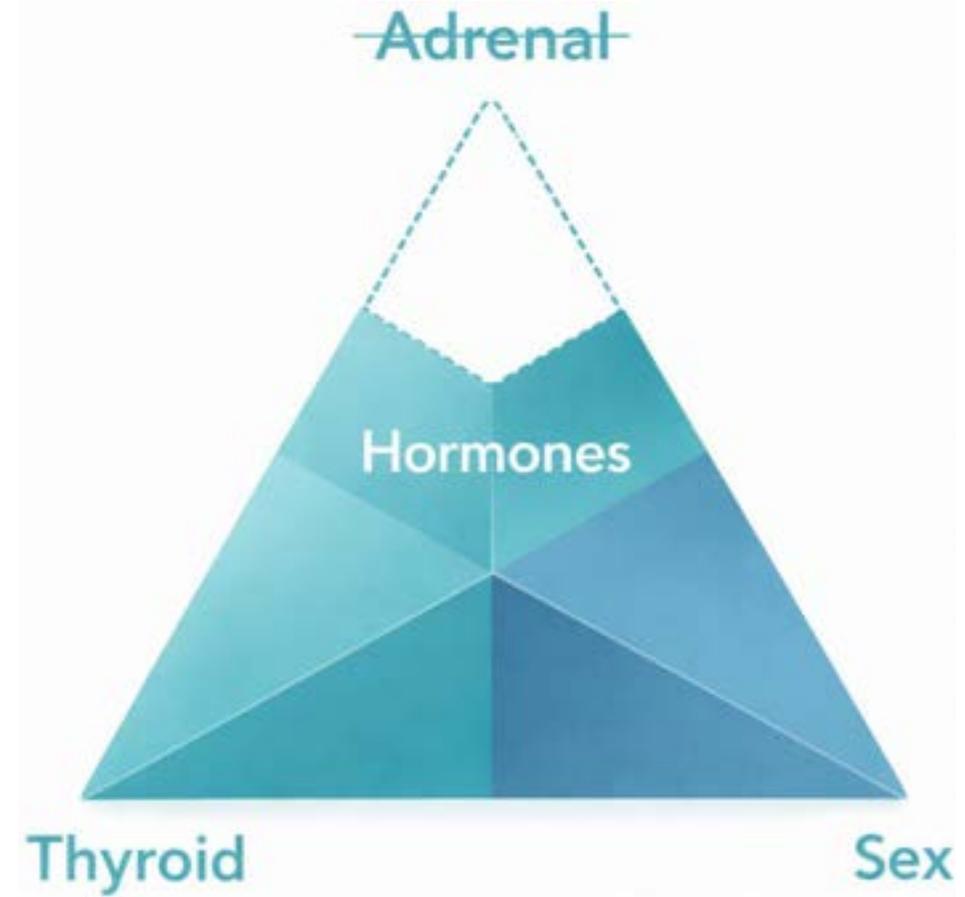


# Serum Testing – Necessary but not sufficient

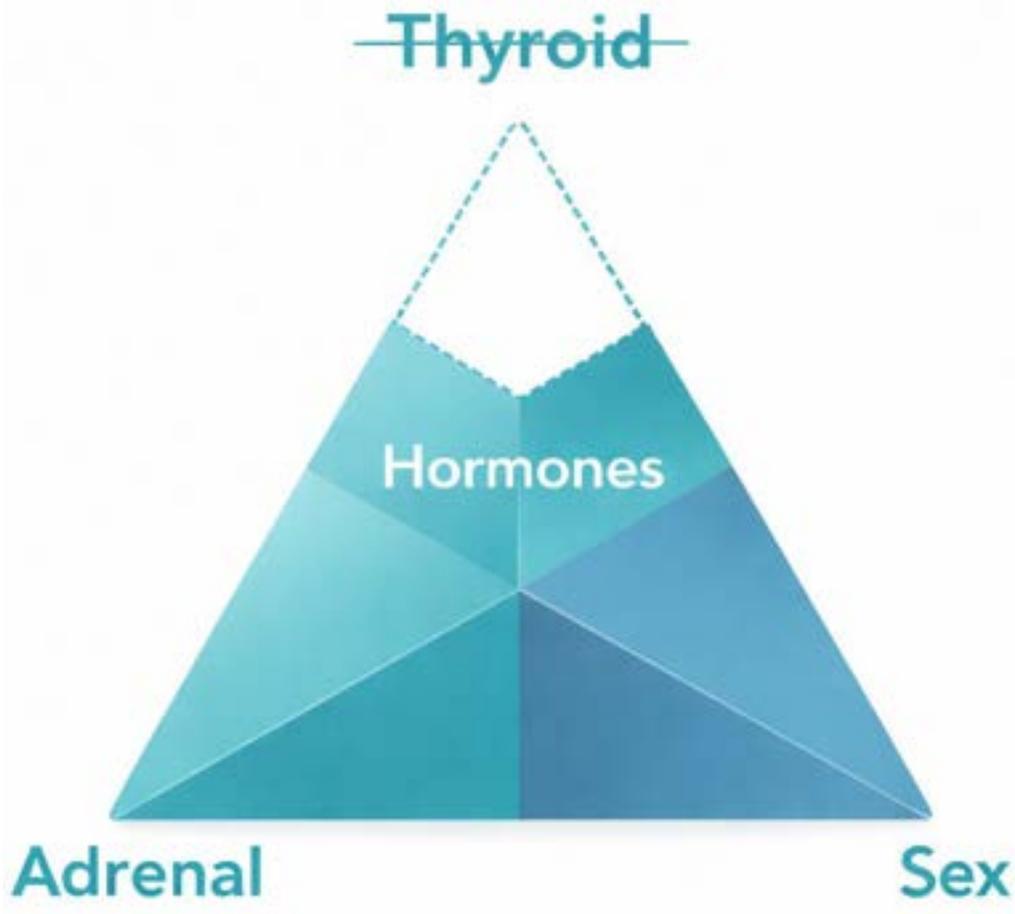


## Serum

Good for many tests  
(but not cortisol)



# DUTCH Testing - "Comprehensive" for reproductive and adrenal hormones



Comprehensive for  
Adrenal & Sex  
Hormones

# Serum and DUTCH Test – Competitive and Complementary

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Good for many tests  
(but not cortisol)



Comprehensive for  
Adrenal & Sex  
Hormones

# Why Hormone Testing?

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The Endocrine Story needs to be told  
when pursuing wellness

Hormone Production  
and Hormone Metabolism:  
Key parts of the Endocrine Story

# Why are we here?

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If you can Interpret the DUTCH Test and integrate with standard lab testing, you can help patients with more competence and confidence

# Why are we here?

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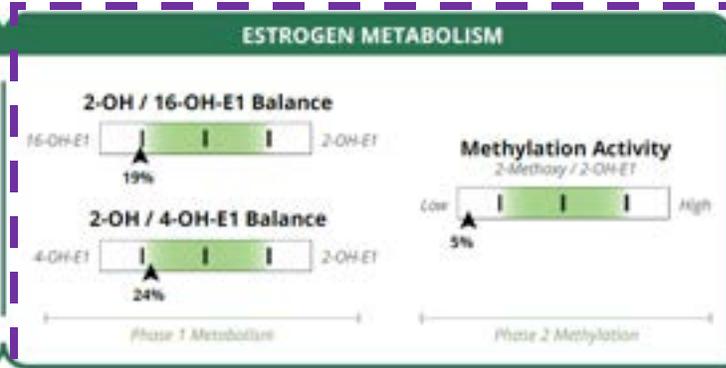
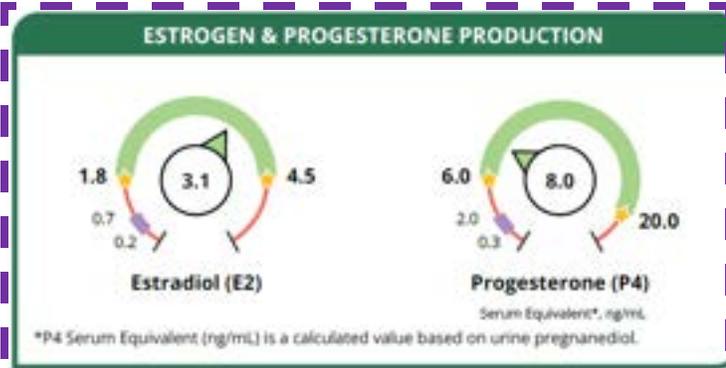
Interpret the DUTCH Test  
with speed, confidence & clarity!



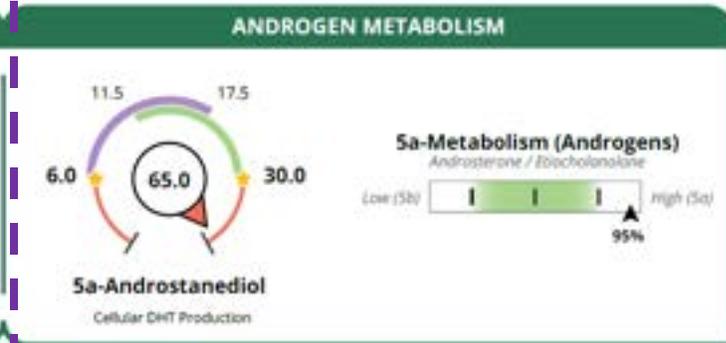
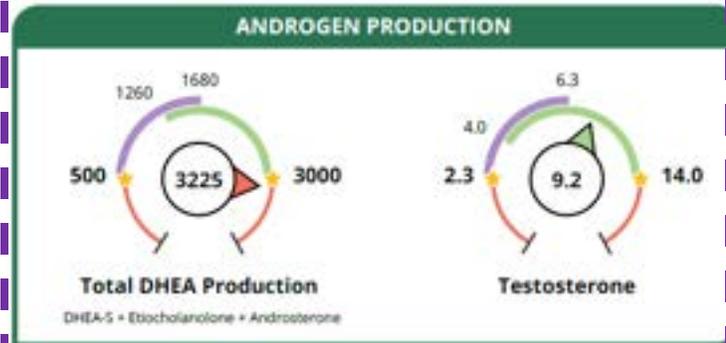
To accomplish our goal, DUTCH Fest can NOT be comprehensive.  
We will focus primarily on female patients and without focusing on HRT.



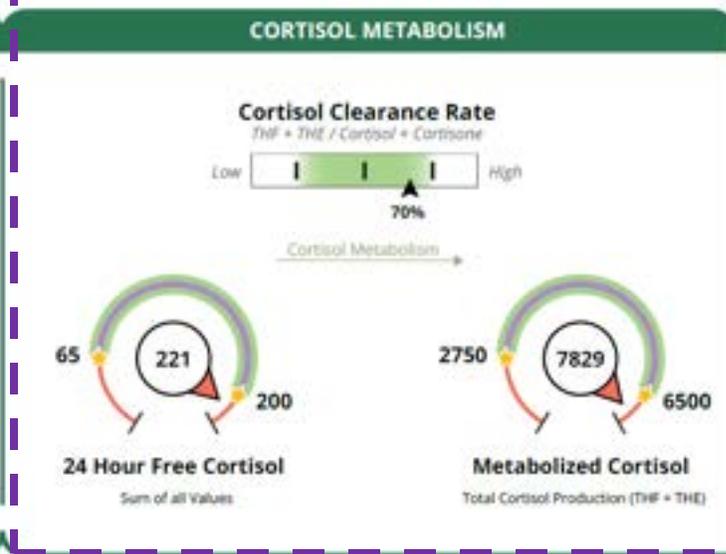
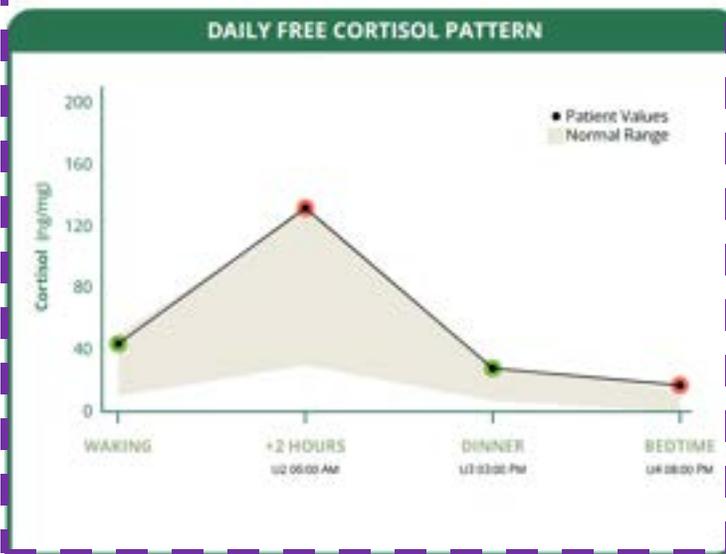
# Estrogen Story



# Androgen Story



# Cortisol Story



Hormone Production

Hormone Metabolism

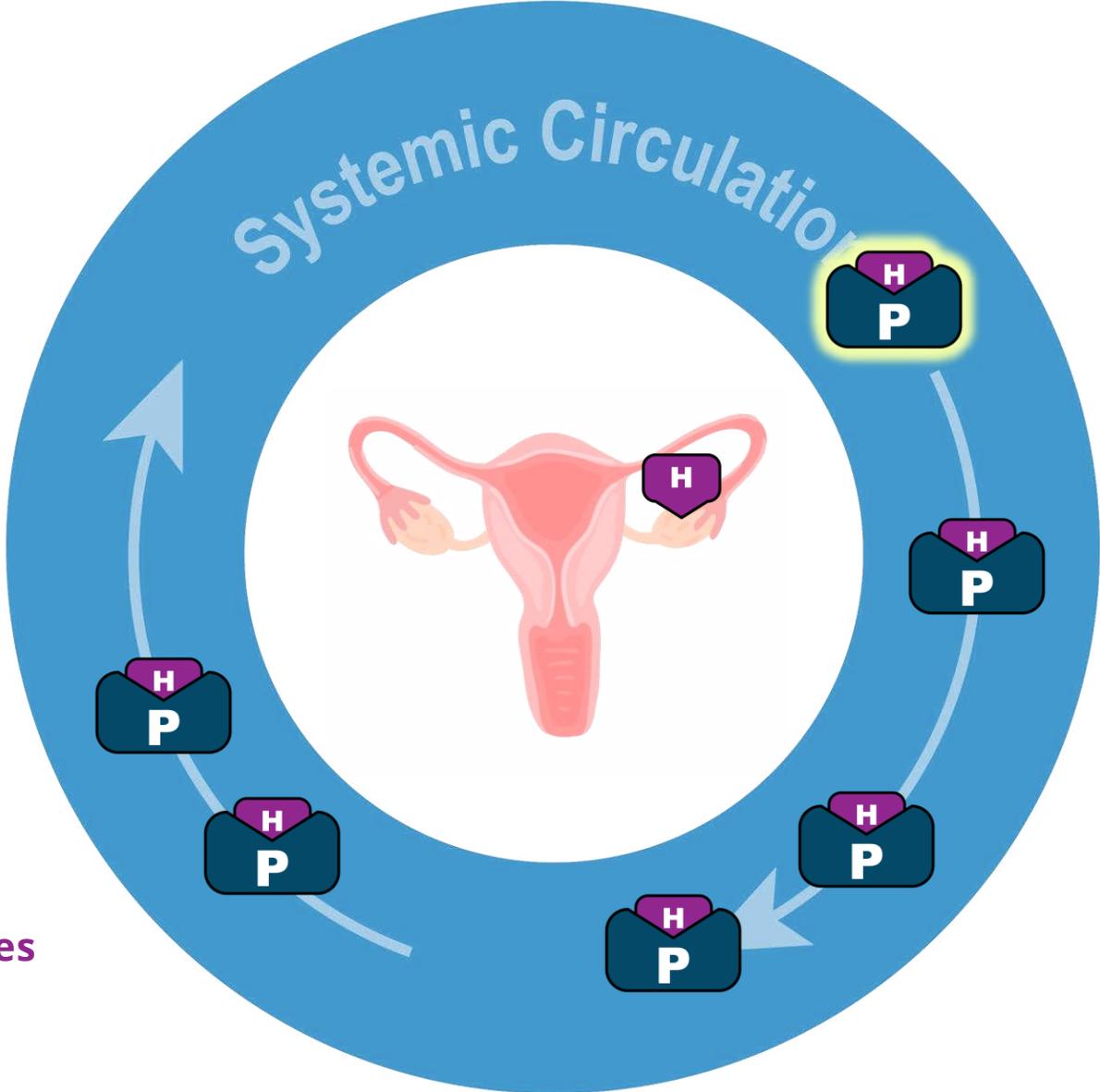
# Hormone Testing Fundamentals

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- Serum, Saliva, DUTCH (Urine) Differences
- Using the Steroid Pathway Responsibly
- Why Test Metabolites? The Issue is the Tissue!
- Applying DUTCH to HRT (not the focus of DUTCH Fest)

# Serum, Saliva, & Urine Testing

What's the Difference?



**P** Protein  
**H** Hormones

Serum

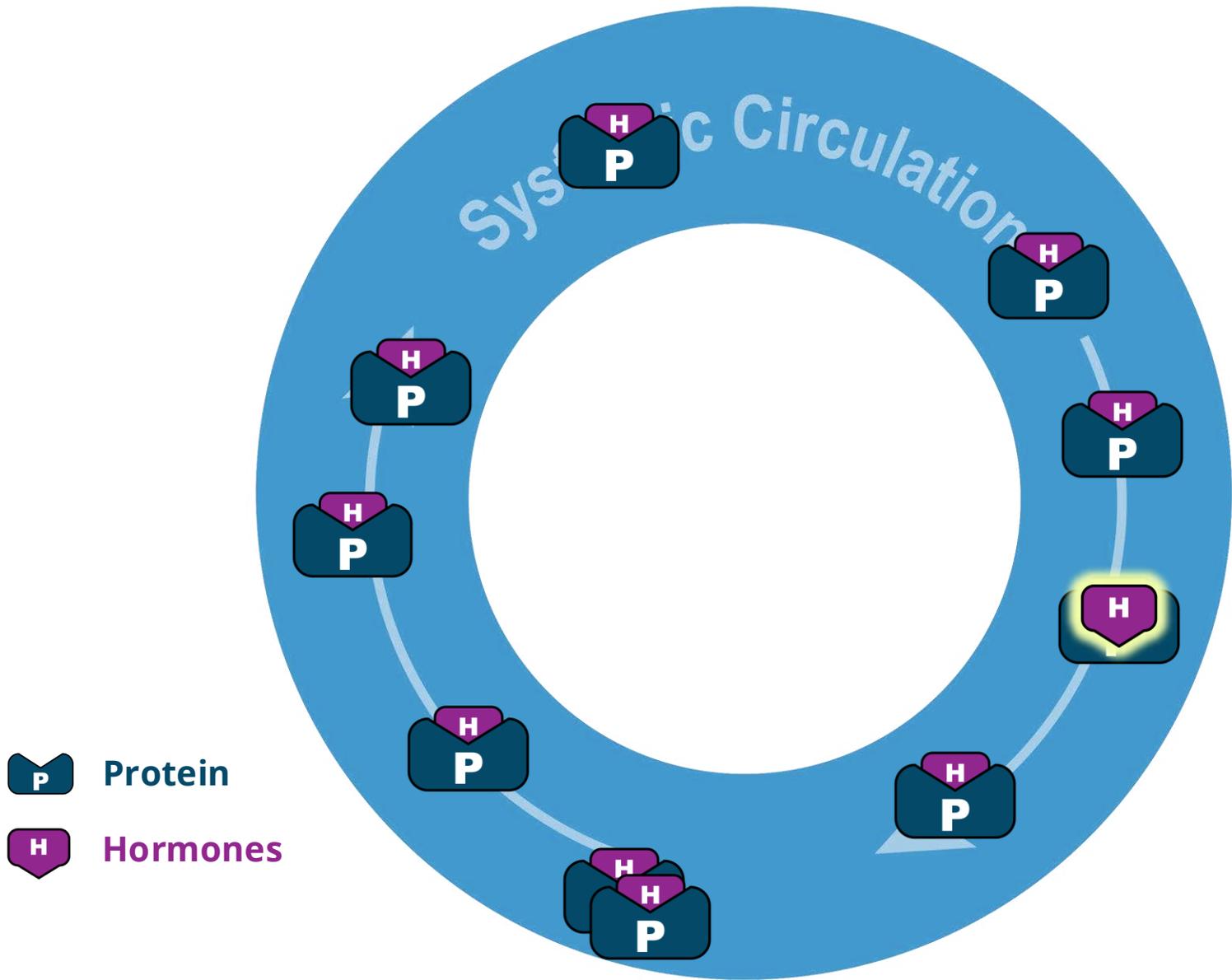
Saliva

Urine



ESTROGEN & PROGESTERONE PRODUCTION	ESTROGEN METABOLISM
<p>Estradiol (E2)</p> <p>Progesterone (P4)</p>	Use LC-MS/MS for E2
ANDROGEN PRODUCTION	ANDROGEN METABOLISM
<p>Total DHEA Production</p> <p>Testosterone</p>	Use LC-MS/MS for female T
DAILY FREE CORTISOL PATTERN	CORTISOL METABOLISM
Hormone Production	Hormone Metabolism







### ESTROGEN & PROGESTERONE PRODUCTION



### ESTROGEN METABOLISM

Sex hormones in saliva – accurate?



### ANDROGEN PRODUCTION



### ANDROGEN METABOLISM

### DAILY FREE CORTISOL PATTERN

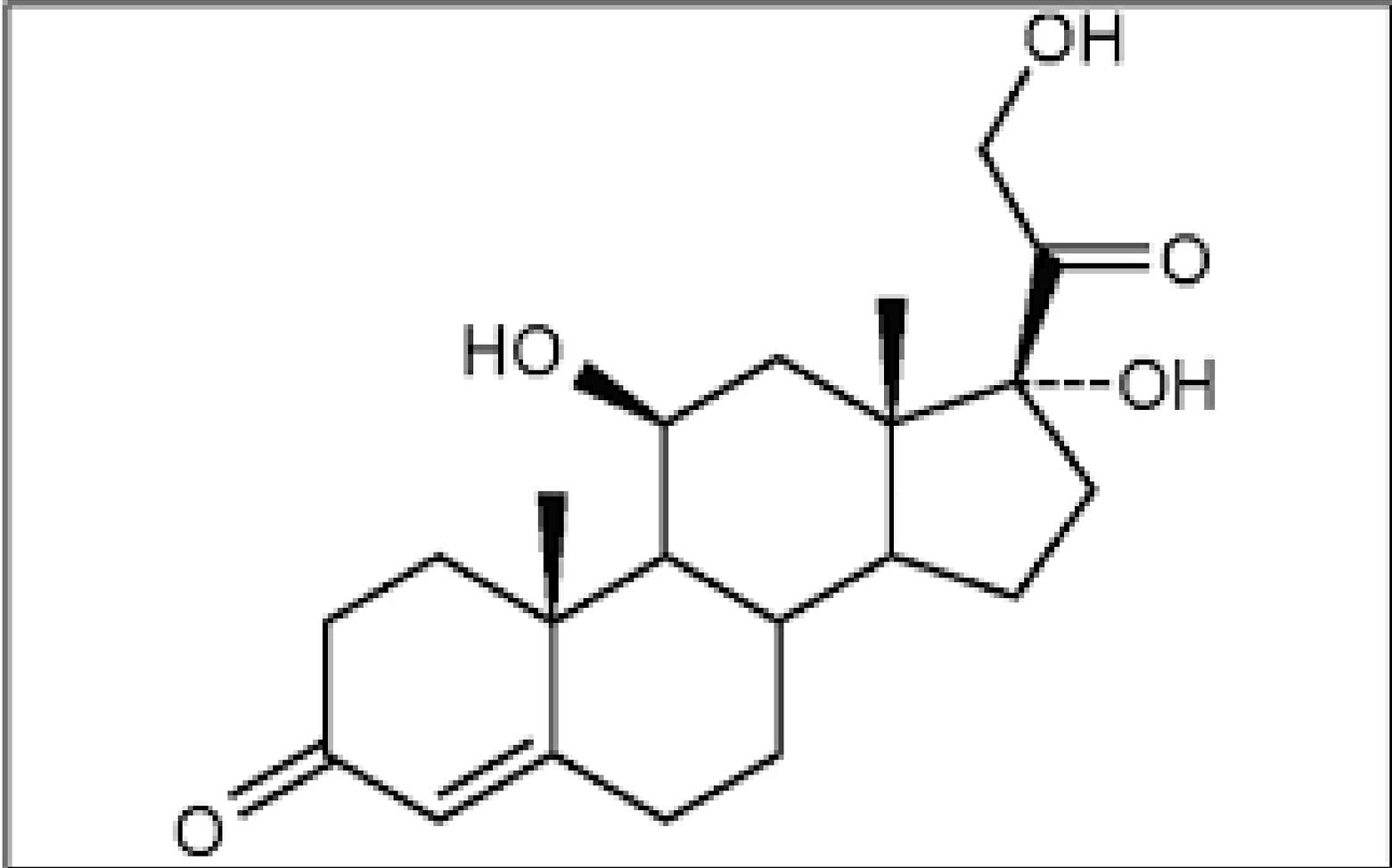


### CORTISOL METABOLISM

Cortisol testing drove popularity in saliva testing (rightly so)

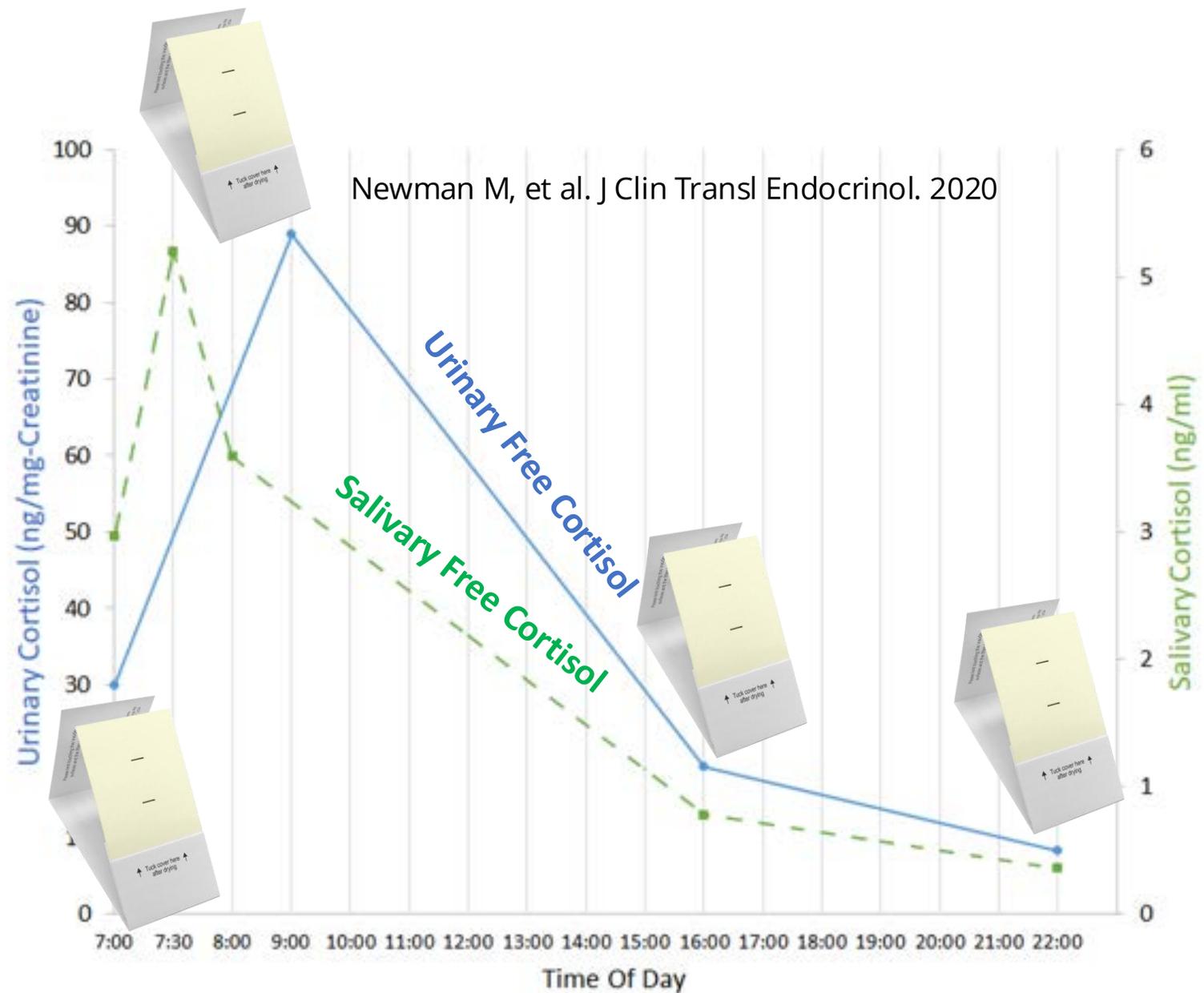
Hormone Production

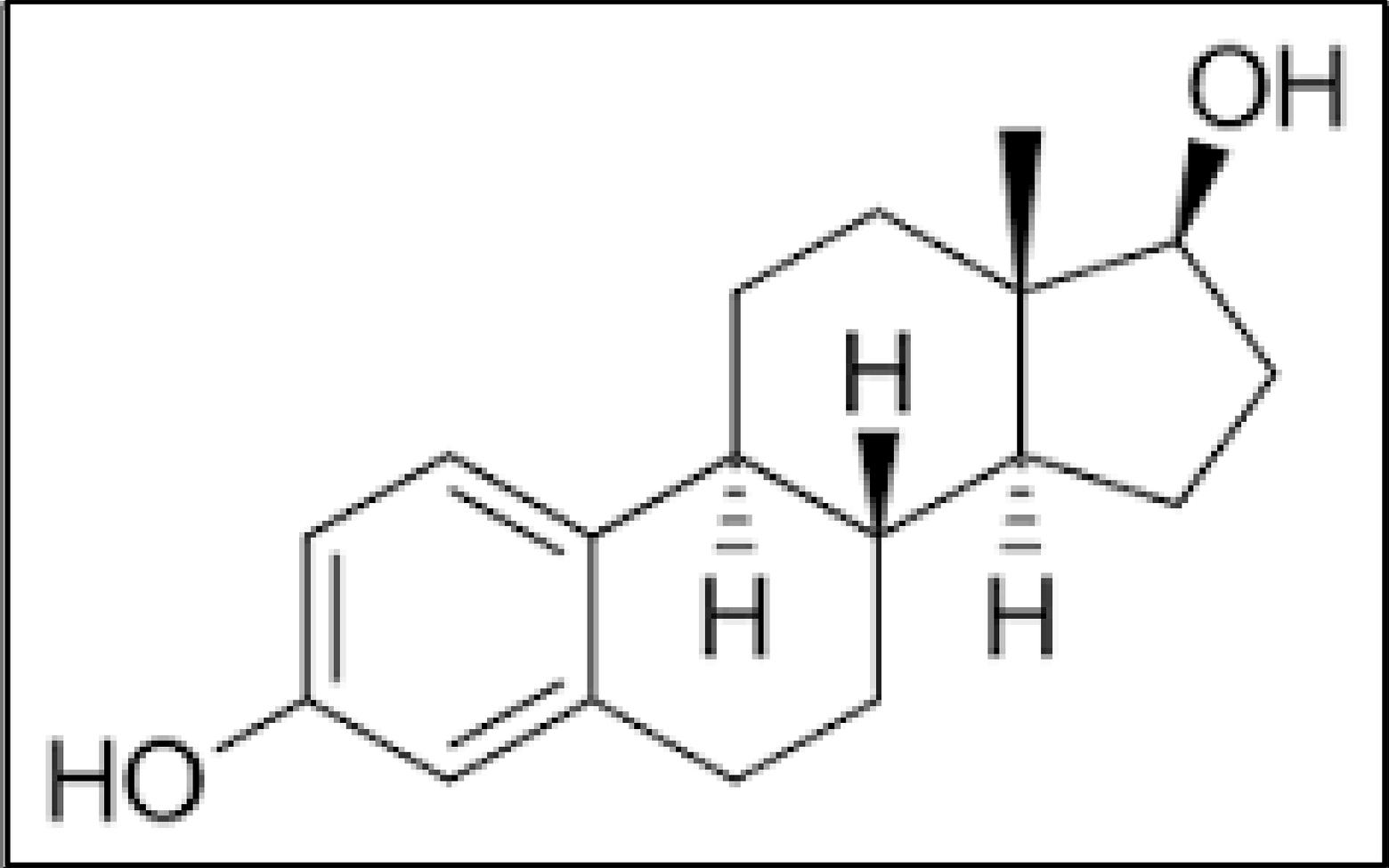
Hormone Metabolism



# Dried Urine & Saliva Free Cortisol

**Precision  
Analytical Data  
N=68  
Peer-Reviewed Published**





Serum



A red cylindrical icon representing a serum sample. It features a dark blue shield-shaped label with the letters 'H' and 'P' stacked vertically.

Saliva



A blue cylindrical icon representing a saliva sample. It features a purple shield-shaped label with the letter 'H' inside.

Urine Cortisol

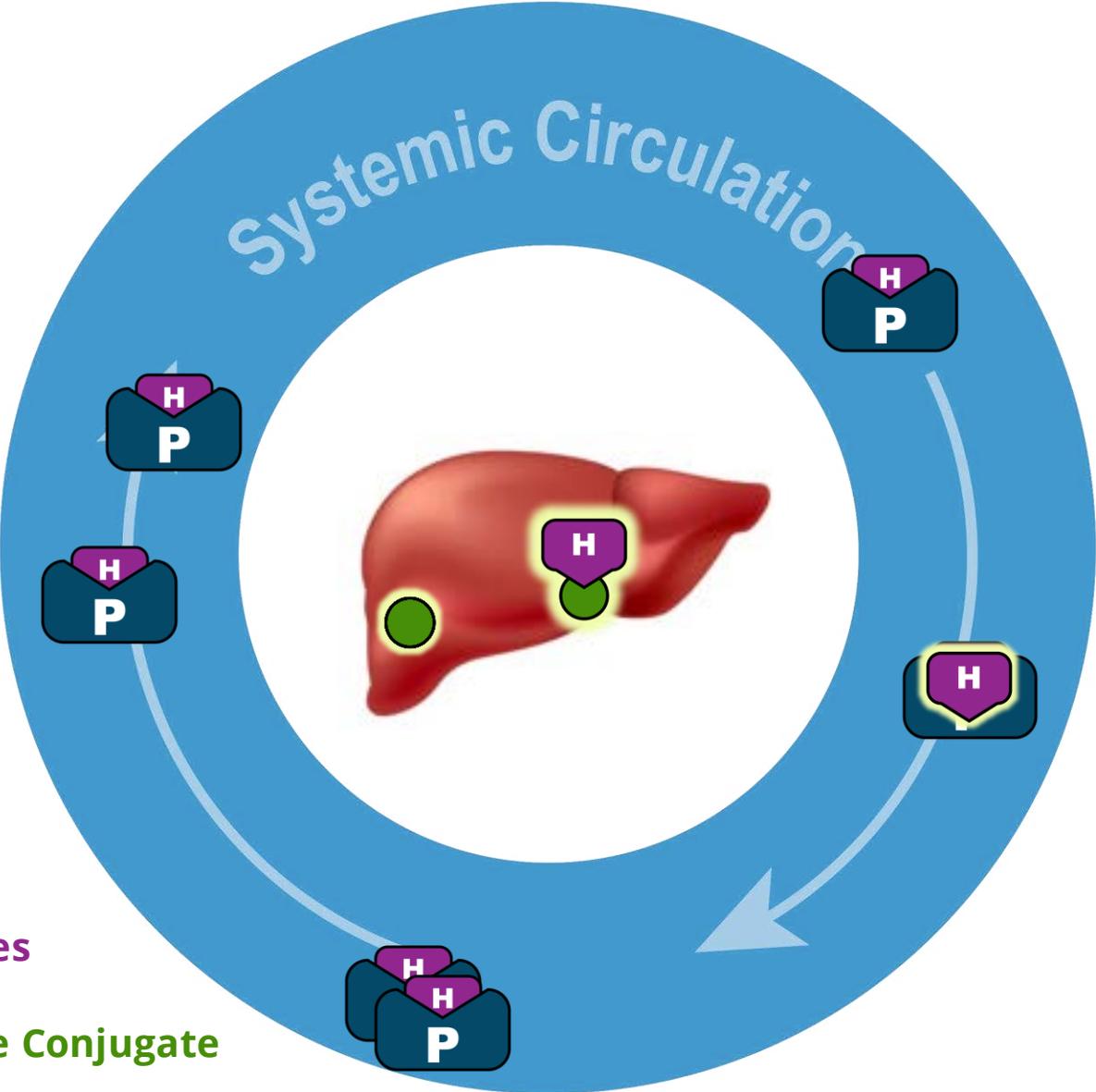


A yellow cylindrical icon representing a urine sample for cortisol measurement. It features a purple shield-shaped label with the letter 'H' inside.

Urine



A yellow cylindrical icon representing a general urine sample. It does not have a label.



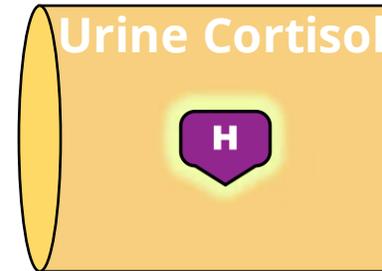
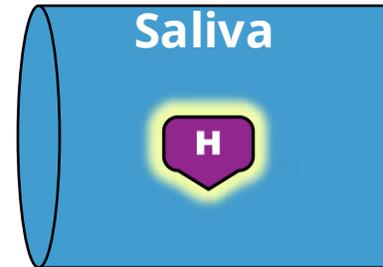
-  Protein
-  Hormones
-  Hormone Conjugate



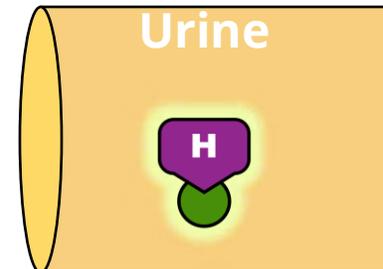
**Protein-bound (SHBG, Albumin)**

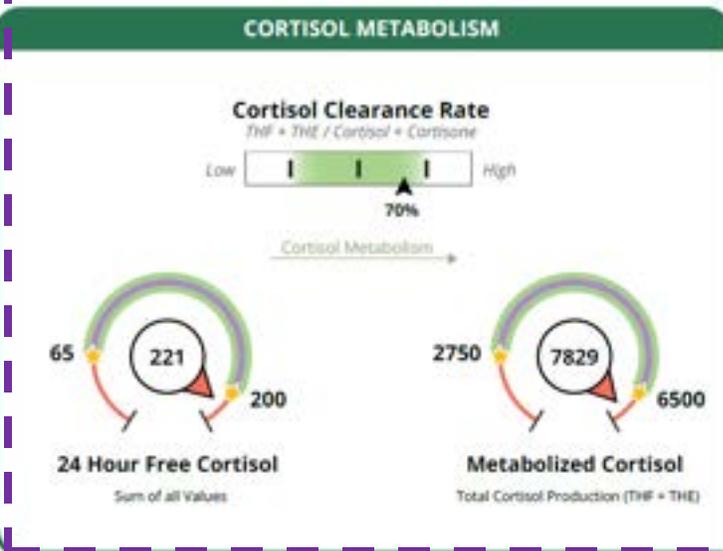
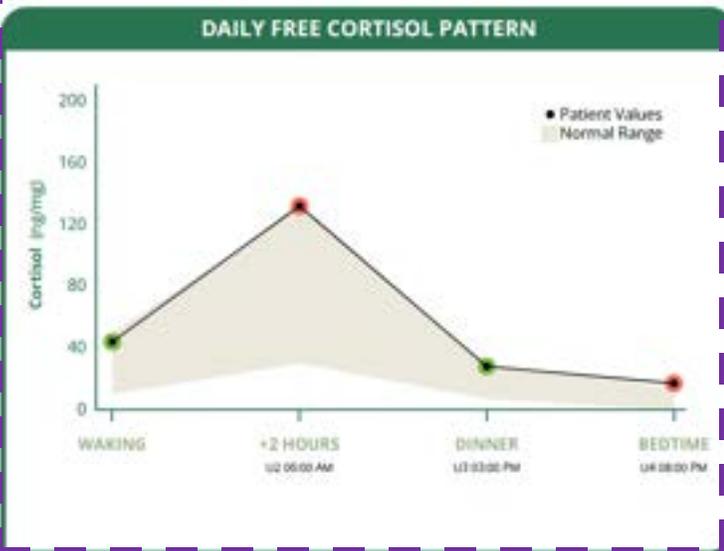
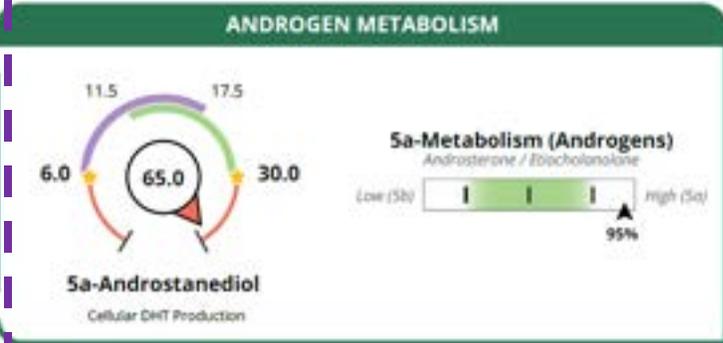
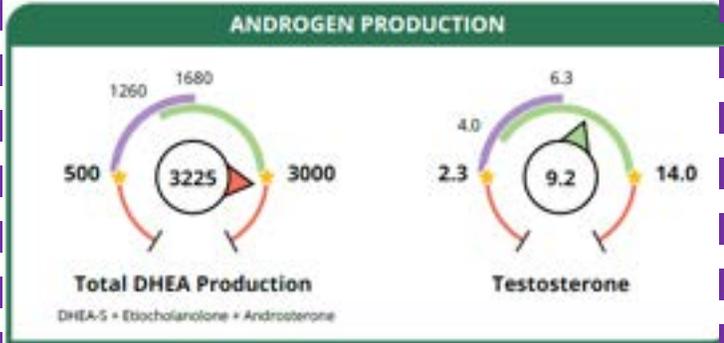
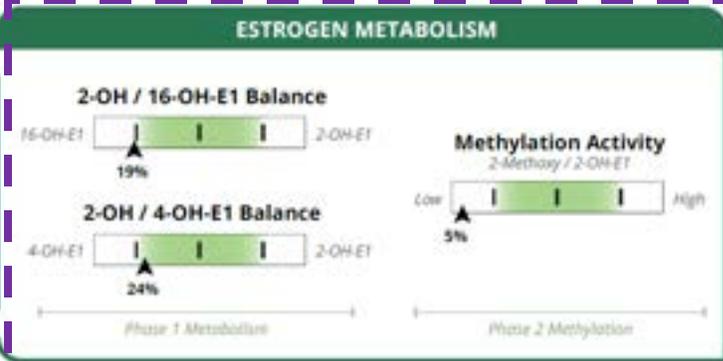
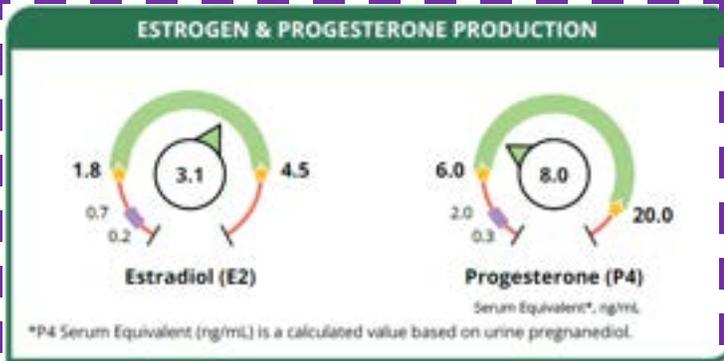


**Free (unbound) Hormone**



**Hormone Conjugate (water-soluble)**

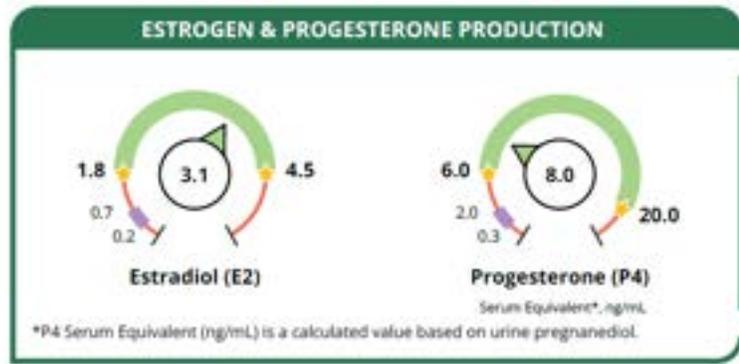




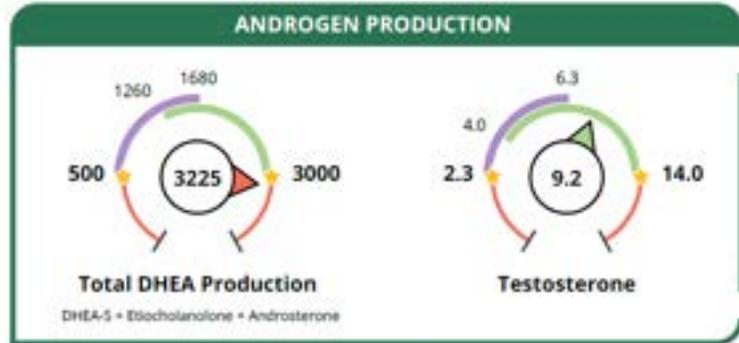
Hormone Production

Hormone Metabolism

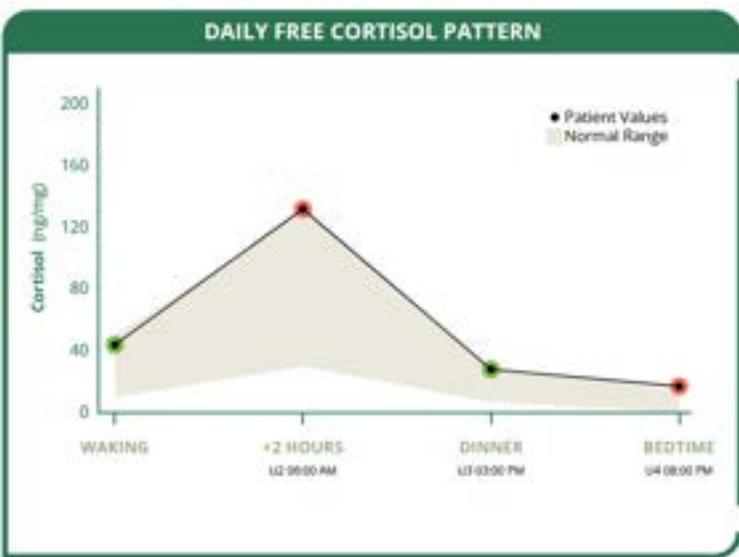




## Estrogen and Progesterone Production

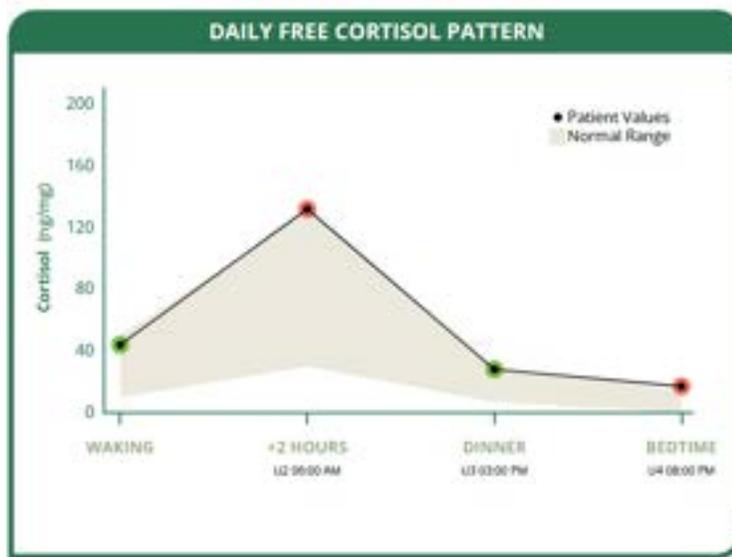
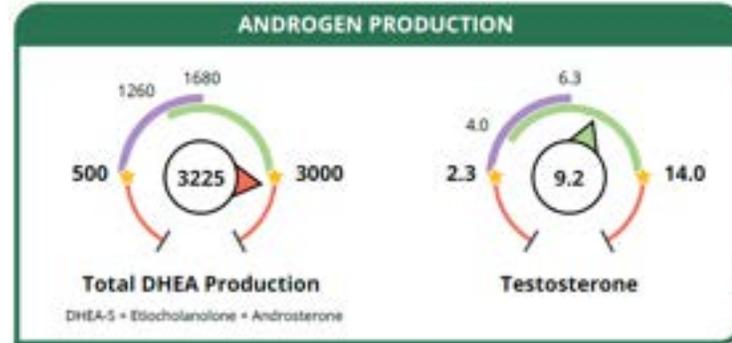
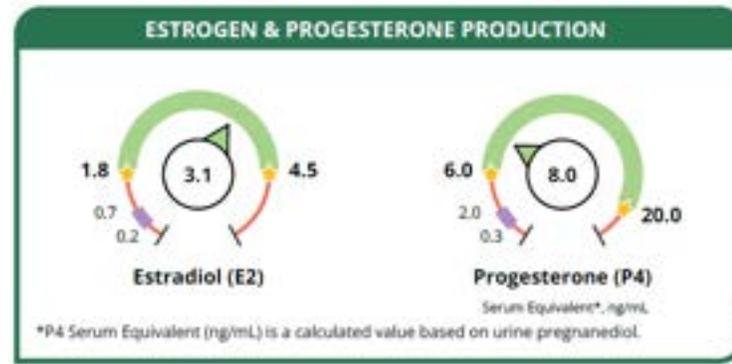


## DHEA(S) and Testosterone Production



## Cortisol Production

Hormone Production

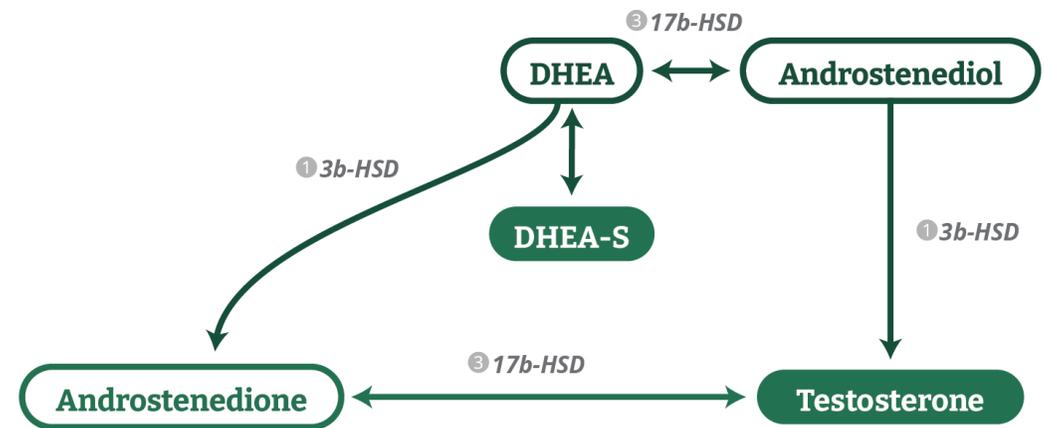


## Hormone Production

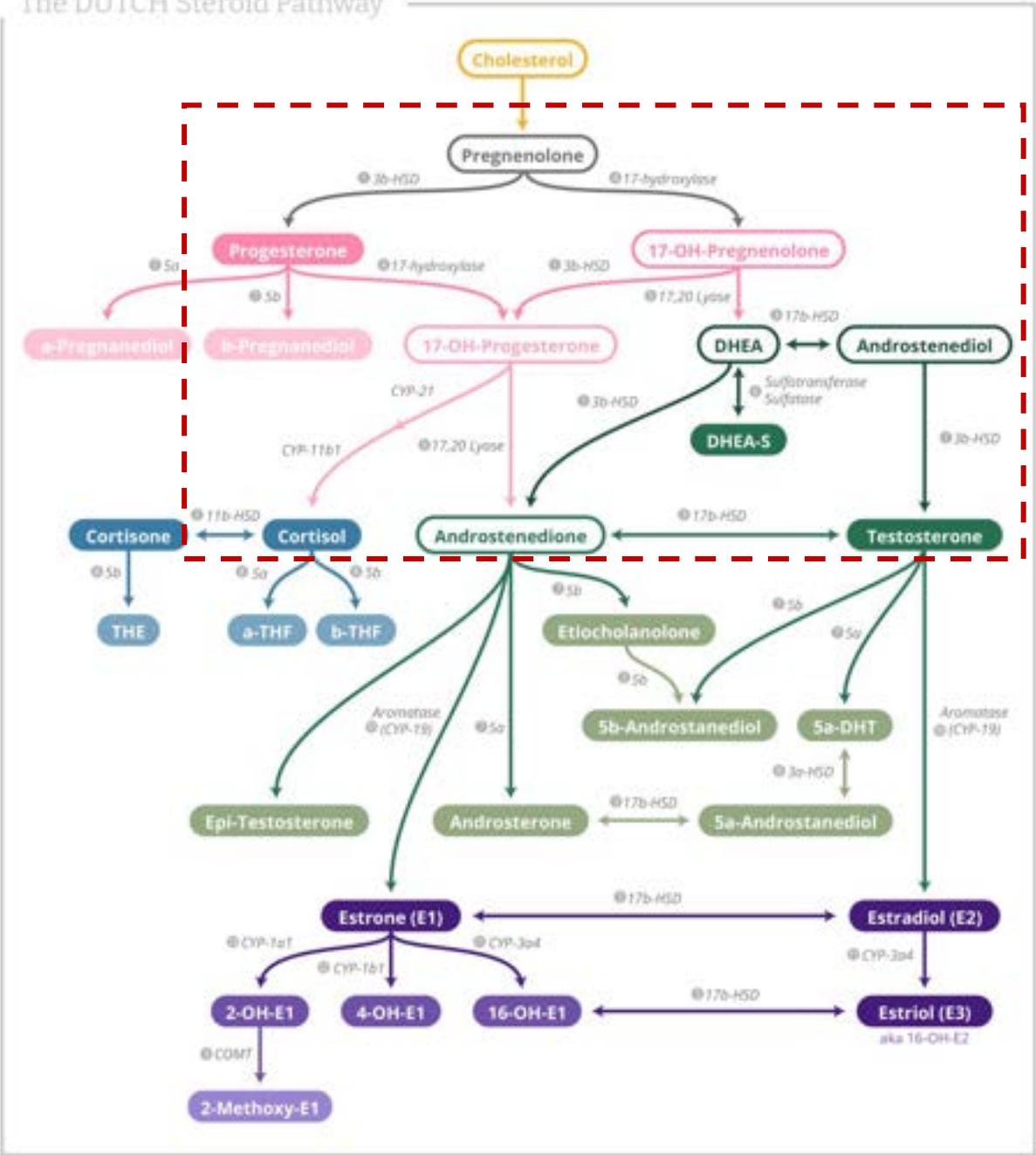


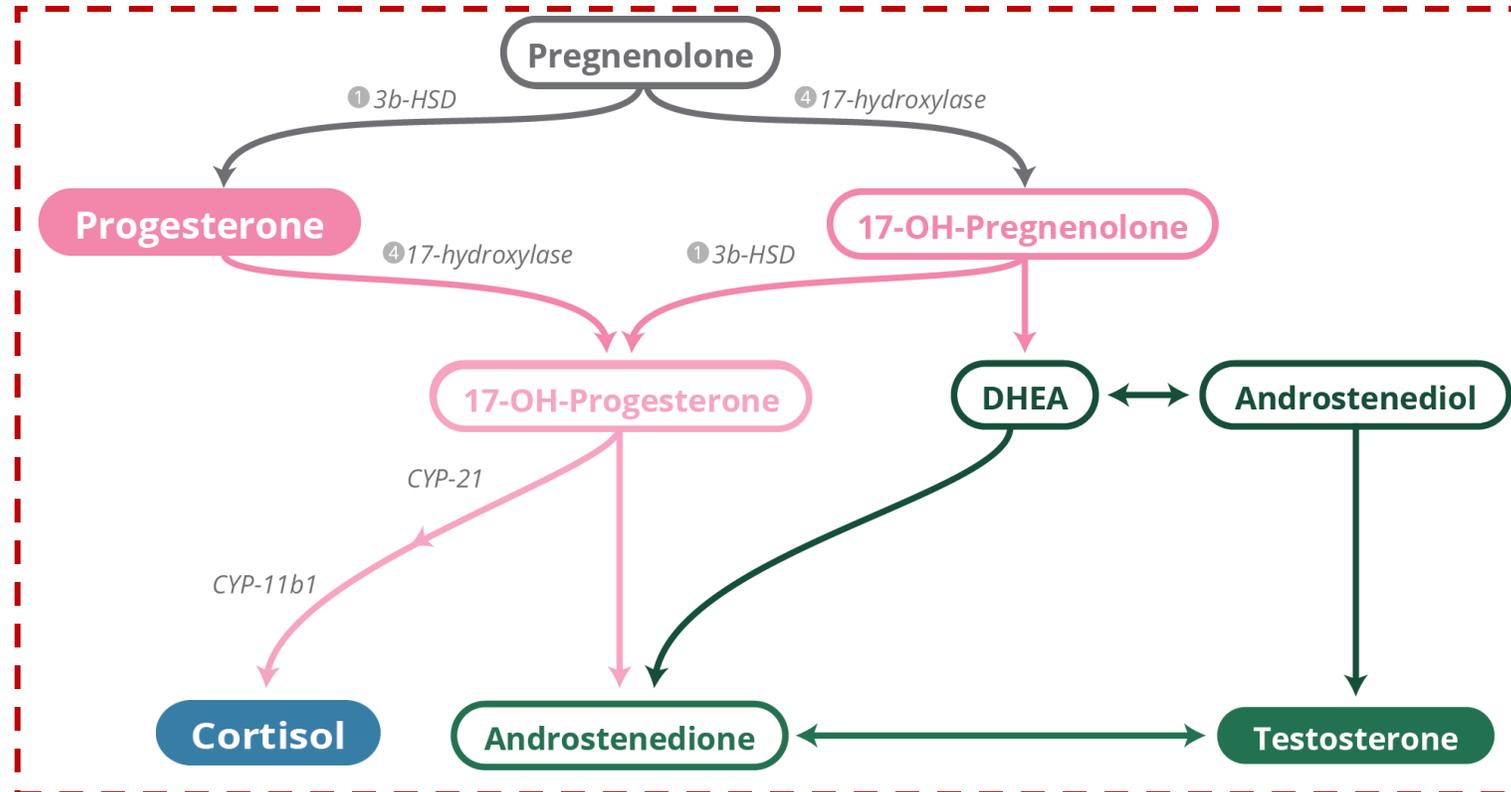
For premenopausal women, hormones are made primarily from glandular production, not “trickle down metabolism”

Exception – Testosterone:  
Primarily comes from adrenal DHEA and ovarian production.



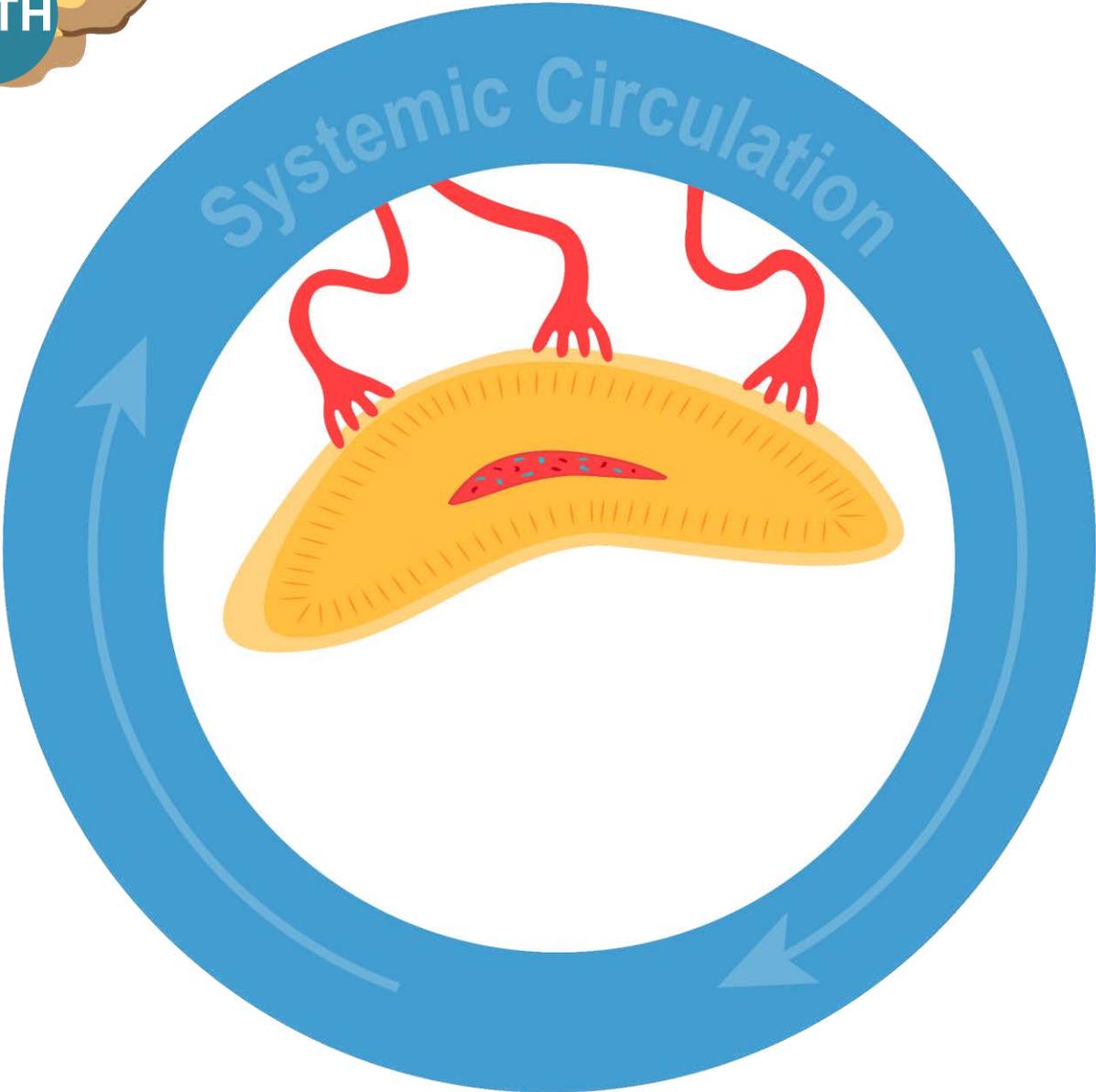
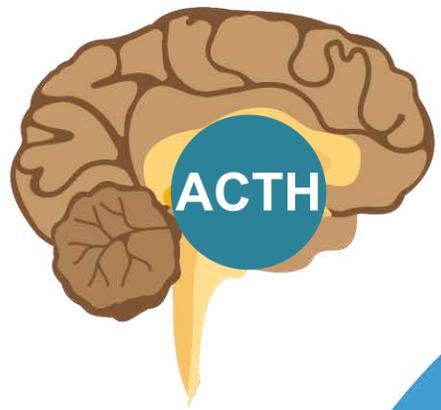
The DUTCH Steroid Pathway



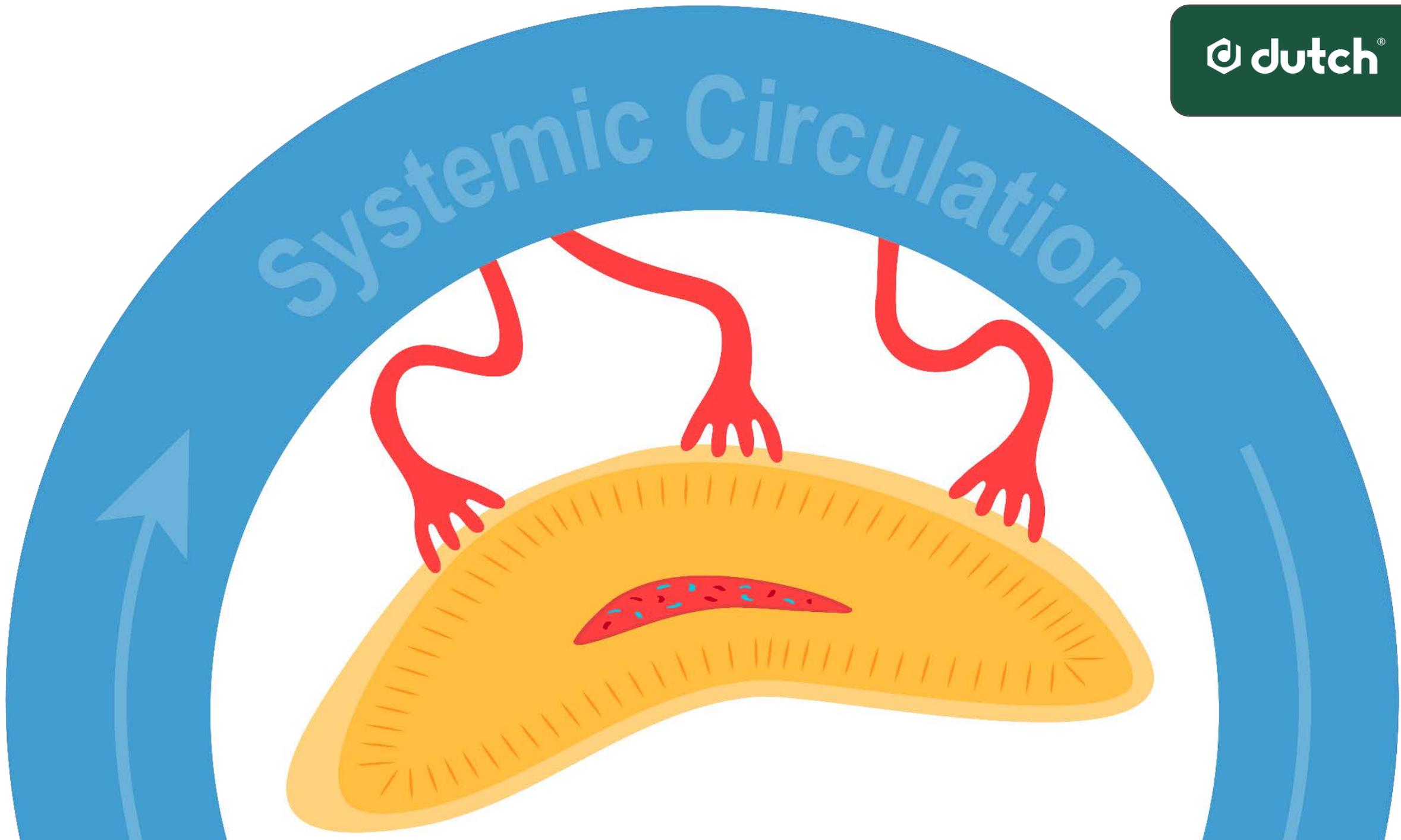


Cortisol: “made from Progesterone and Pregnenolone?”

What does that mean?



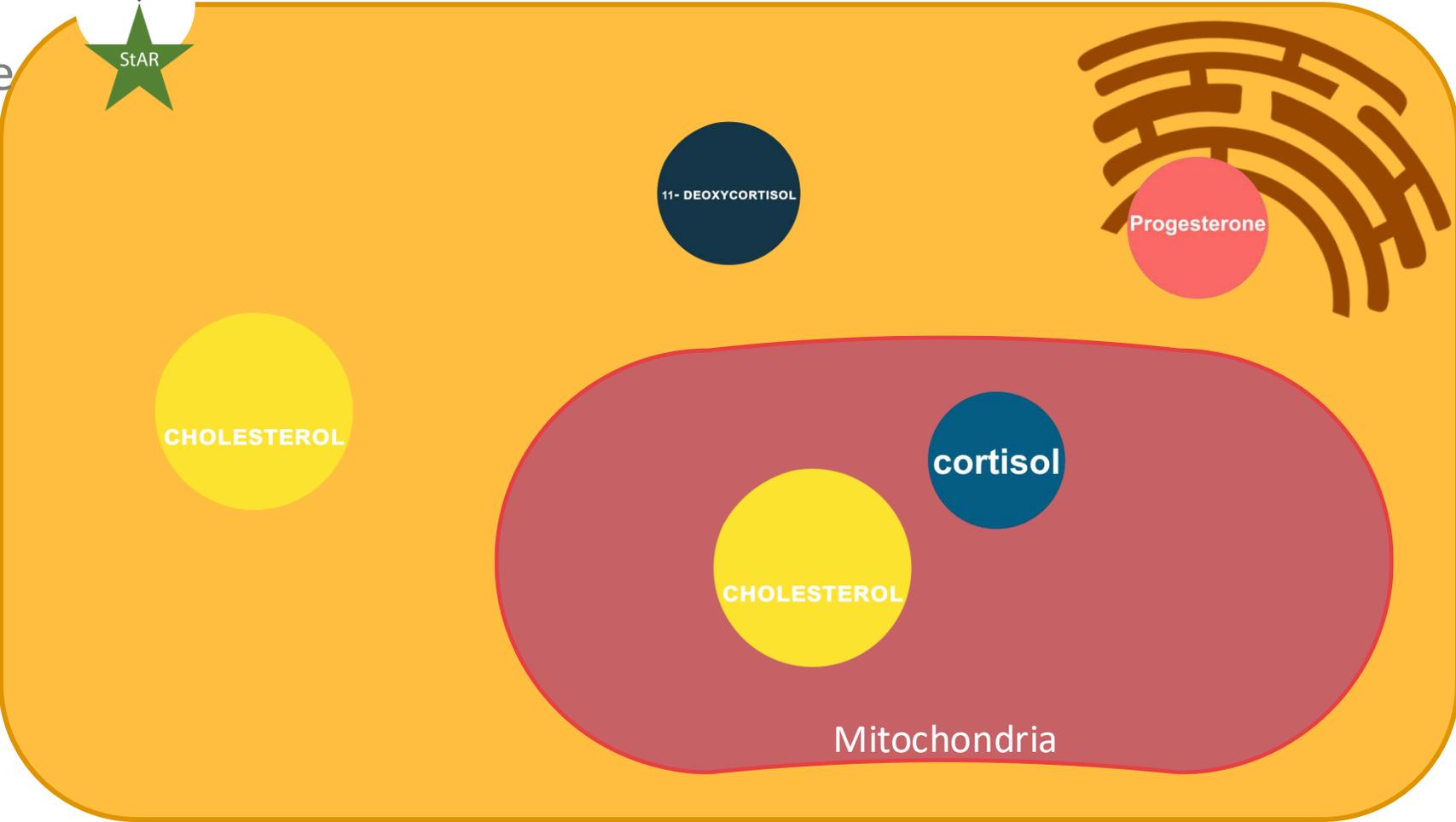
# Systemic Circulation

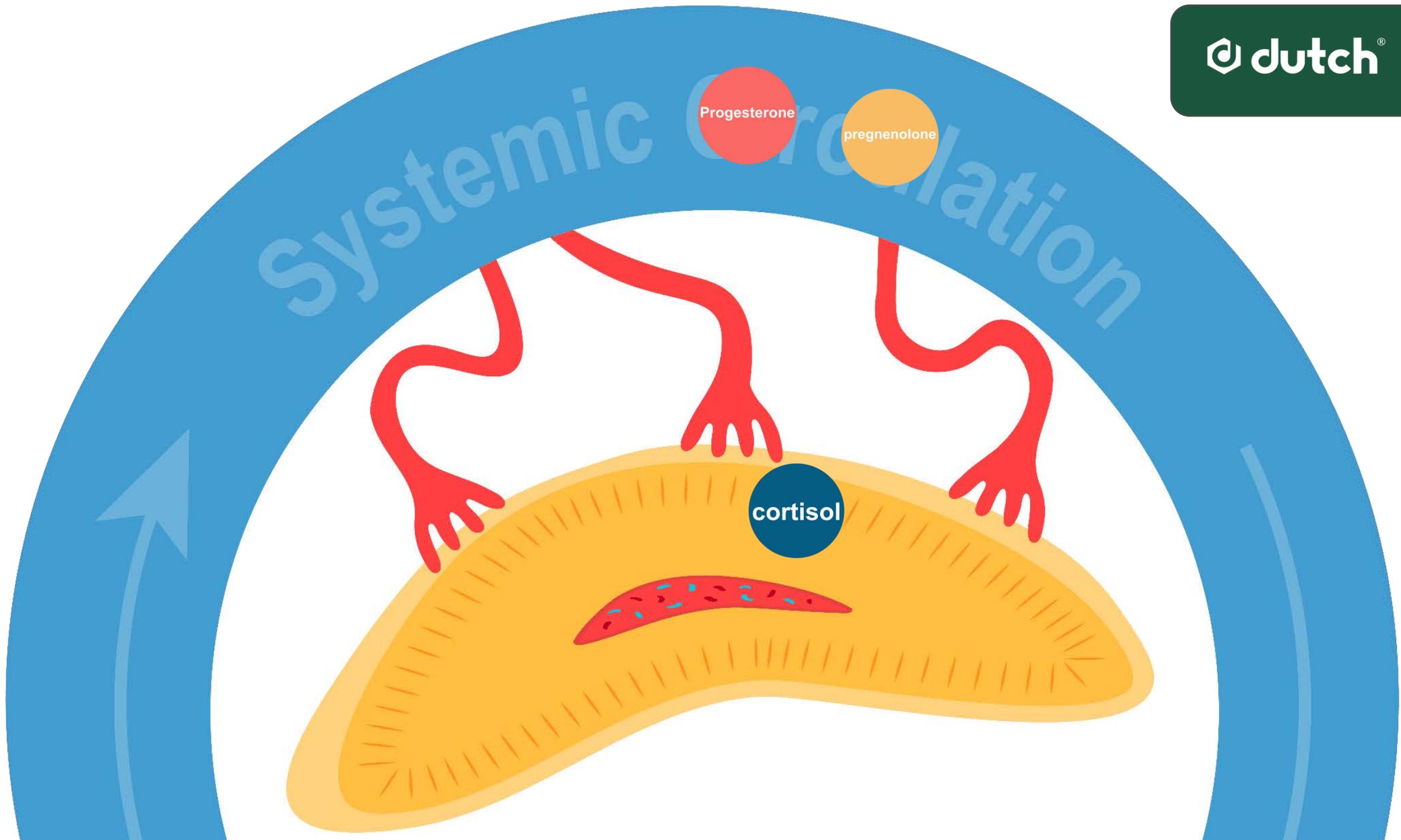


# Adrenal Cortex Cell



StAR abundance  
T3 related





Progesterone

pregnenolone

cortisol

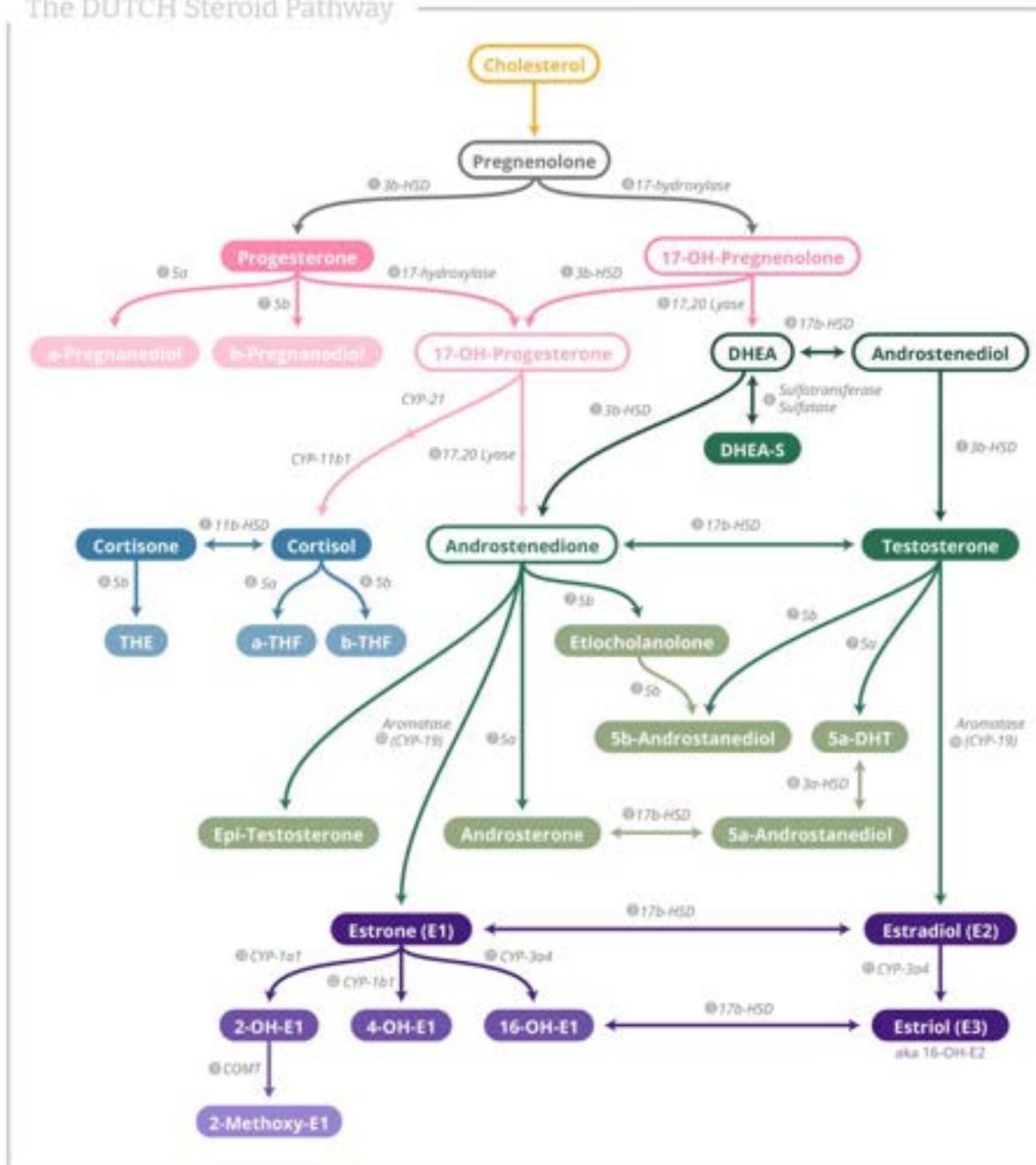
Systemic Circulation



## Use the Steroid Pathway Responsibly!

The Steroid Pathway is full of interesting and useful insights:

BUT “trickle down metabolism” cannot compete with glandular production (DHEA, Cortisol, Pre-menopausal E2, Pg, male T)



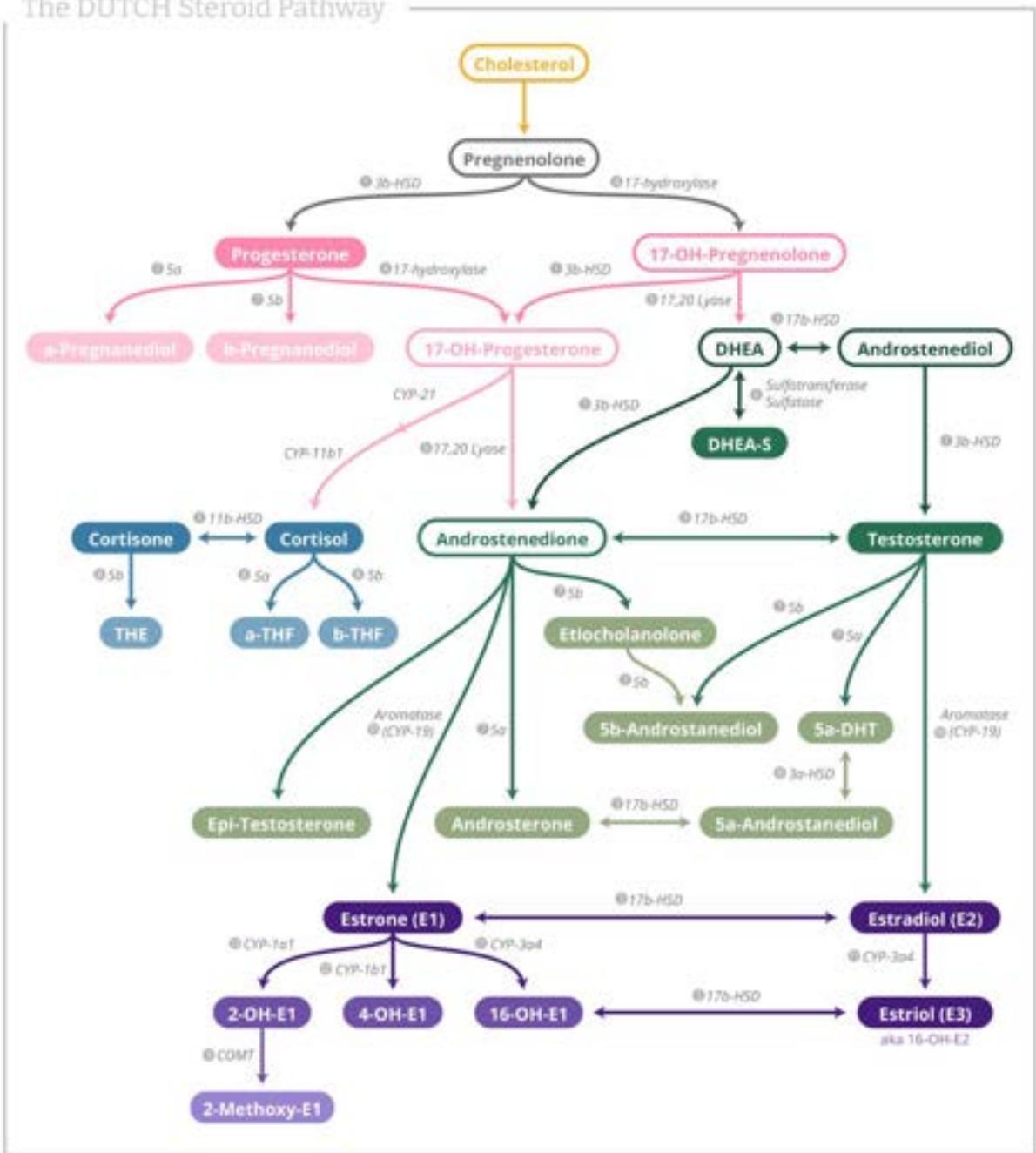


## Use the Steroid Pathway Responsibly!

The Steroid Pathway is full of interesting and useful insights:

Giving DHEA can produce “female” levels of testosterone but can’t compete with testicular testosterone or ovarian estrogen production

Giving progesterone can’t increase cortisol levels significantly





## Use the Steroid Pathway Responsibly!

The Steroid Pathway is full of interesting and useful insights:

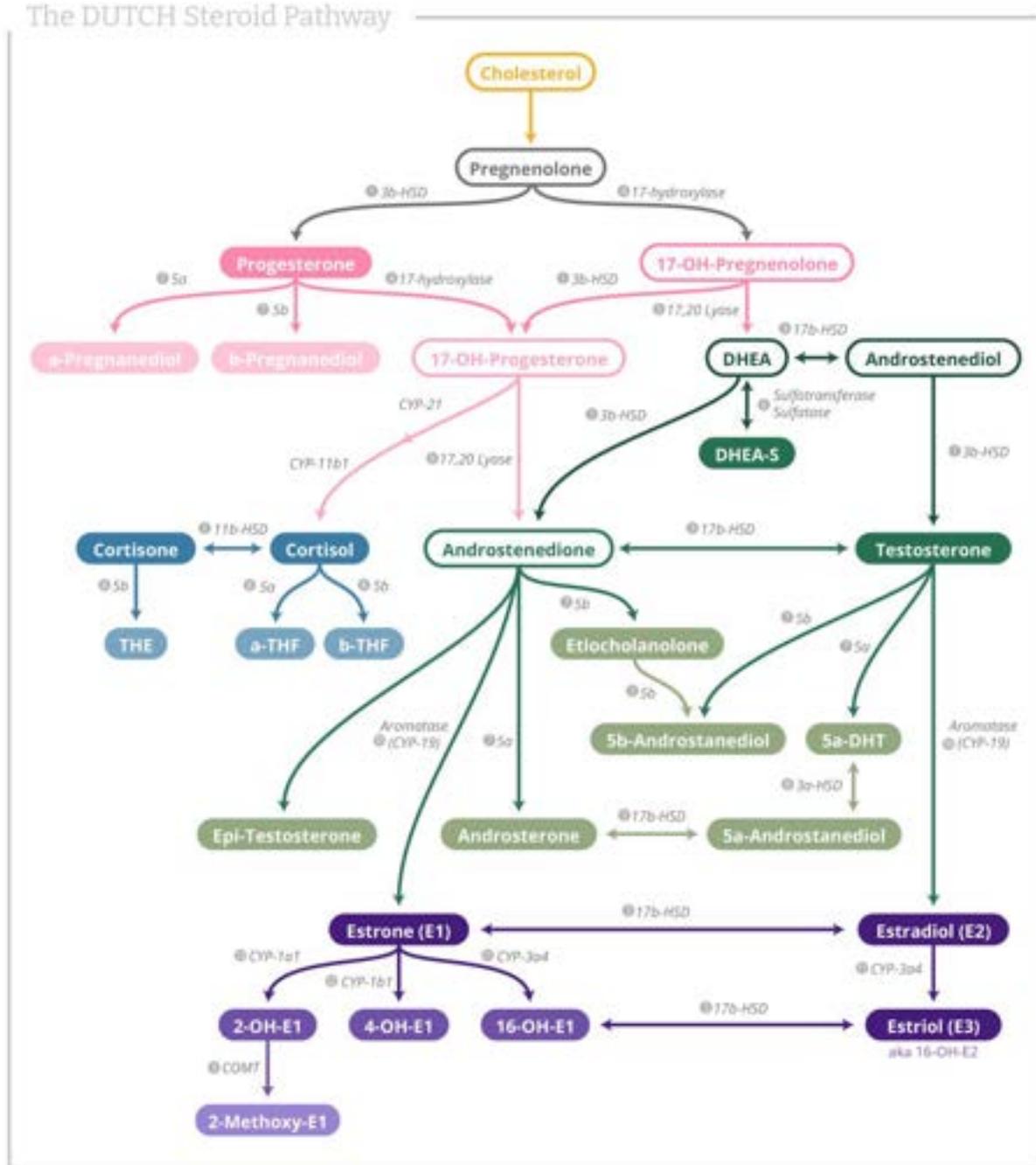
DHEA → Testosterone in women

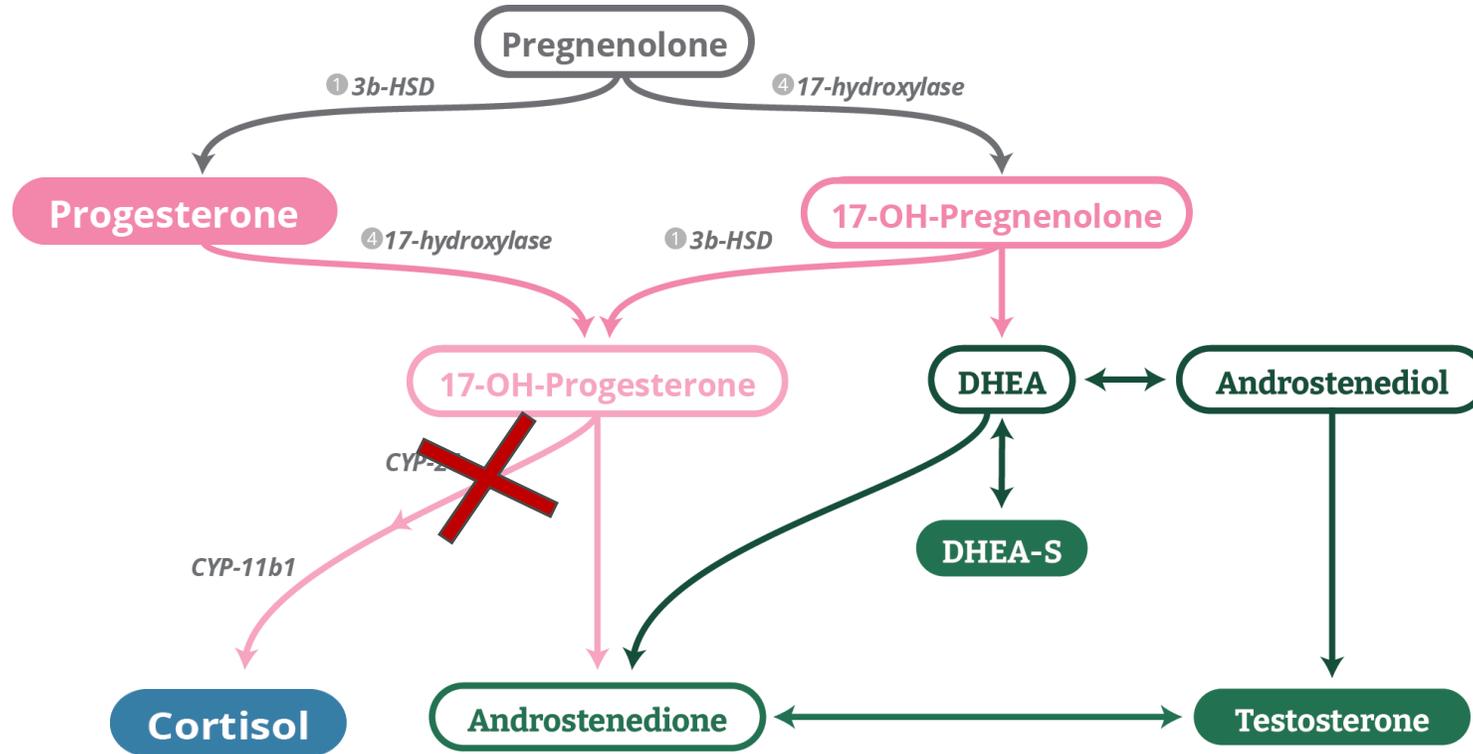
Androgen → Estrogen (post-meno)

Estrogen Metabolism

5a-Androgen Metabolism

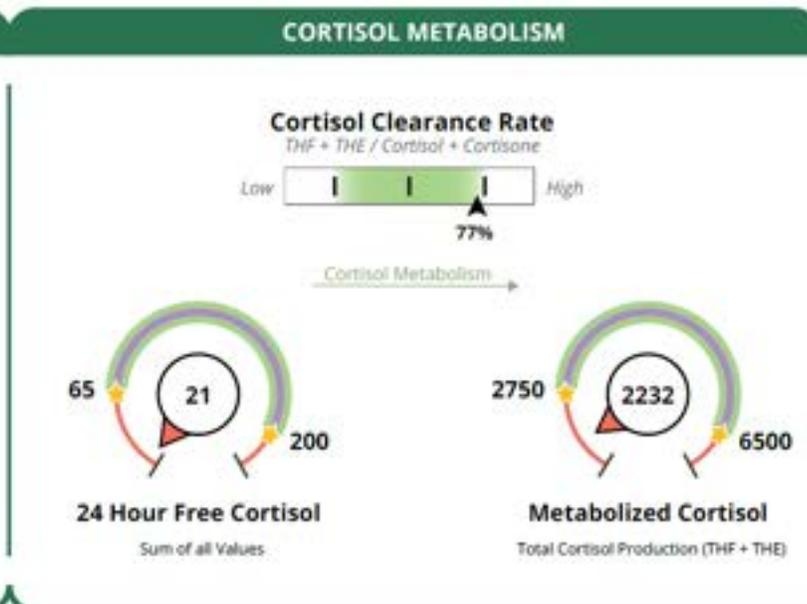
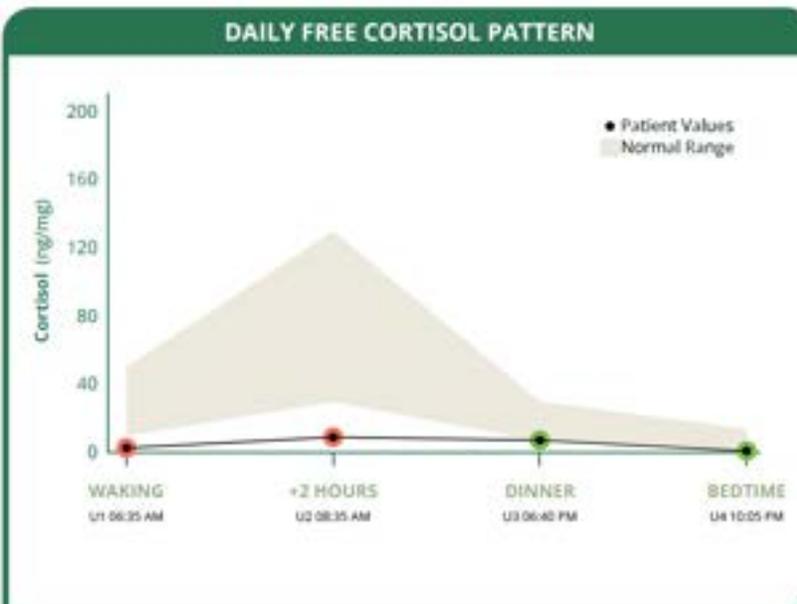
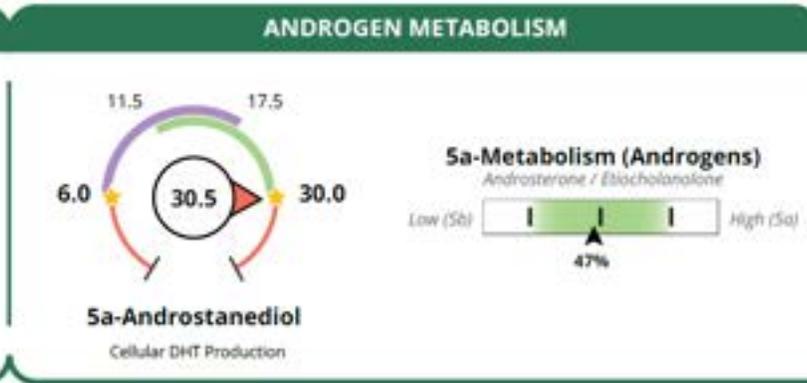
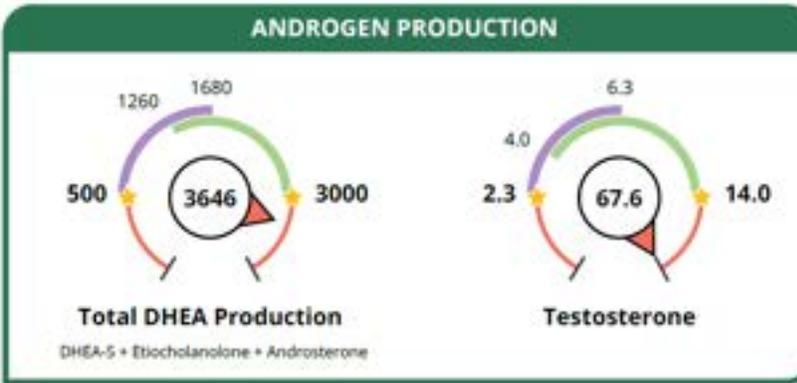
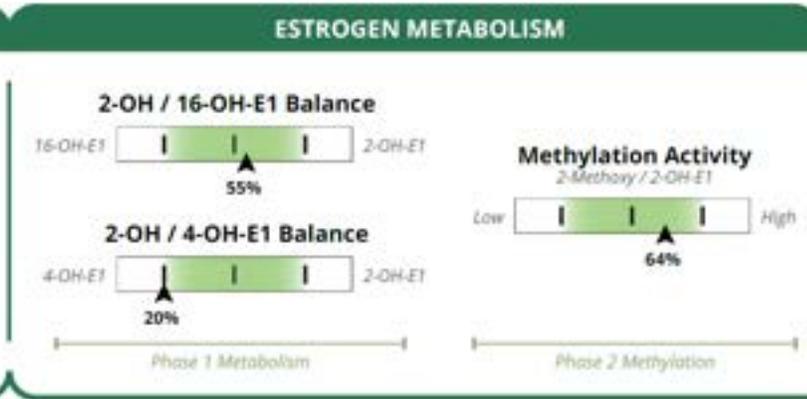
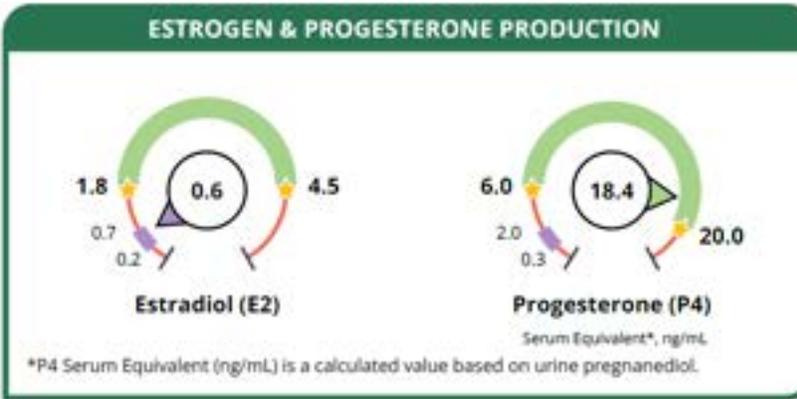
Cortisol Metabolism





**In Congenital Adrenal Hyperplasia (CAH), a missing enzyme pushes 17OH-Progesterone towards DHEA and Testosterone**

Patient with CAH



# DUTCH Test – use cases

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- Disease States (DUTCH is not diagnostic!)
  - CAH
  - Cushing's, Addison's Disease
  - Hormone producing tumor
- Age-related hormone deficiency
- HRT Monitoring (not covered in detail today)
- Hormone Dysfunction

# Abnormal Results – Two Categories

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## **See it, Explain it**

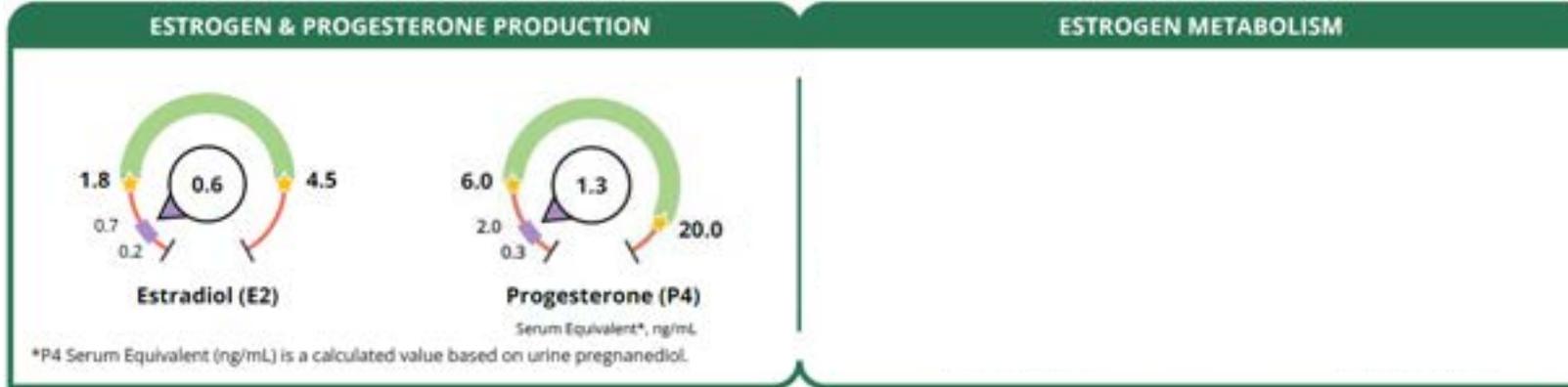
- Some abnormalities need to be understood but not fixed.

## **See it, Explain it, Fix it!**

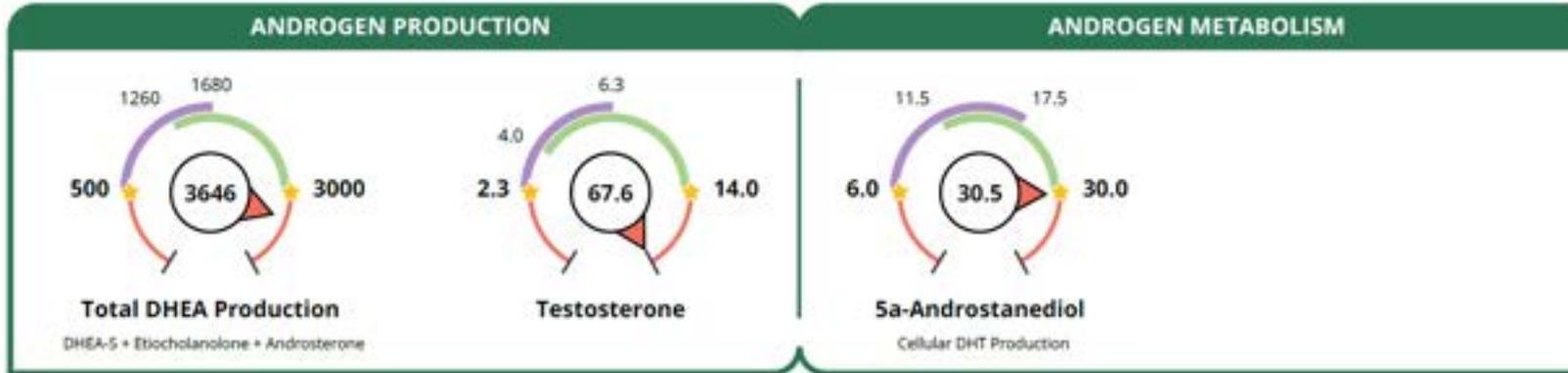
- Your job is to find abnormalities that need addressing.

# What is the Story?

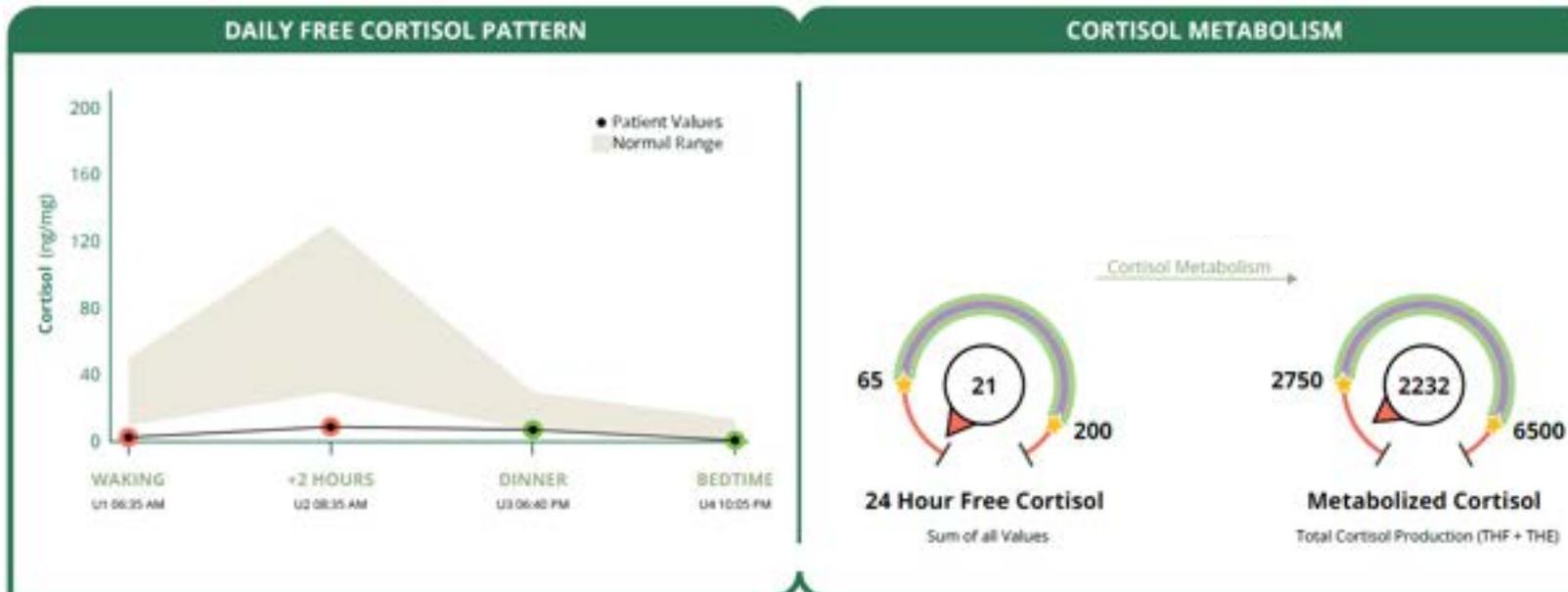
Birth Control Use  
Or POI?



Sublingual  
Testosterone  
Or PCOS?



Etomidate use day  
of test (surgery)  
Or Adrenal  
Insufficiency?



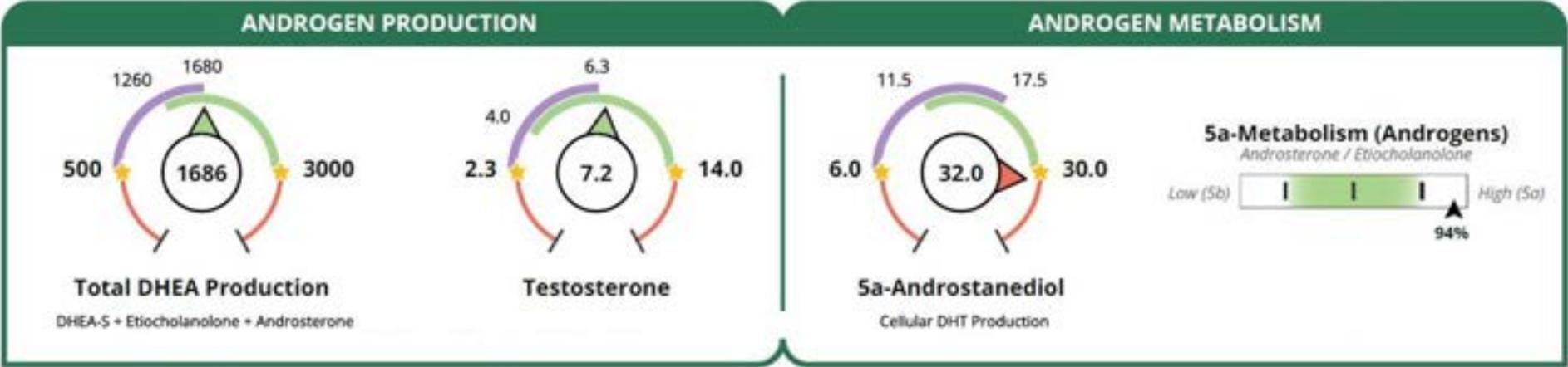
# Why do we care about Metabolites?

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Hormone production is usually sufficient for observing disease states.  
Hormone metabolism is often valuable for hormone dysfunction or nuanced cases.

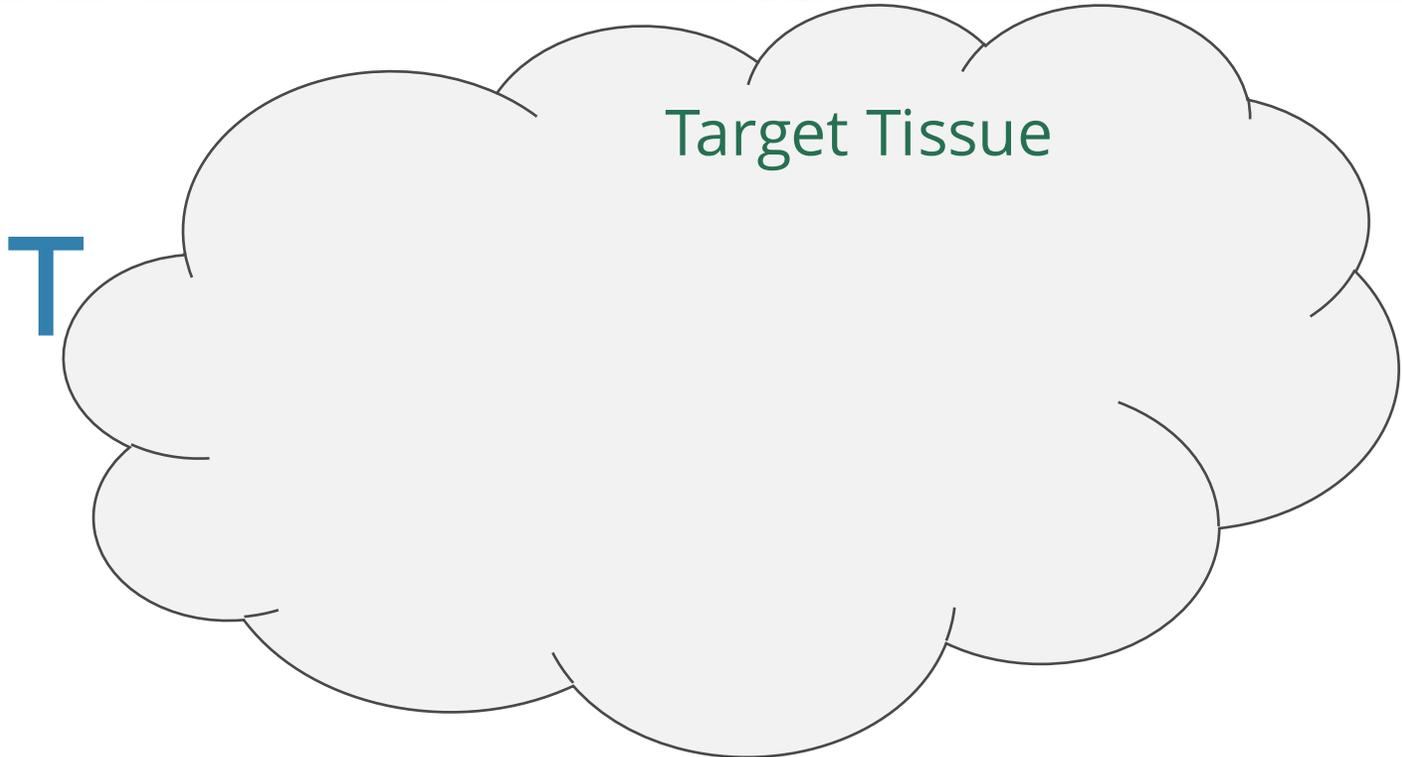
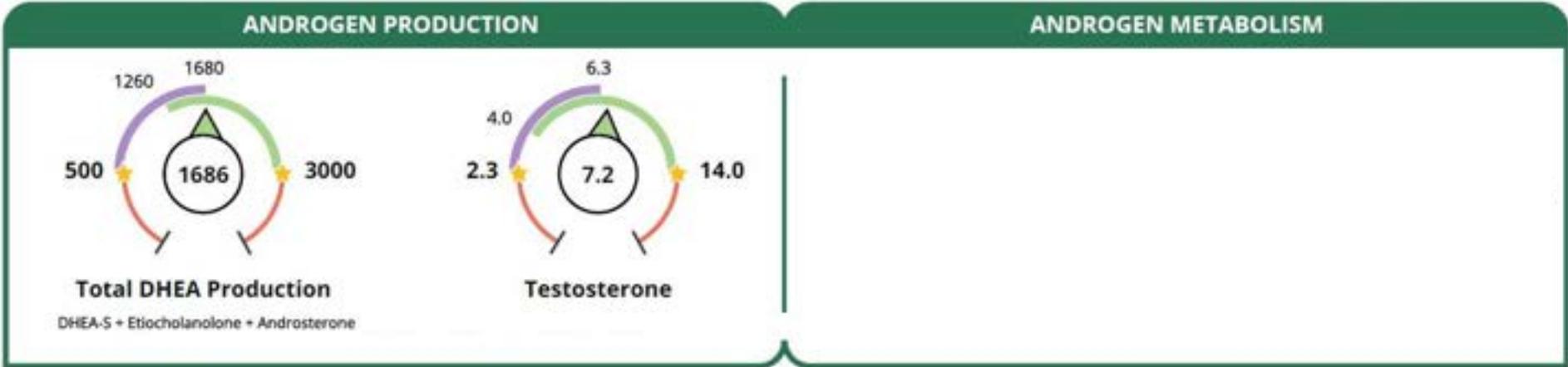
The ISSUE is the TISSUE

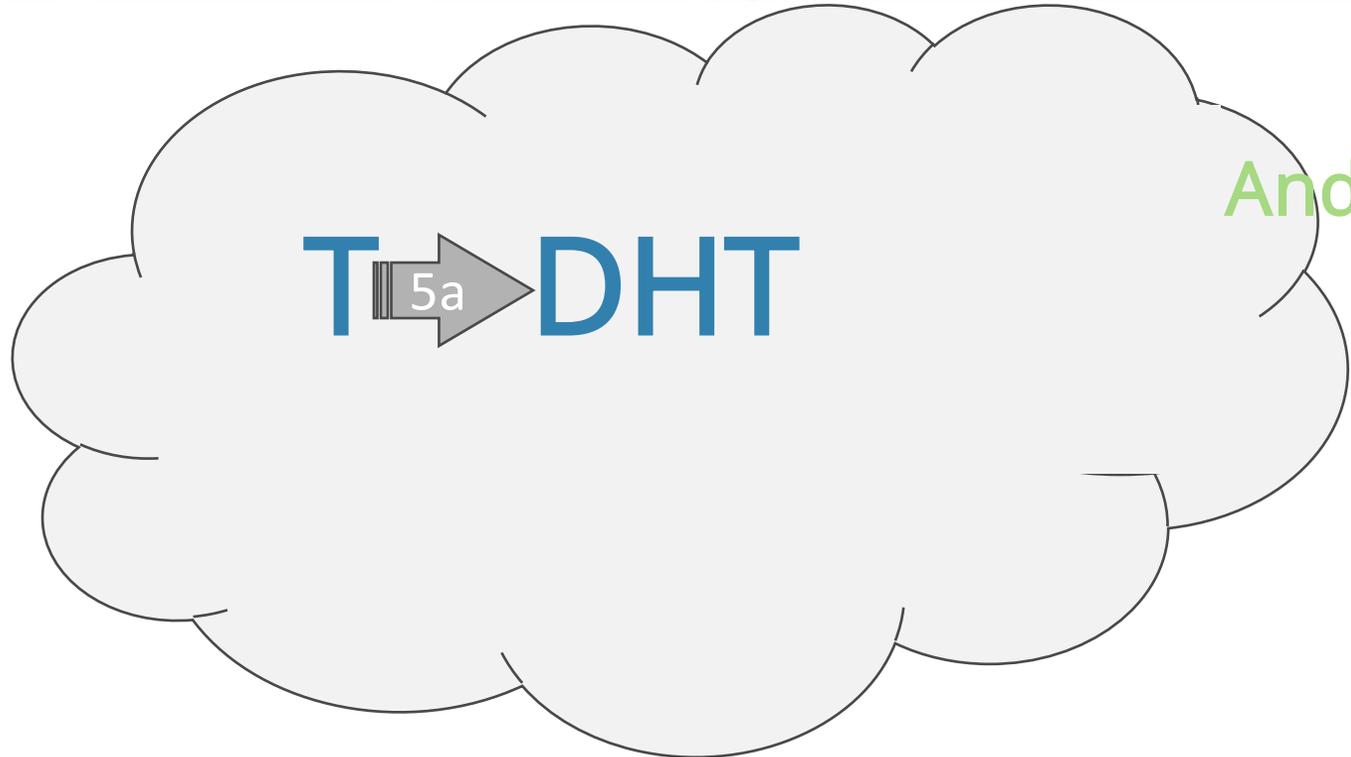
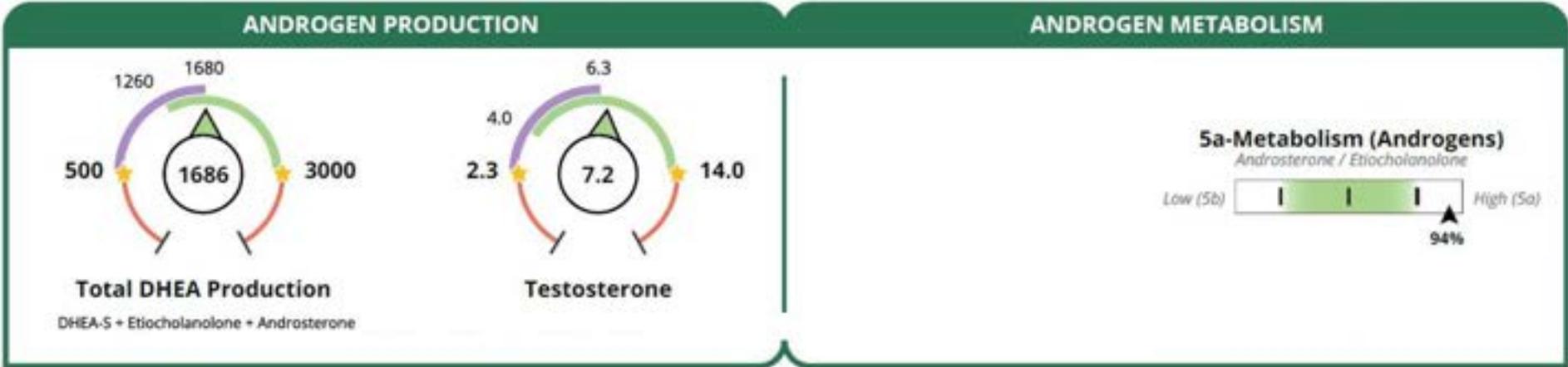
# Why do we care about Metabolites?



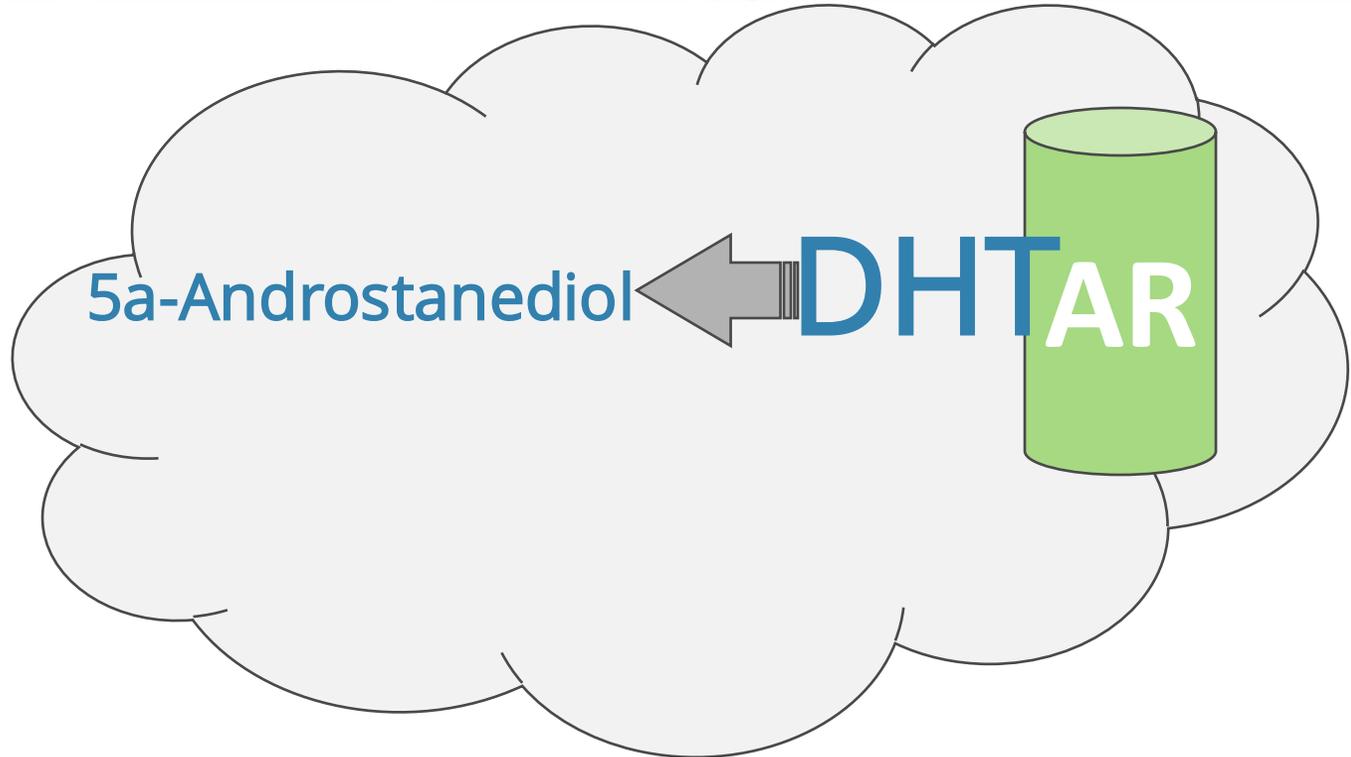
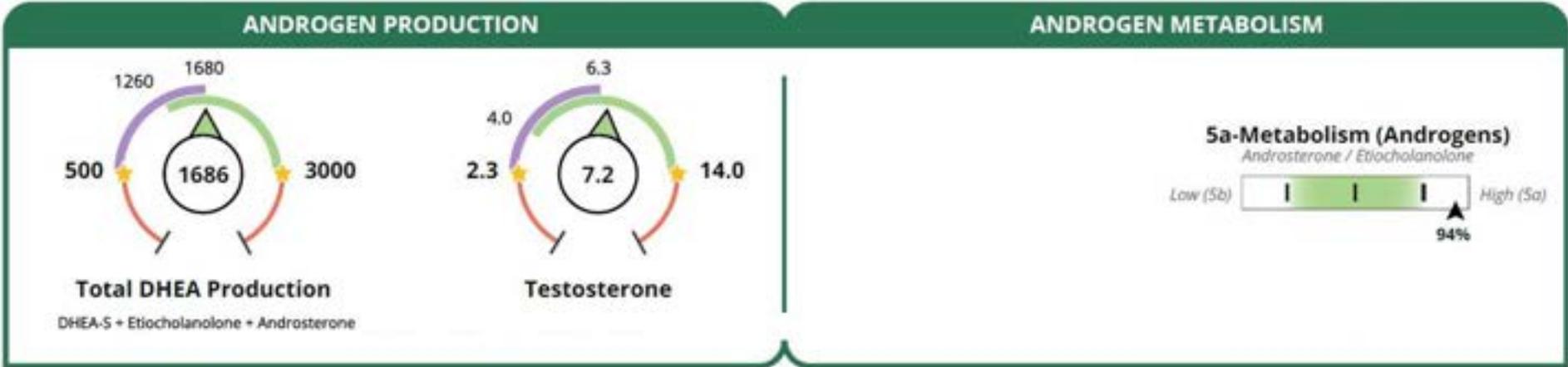
The ISSUE is the TISSUE

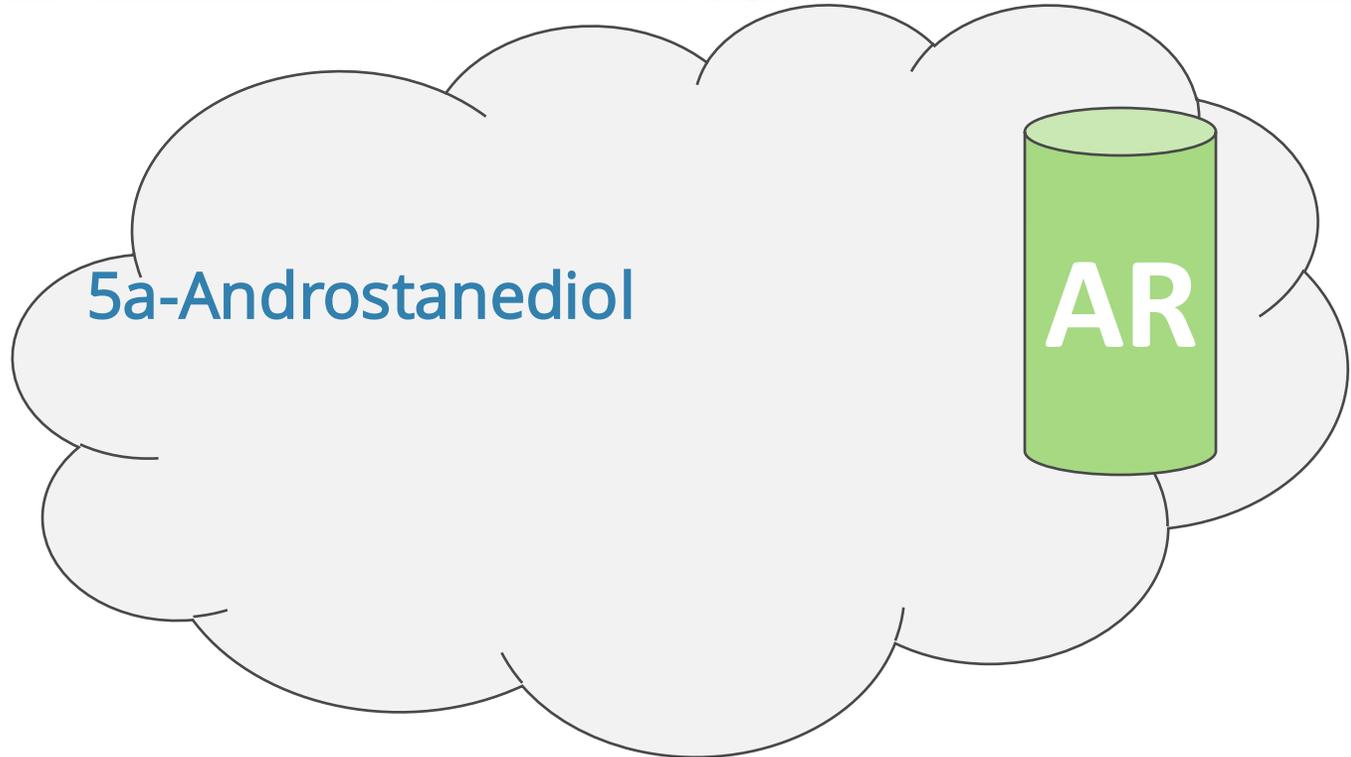
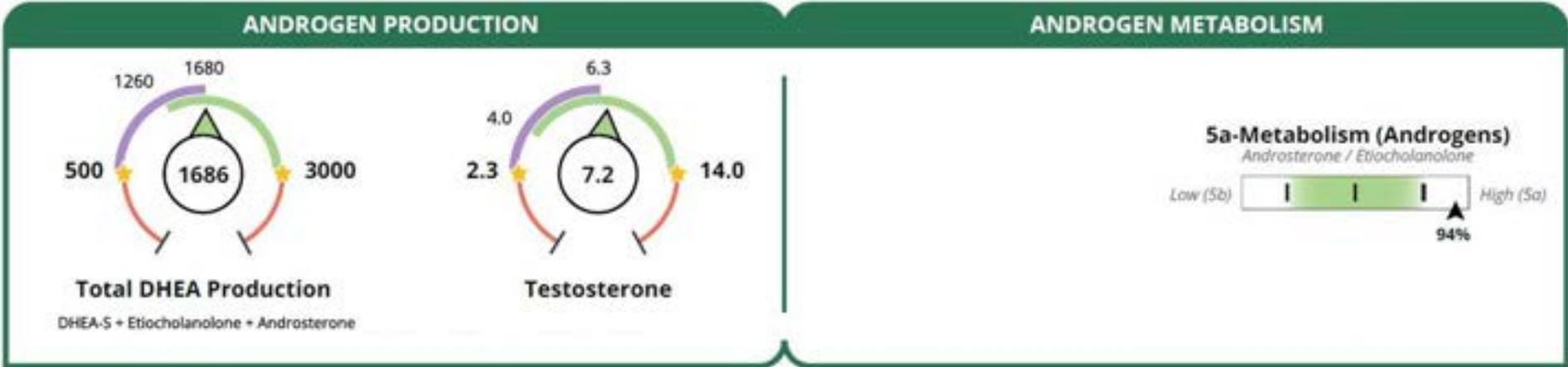
# Tissue Androgenic Activity





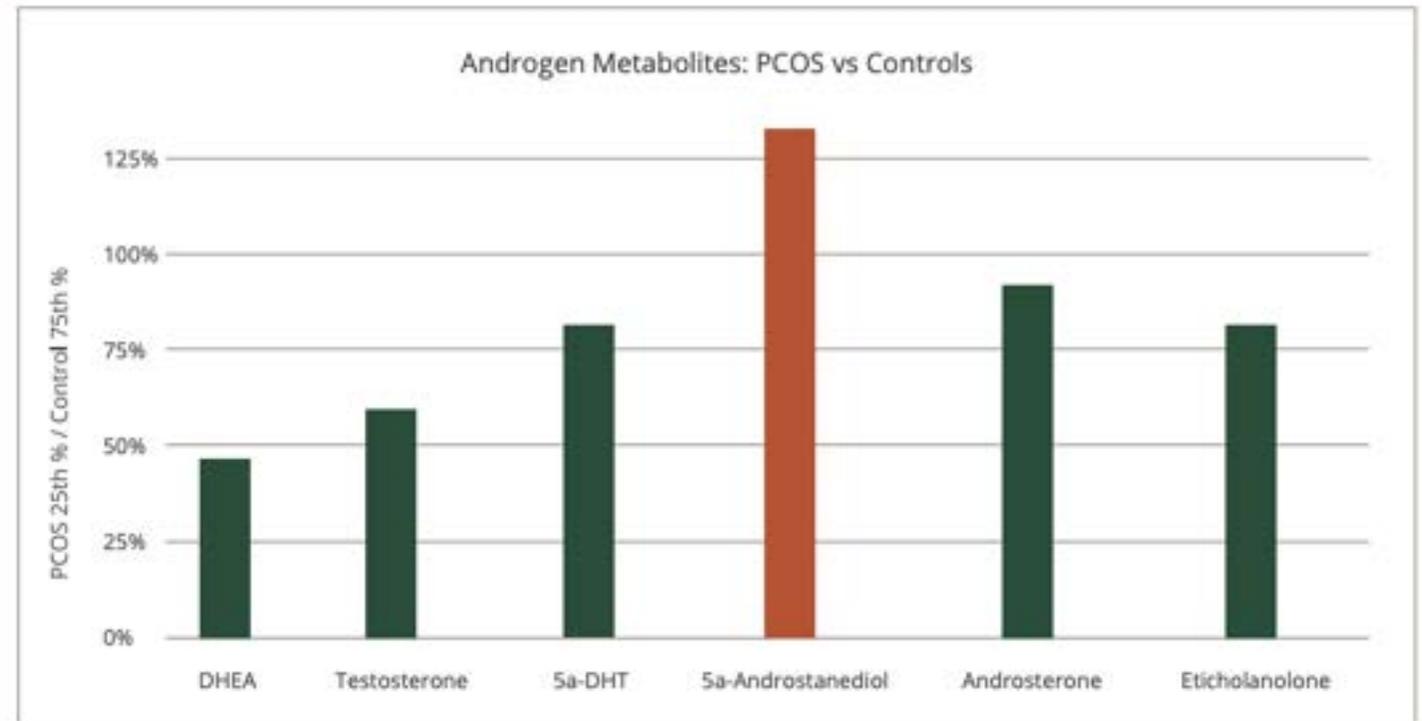
Androgenic impact



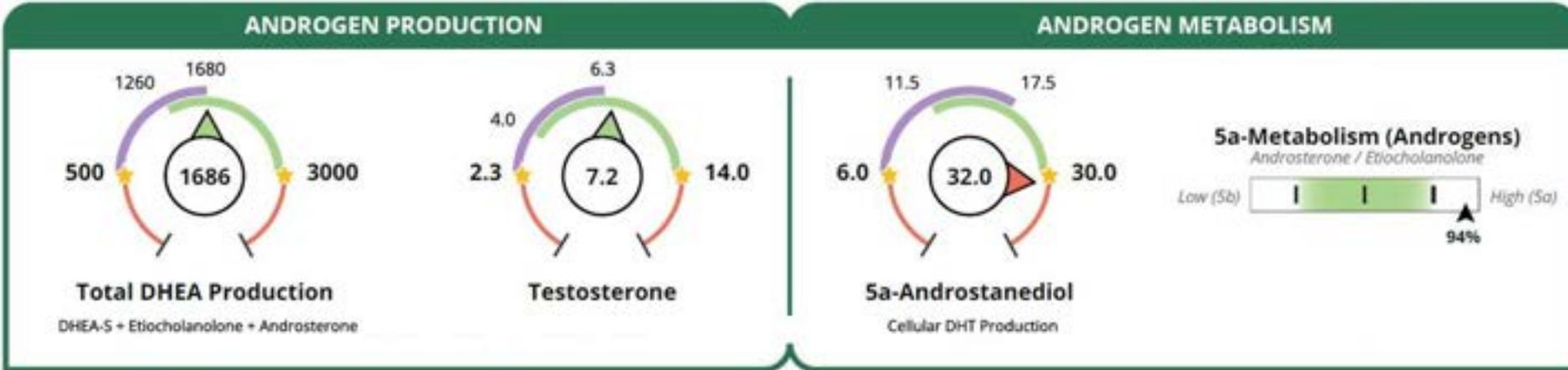


# 5 $\alpha$ -Androstenediol is the most differentiating androgen metabolite

**Figure 2:** An analysis of androgen metabolites in 24-hour urine (nmol/24h) in women with or without PCOS shows that, for 5 $\alpha$ -androstenediol, the 25th percentile value for PCOS patients is more than 125% of the 75th percentile value for normal controls. Essentially, even the lower end of the PCOS range (25th percentile) exceeds the upper end of the normal range (75th percentile) for healthy controls, suggesting no overlap between the normal range and the PCOS range for 5 $\alpha$ -androstenediol. [98]

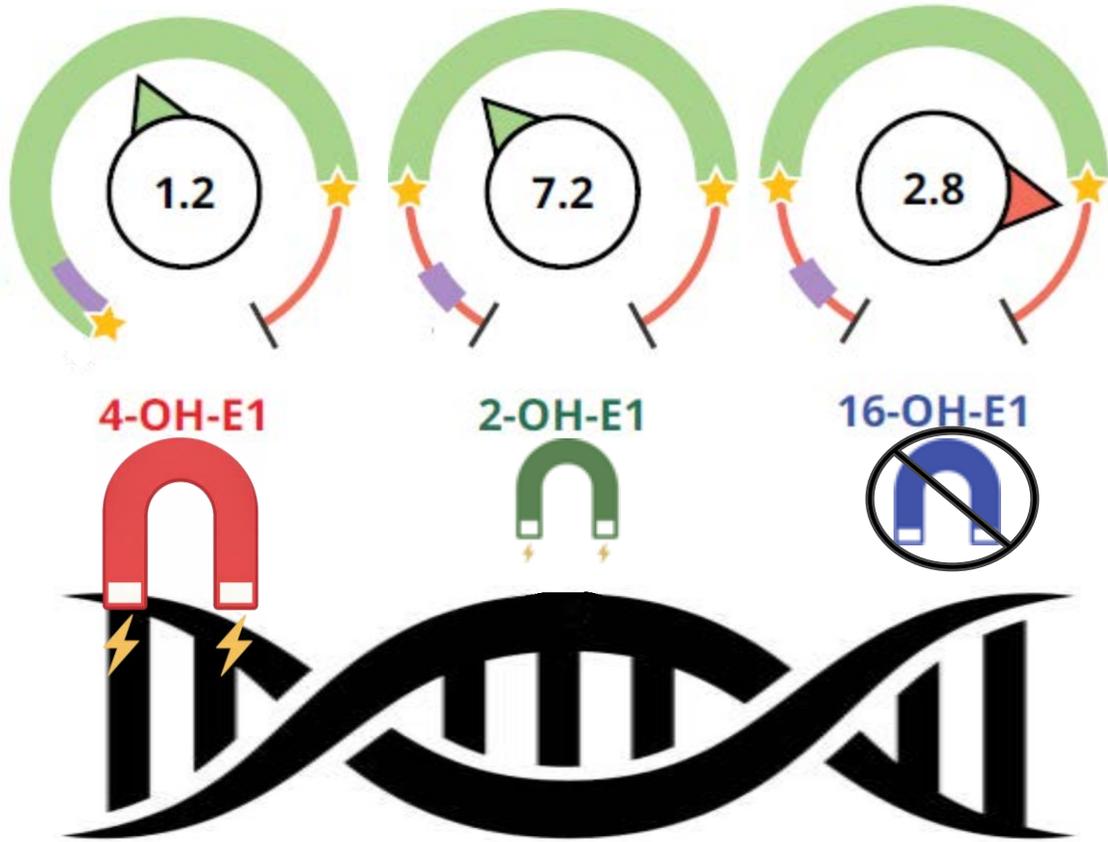


Dhayat NA, Marti N, Kollmann Z, et al. Urinary steroid profiling in women hints at a diagnostic signature of the polycystic ovary syndrome: A pilot study considering neglected steroid metabolites. PLOS ONE. 2018; 13(10):e0203903. doi:10.1371/journal.pone.0203903



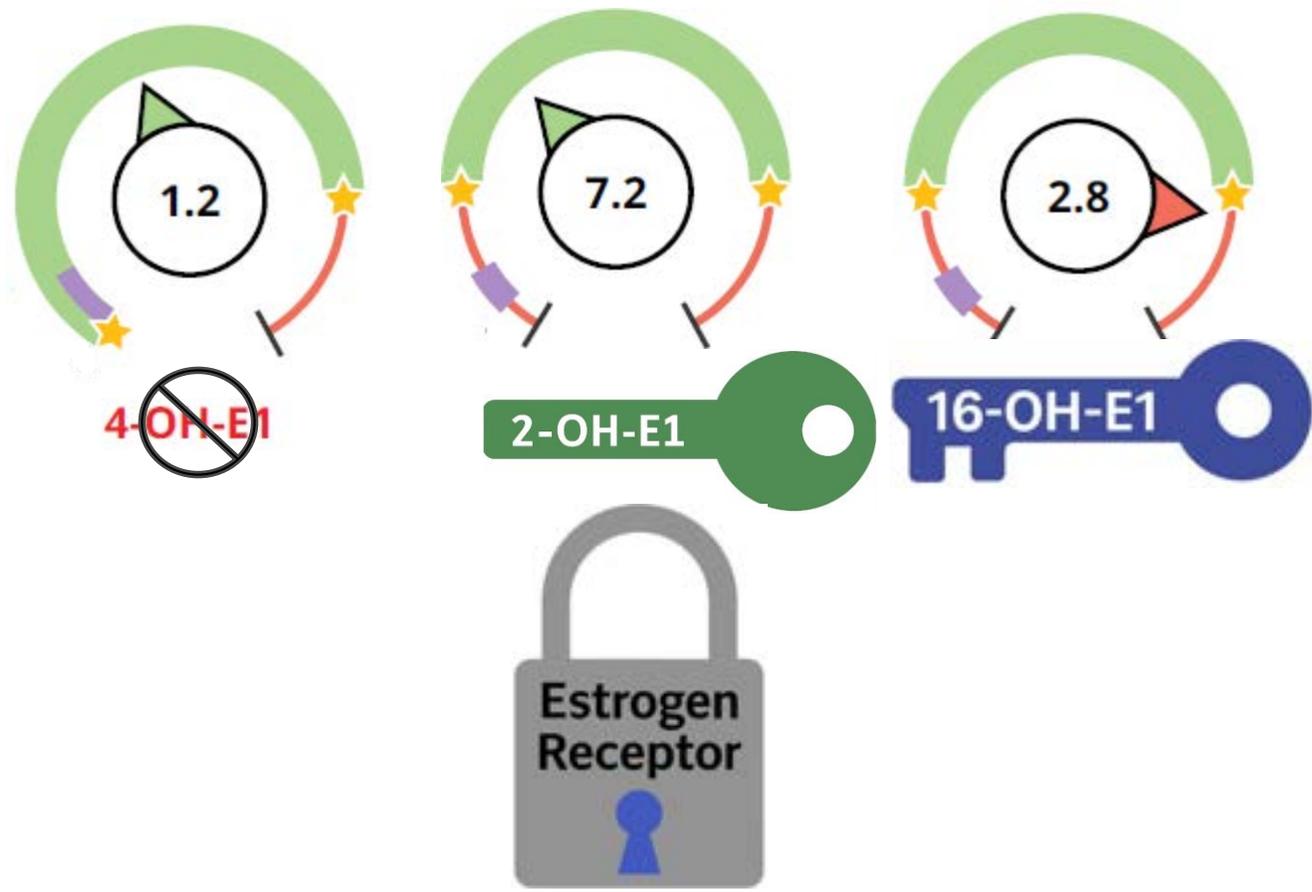
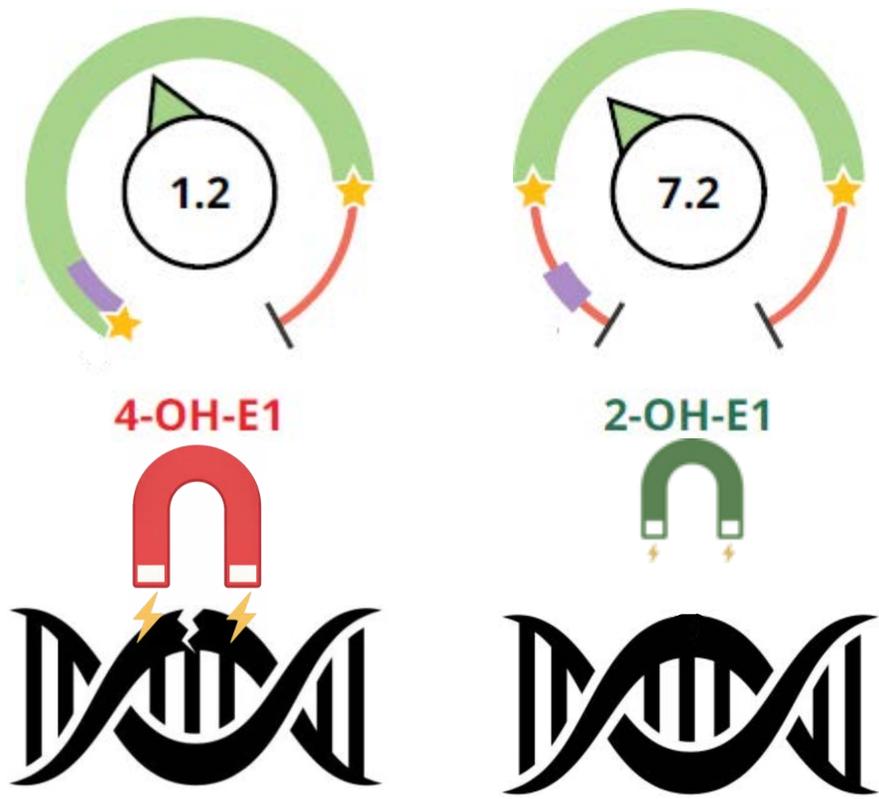
# The ISSUE is the TISSUE

- 5a-Androstenediol best represents tissue DHT
- Parent hormones AND metabolites matter



## Estrogen Metabolites:

Balance of these three metabolites matter at the DNA and at the receptor – both are important!



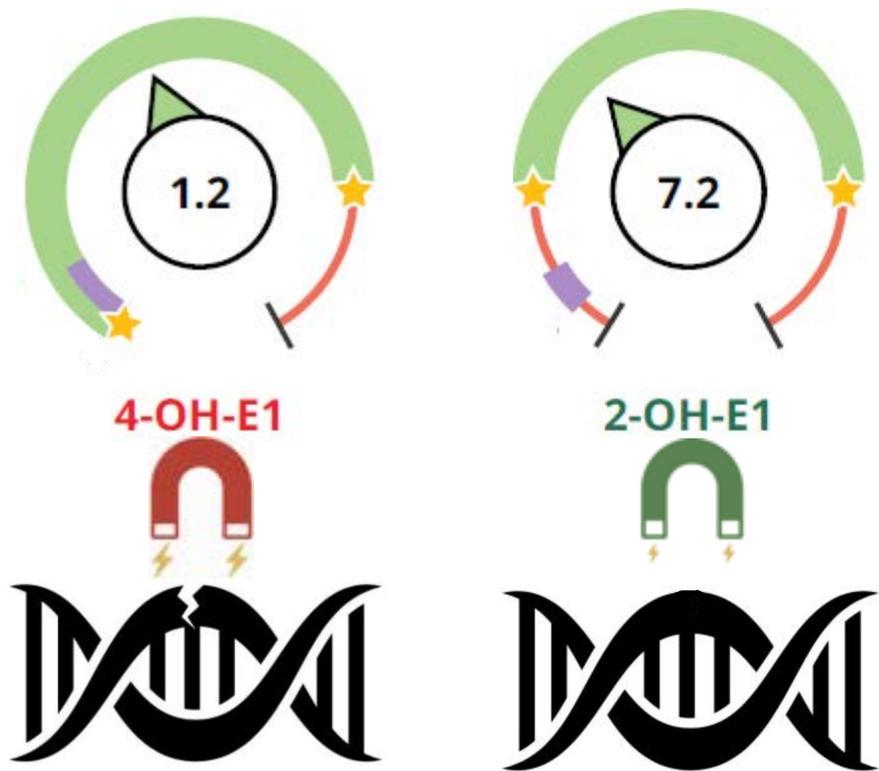
Genotoxic

Protective

2-OH / 4-OH-E1 Balance

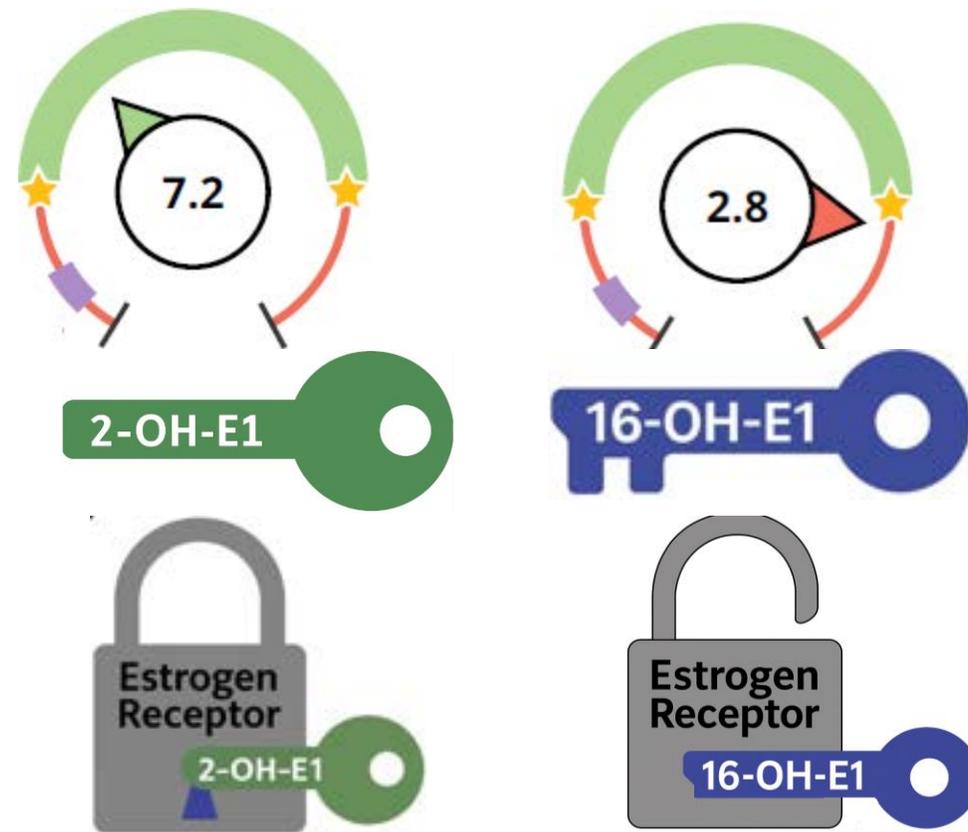
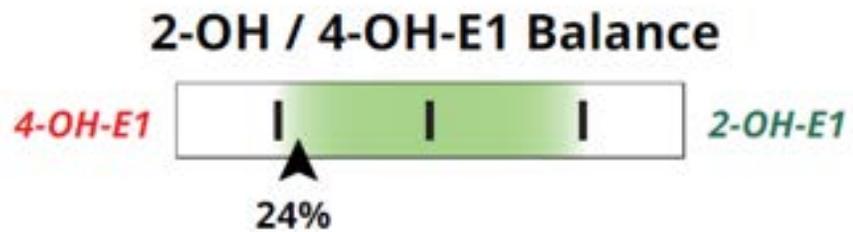


Estrogenic?  
(Proliferative?)



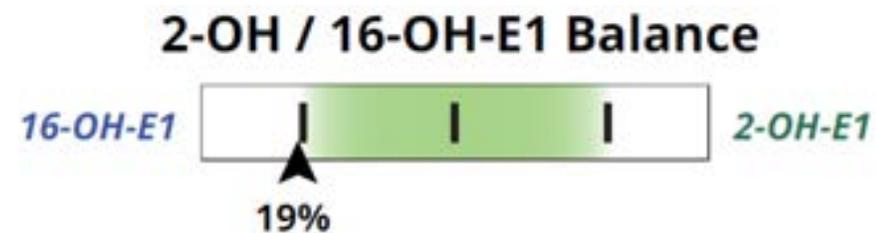
Genotoxic

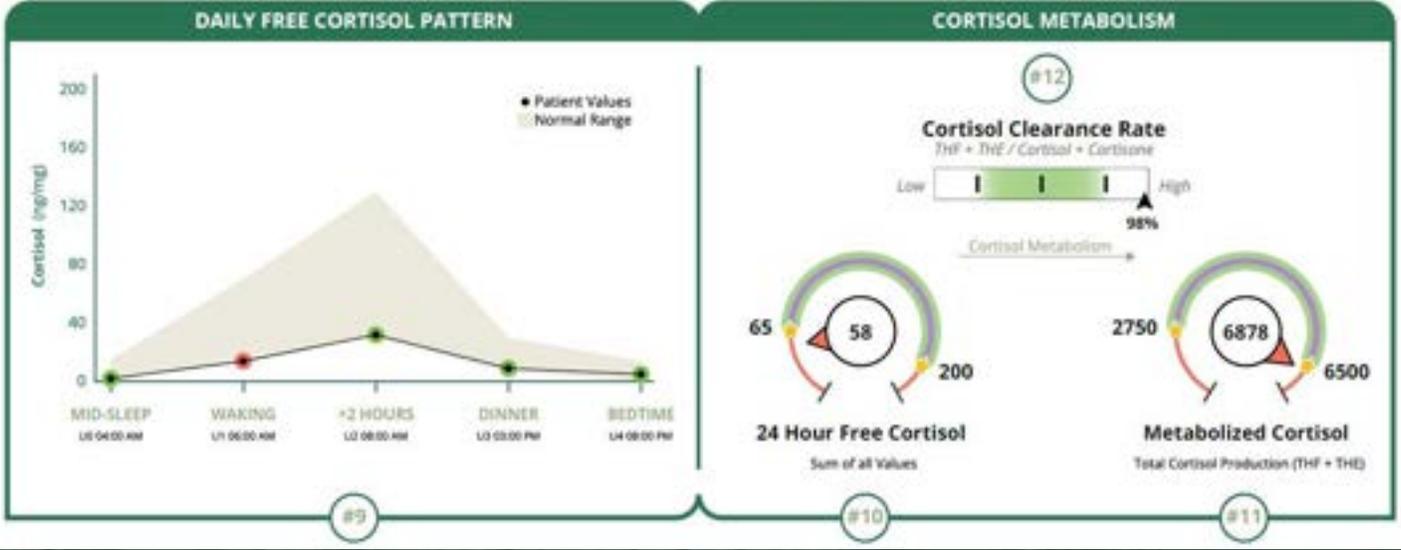
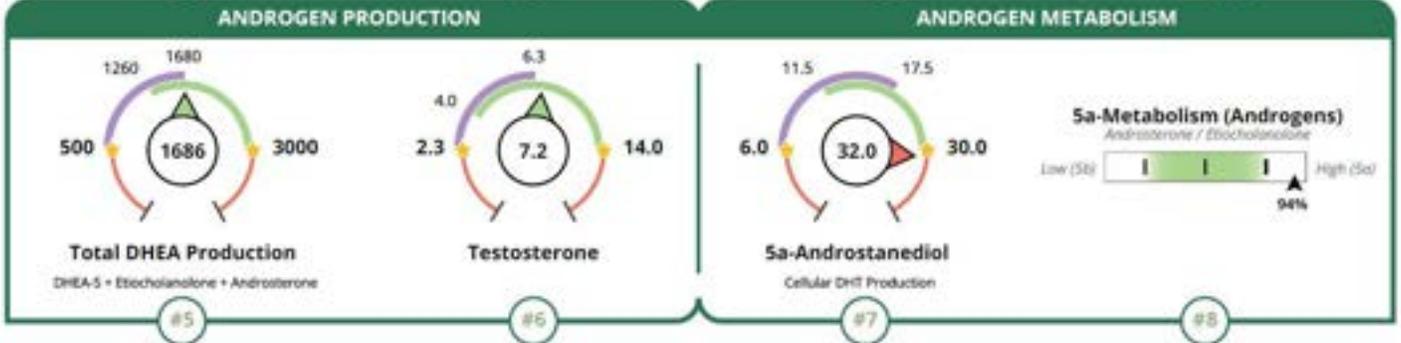
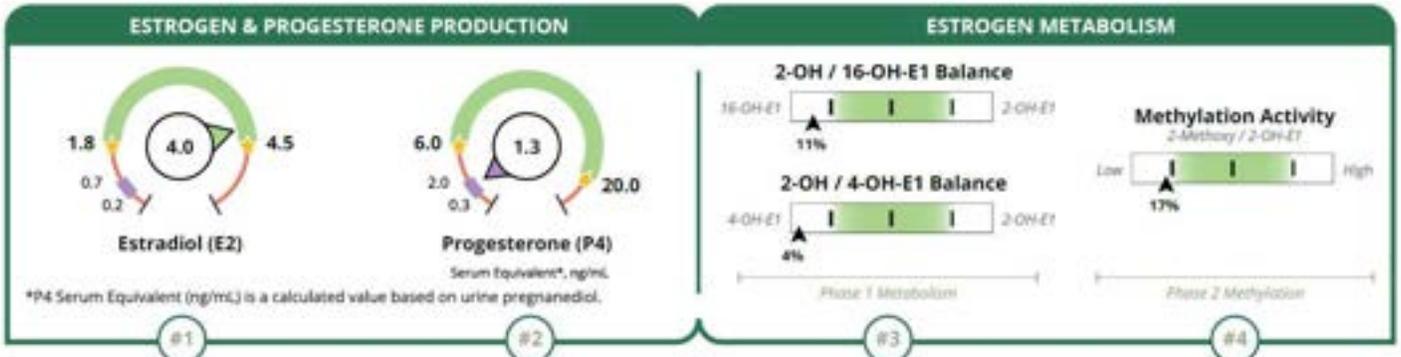
Protective



Anti-Estrogenic

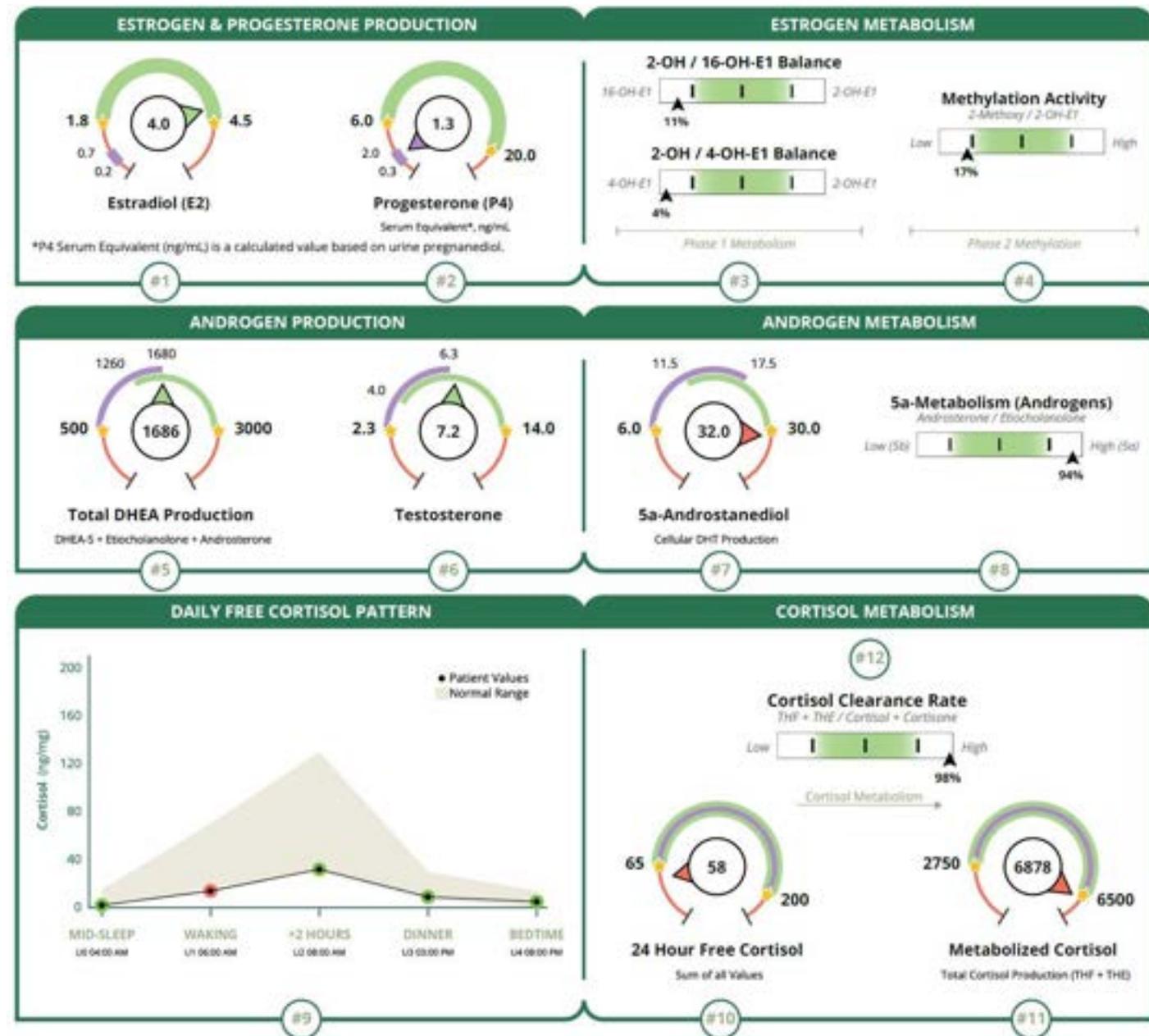
Estrogenic





# Introducing the DUTCH Dozen

- DUTCH Test framework for interpretation
- Understand the basics of a DUTCH Test quickly
- Dig deeper as needed



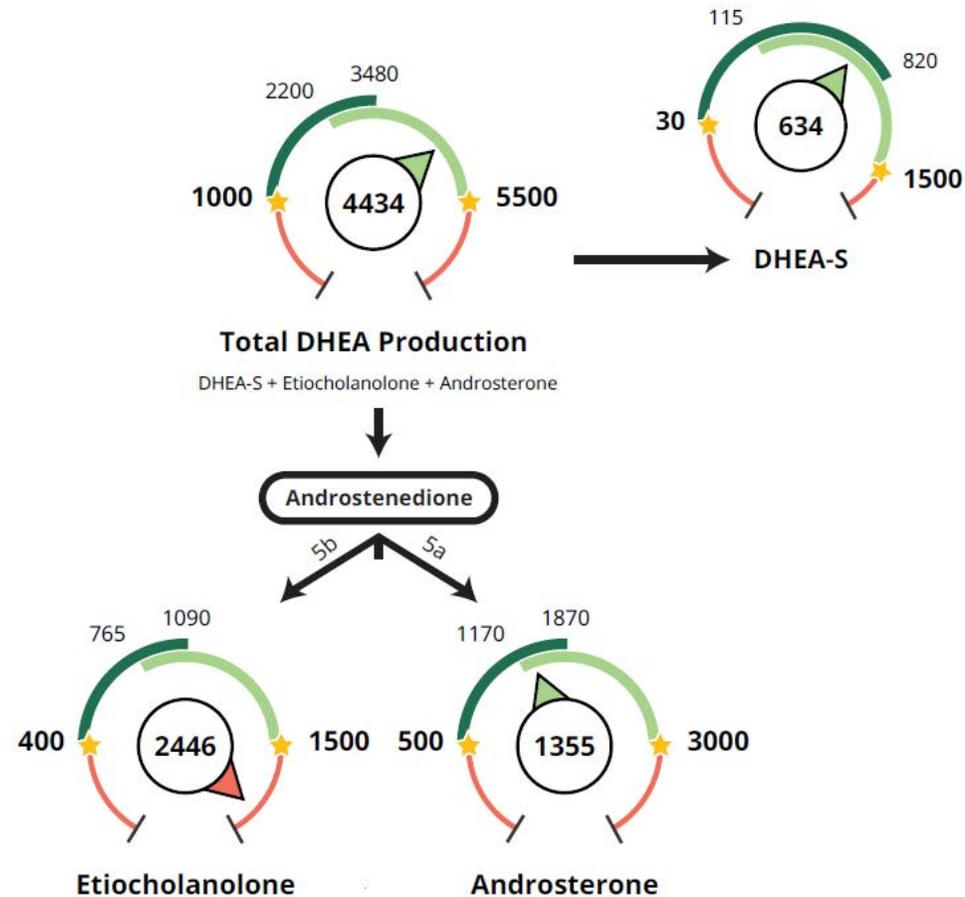
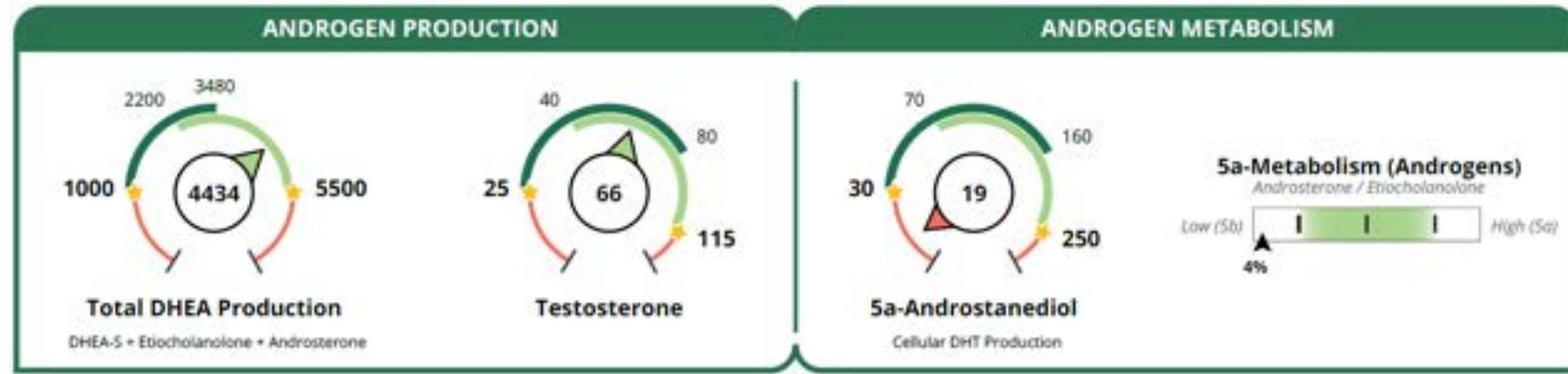
# Introducing the DUTCH Dozen

- Androgen Evaluation
  - High normal adrenal androgens
  - Normal Testosterone (66)
  - Low 5a-DHT production
  - Extreme 5b-metabolism
- Normal estrogen
- High methylation
- High bedtime cortisol
- Low cortisol clearance
- B12, Biotin, Glutathione deficiency

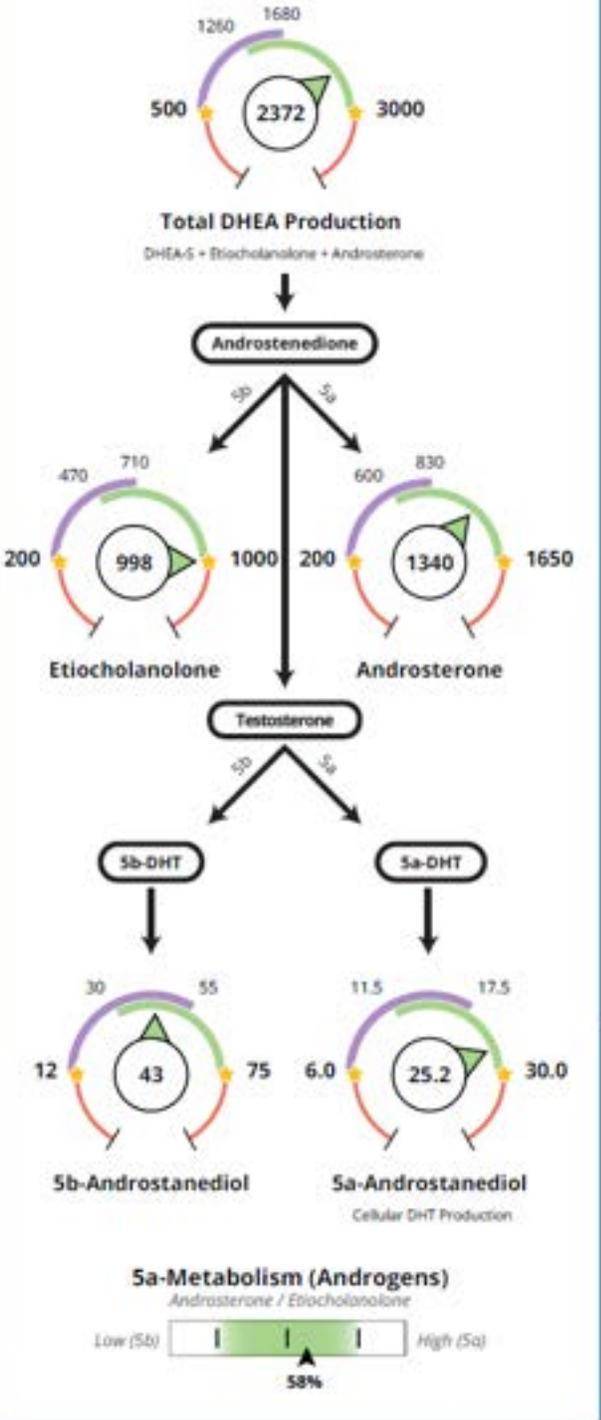


# Where to Focus?

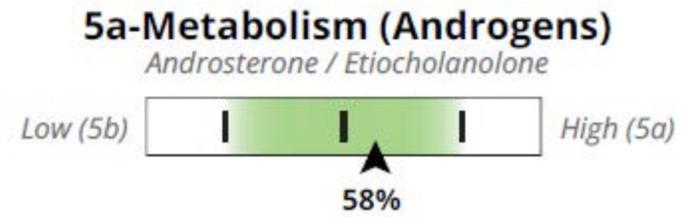
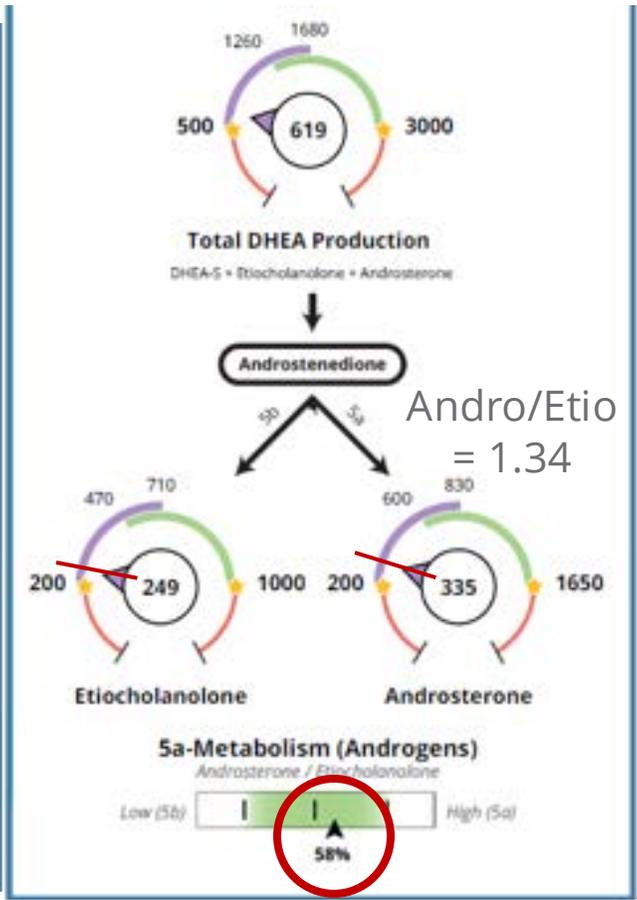
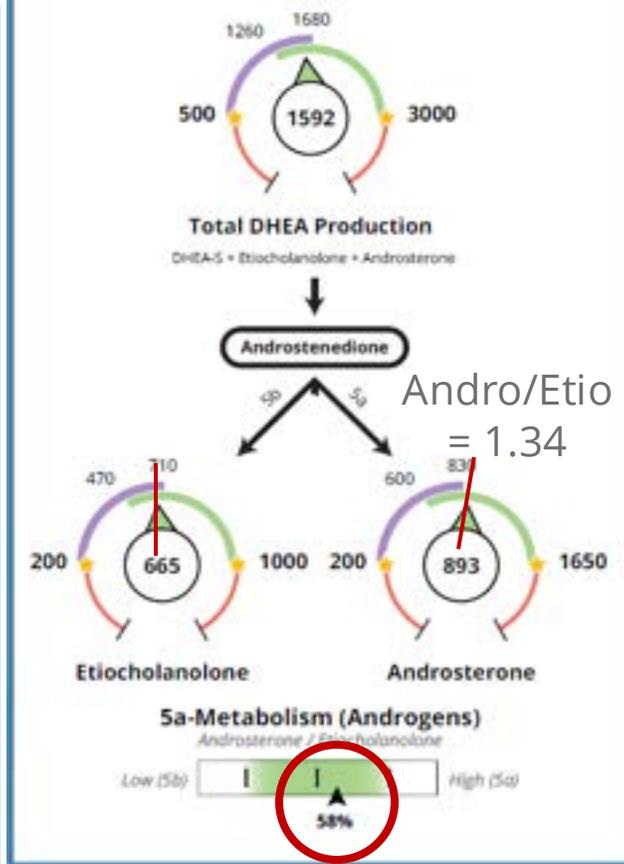
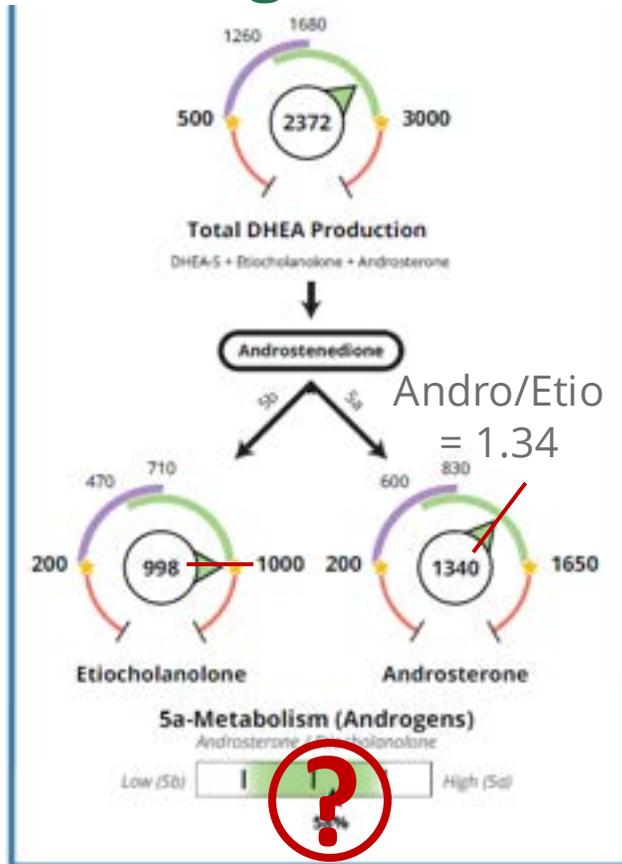
- Androgen Evaluation
  - High normal adrenal androgens
  - Normal Testosterone (66)
  - **Low 5a-DHT production**
  - **Extreme 5b-metabolism**
- High Etiocholanolone???
  - Do I have to care?



# A word of warning about ratios



# A word of warning about ratios



- Ratio ranges are given as population percentiles
- The ratio range is currently the same across all concentrations
- At times this may create counterintuitive ratio results compared to the "picture"

# Agenda for DUTCH Fest

- DUTCH Test and DUTCH Fest follow the same structure
  - Estrogen + Progesterone
  - Androgens
  - Cortisol
- Interpreting each section
  - Identifying Dysfunction
- Causes & Effects of Dysfunction
- Treatment Considerations
- Dig in deeper!





What About Applying  
DUTCH to HRT?

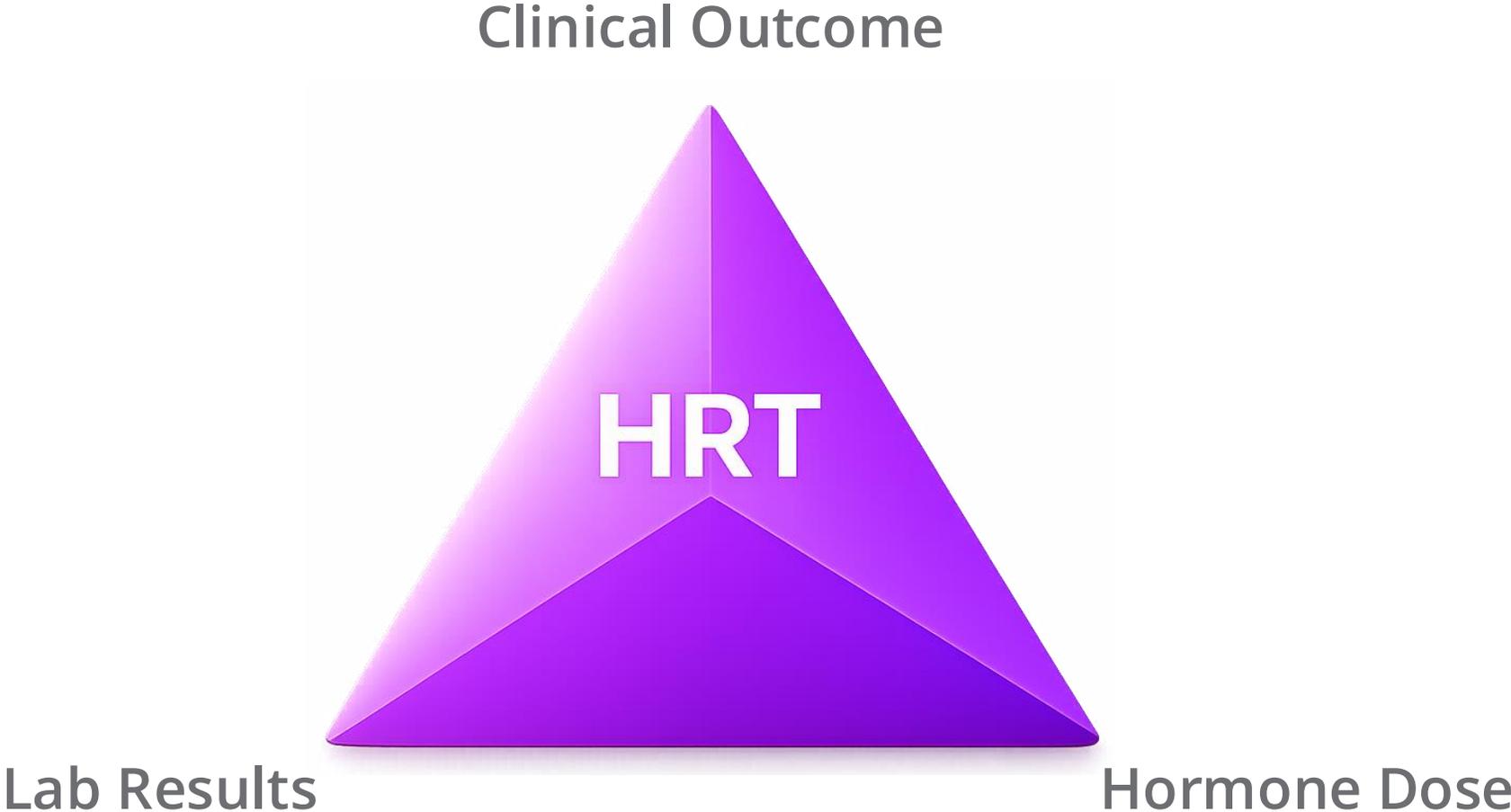
# Two Primary Reasons to Use DUTCH for HRT

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1. The many complementary uses of DUTCH with HRT
  - Estrogen Metabolites
  - Progesterone Metabolites (particularly with swallowed P4)
  - Androgen Metabolites (heavy DHT production?)
  - Cortisol Assessment (impact on hot flashes, general wellbeing)
  - OATs
- For the above, all DUTCH Fest education is relevant with or without HRT
2. Did I get the dose right?
  - Does DUTCH help answer this question? It depends!

# Testing Options with HRT – Can you triangulate testing with treatment?

---



# Testing Options with HRT – What does NOT work ?

---

- DUTCH – If hormones are swallowed, gives big, useless numbers
  - Metabolite patterns may still be relevant

# A Common Caveat to Urine Testing

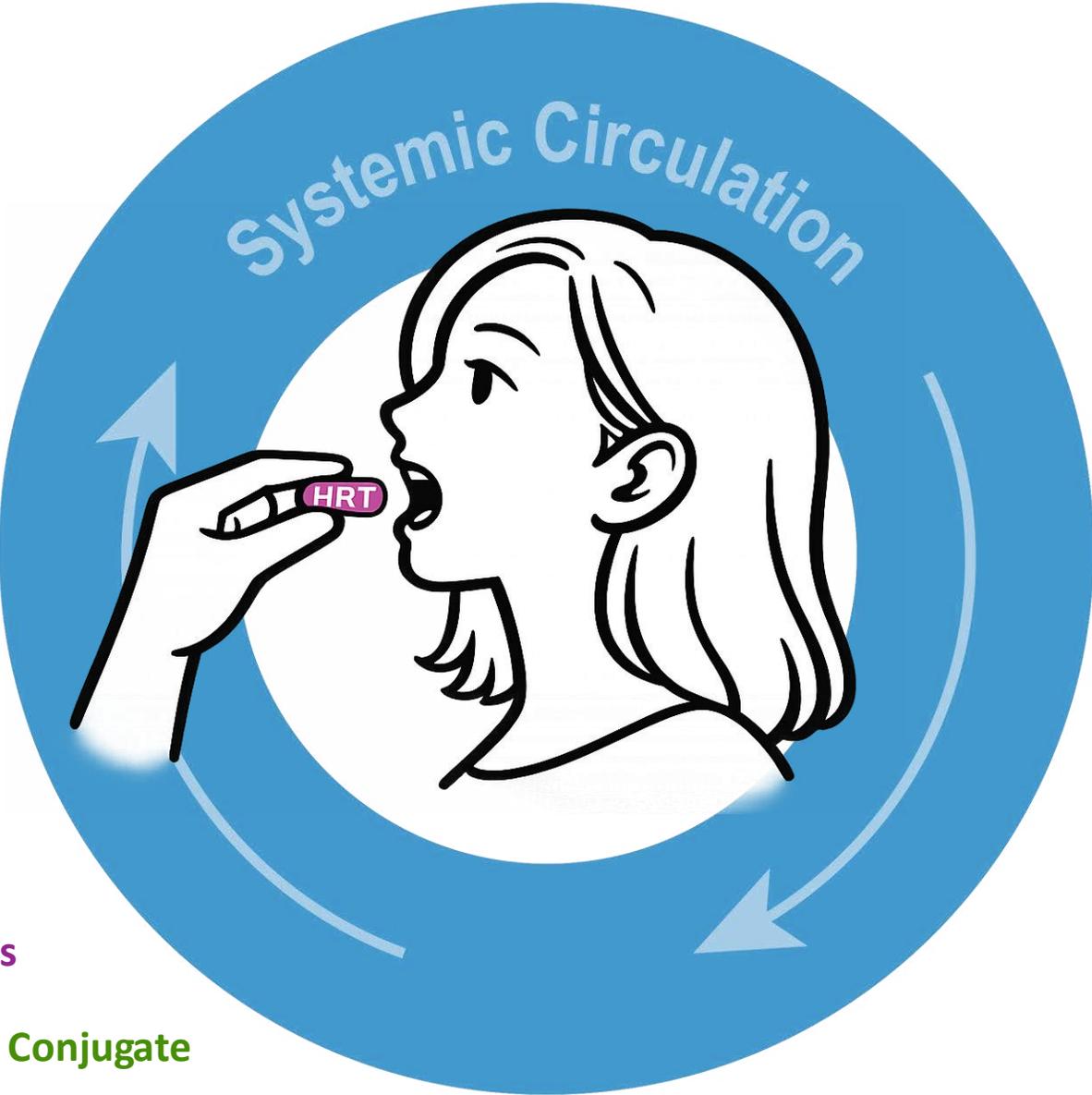
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## First-Pass Metabolism

When something is taken orally and heavily conjugated by the gut and liver, the urine is flooded with an inactive compound that was never in circulation in its active form.

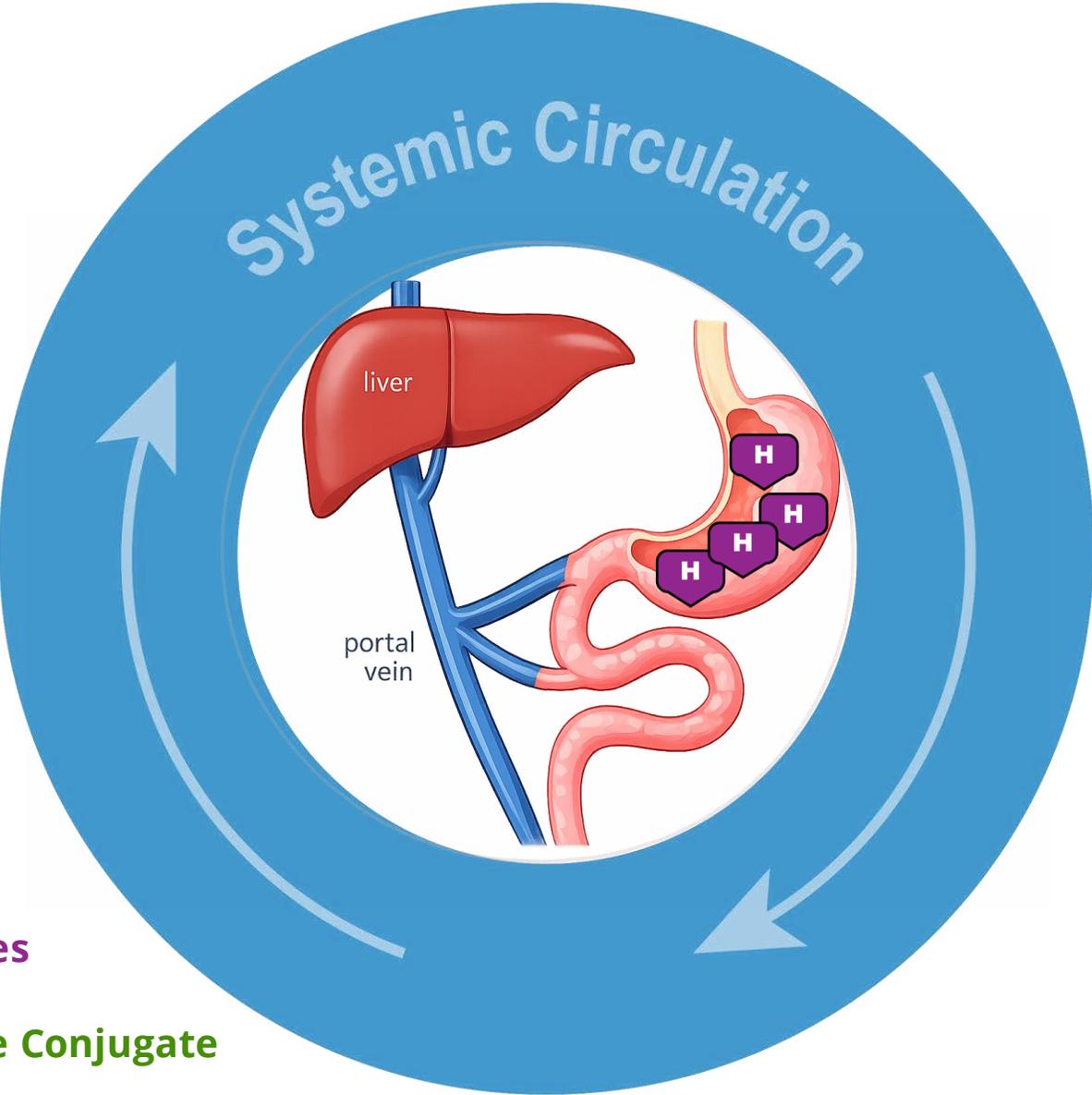
# First-Pass Metabolism



- Protein
- Hormones
- Hormone Conjugate



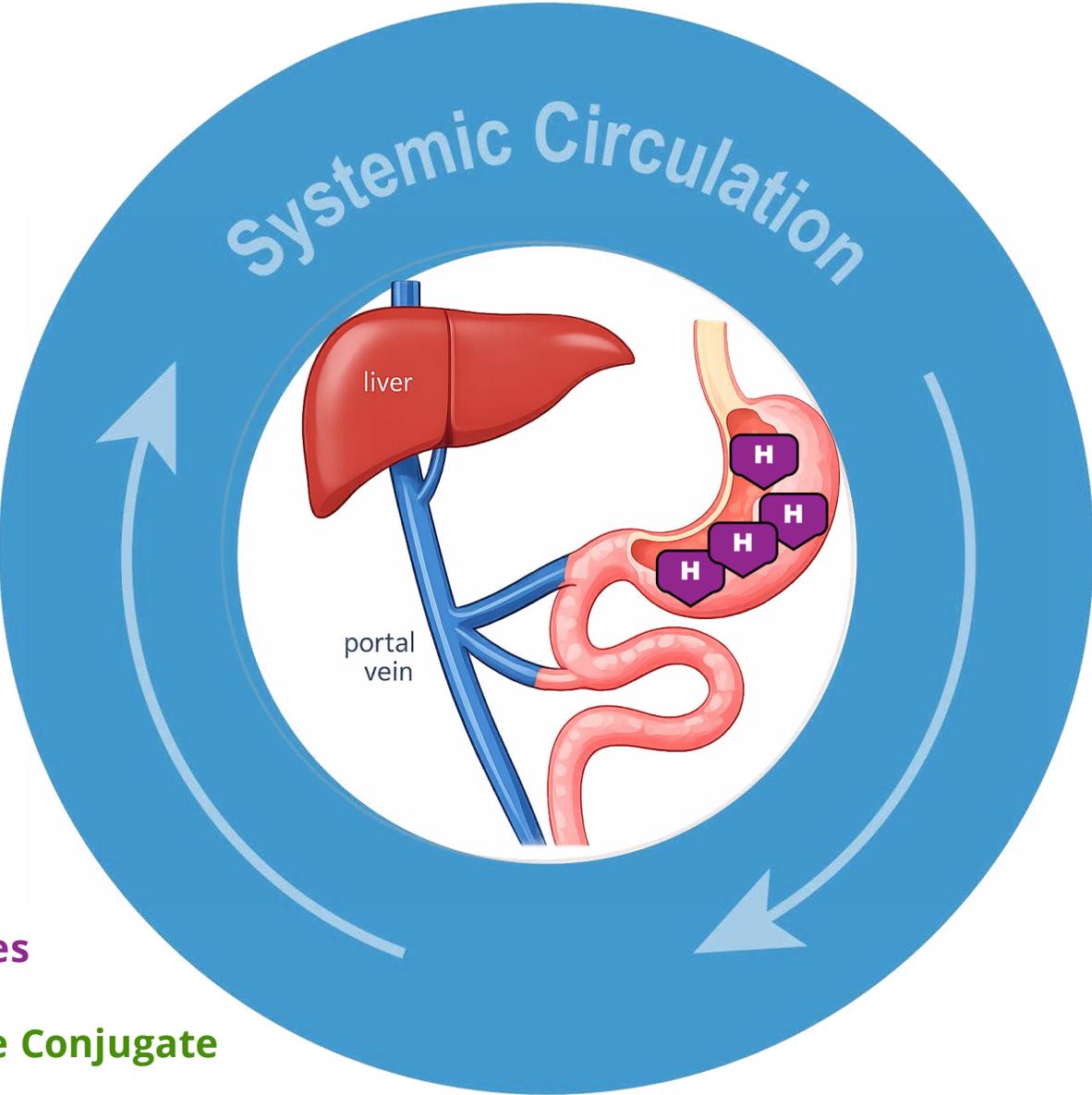
# First-Pass Metabolism



- Protein
- Hormones
- Hormone Conjugate



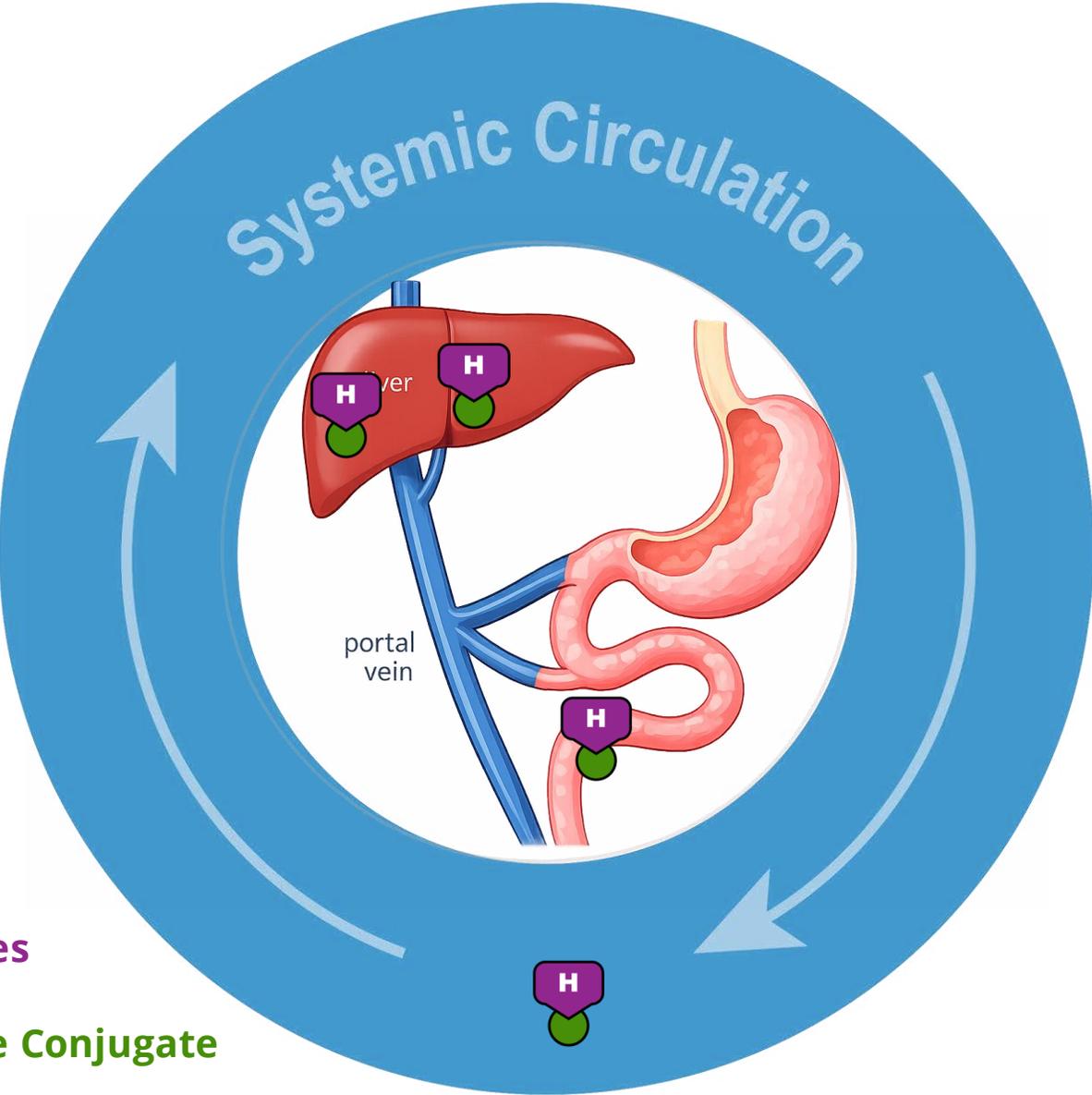
# First-Pass Metabolism



- Protein
- Hormones
- Hormone Conjugate



# First-Pass Metabolism



- Protein
- Hormones
- Hormone Conjugate



# Testing Options with HRT – What does NOT work ?

---

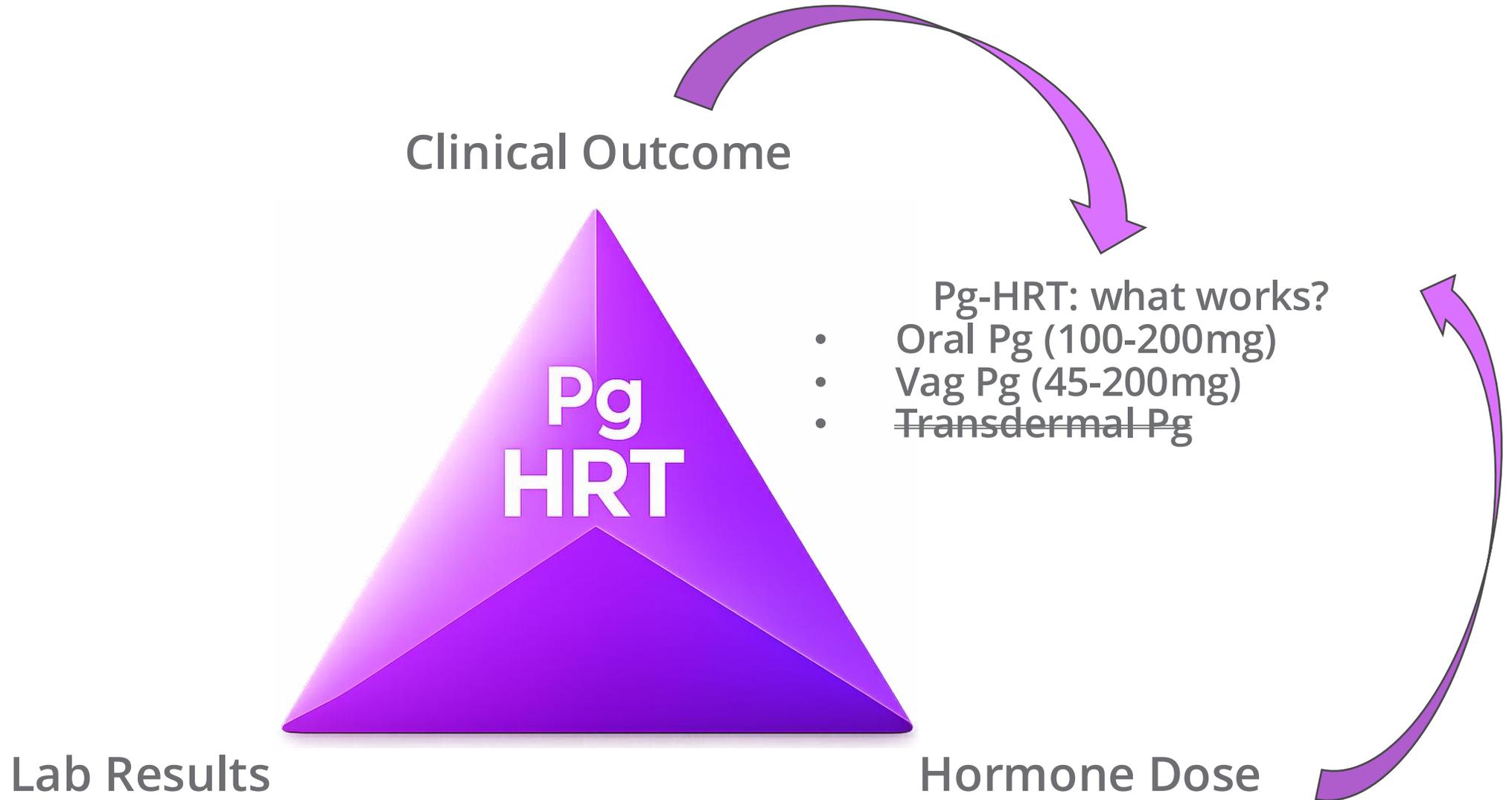
- DUTCH – If hormones are swallowed, gives big, useless numbers
  - Metabolite patterns may still be relevant
- Serum – HRT scenarios with a fast up-and-down pattern
  - Estrogen creams and gels can “disappear” in <12 hours
  - Oral, sublingual Pg, T particularly fast
- Saliva – Hormone creams and gels give big, useless numbers
  - No HRT scenarios have data suggesting saliva is a better option
- Prog – Testing does NOT help get dosing right for endometrium

# Testing Options with HRT – What **DOES work?**

---

- DUTCH – use as a primary or secondary testing option for all estrogen therapy that is not swallowed (oral, sublingual doses cannot be guided by urine testing)
- DUTCH – use as a complementary option for most androgen therapy
- DUTCH – use metabolite patterns, HPA Axis, OATs in most scenarios
  
- Serum – best primary test for TRT, oral E2, DHEA

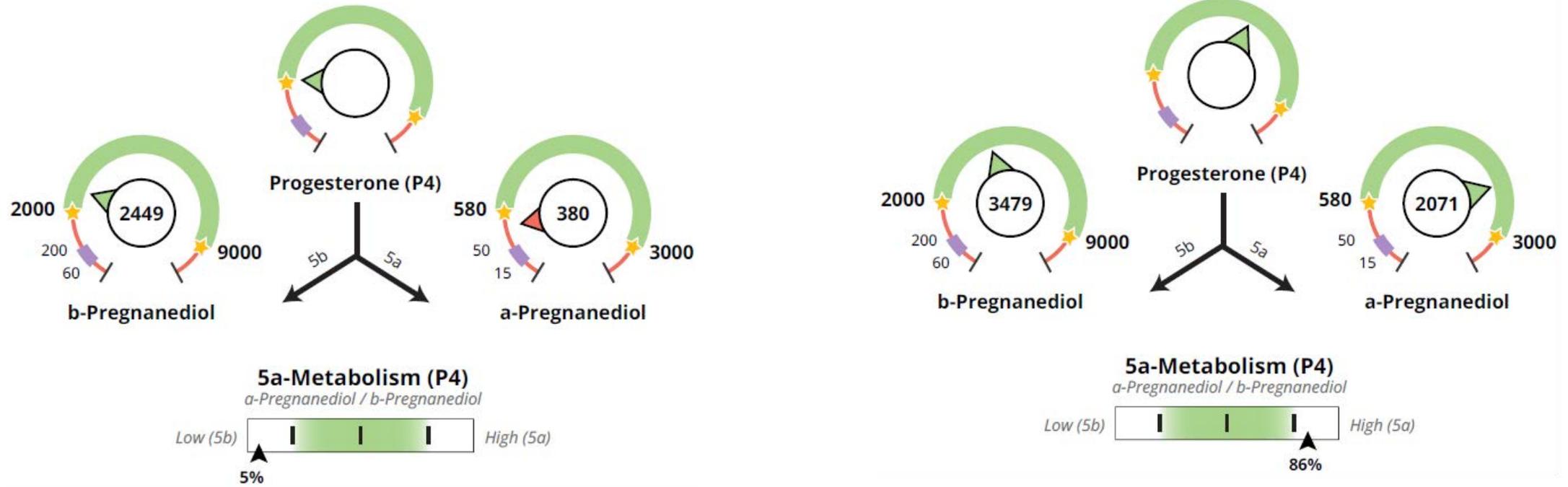
# Testing Options with HRT – Can you triangulate testing with treatment?



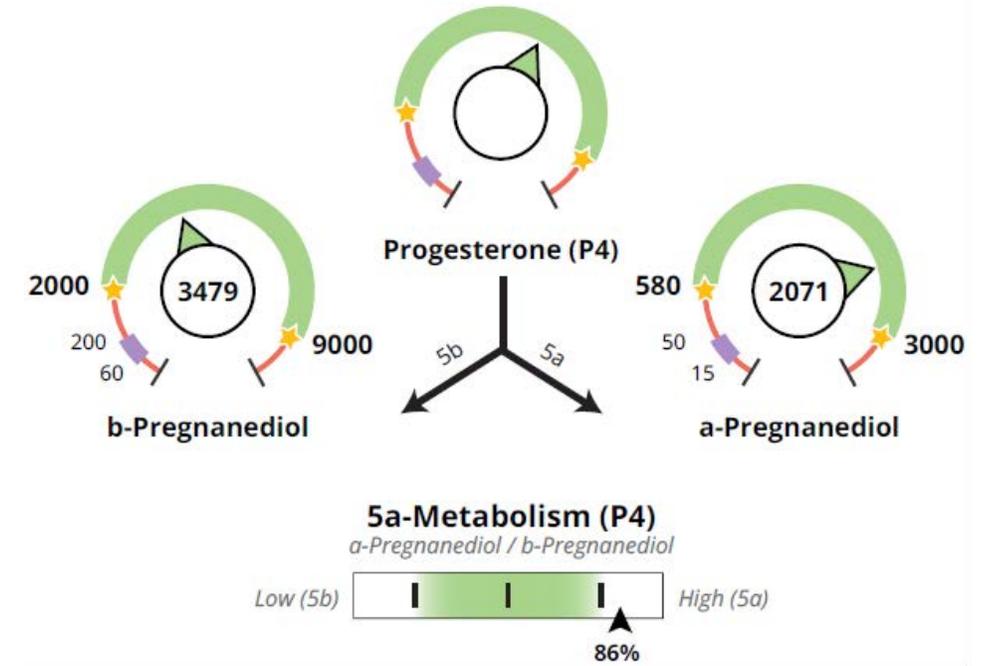
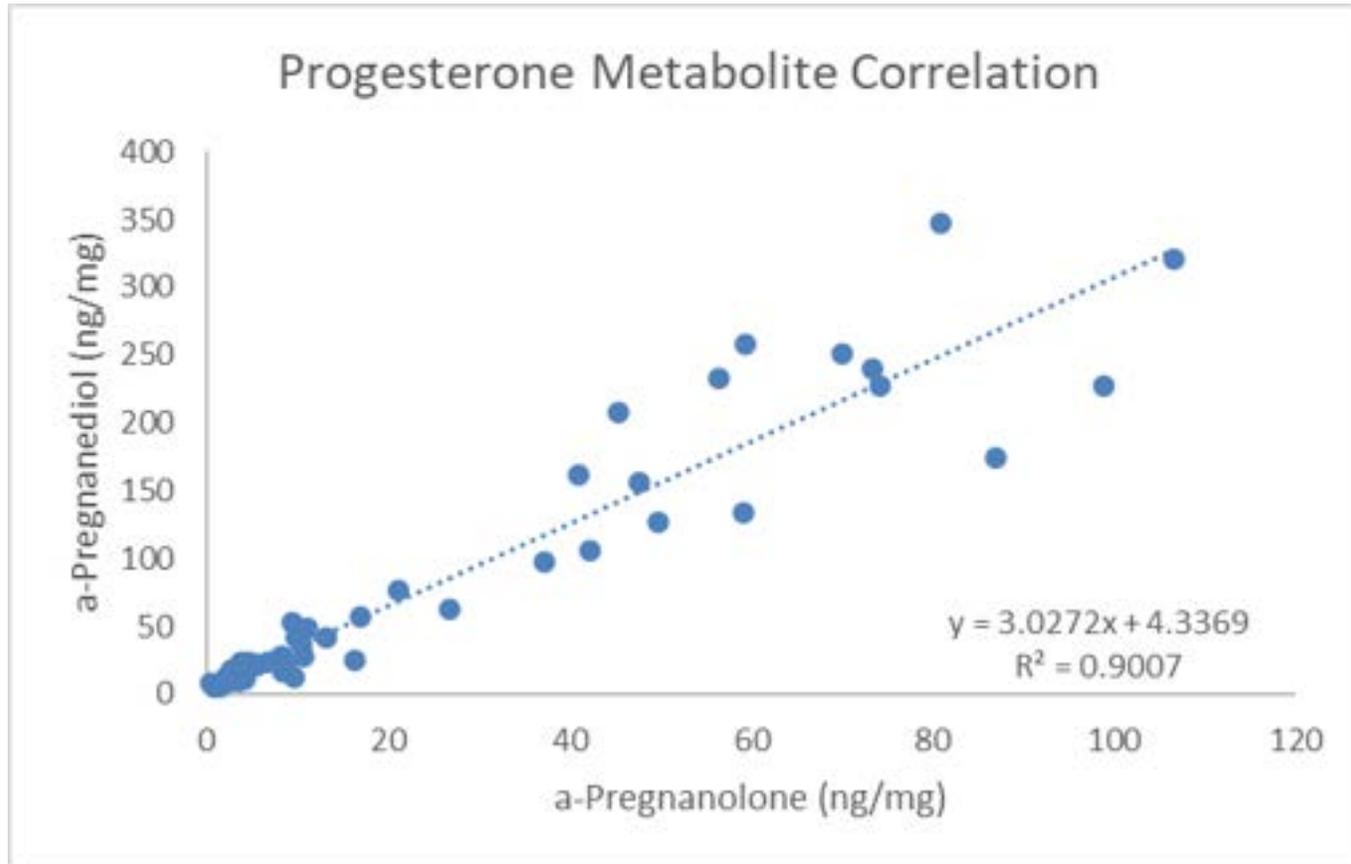
Urine testing tells us which metabolites are preferentially made, but levels tell you **NOTHING** about the endometrium

Note: ranges with oral P4 are higher

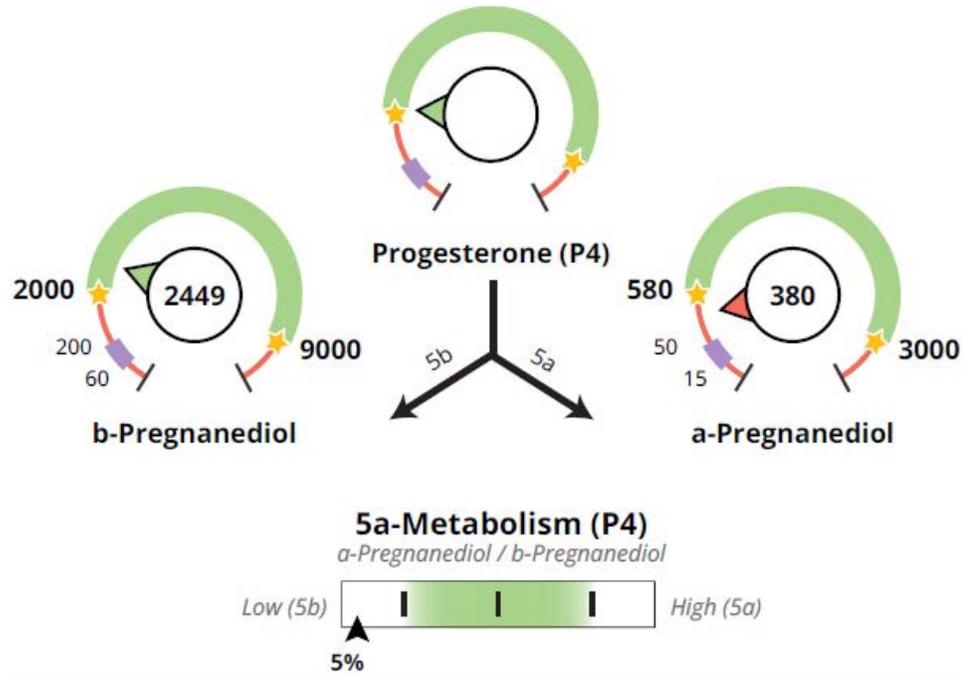
# OMP DUTCH Case Studies



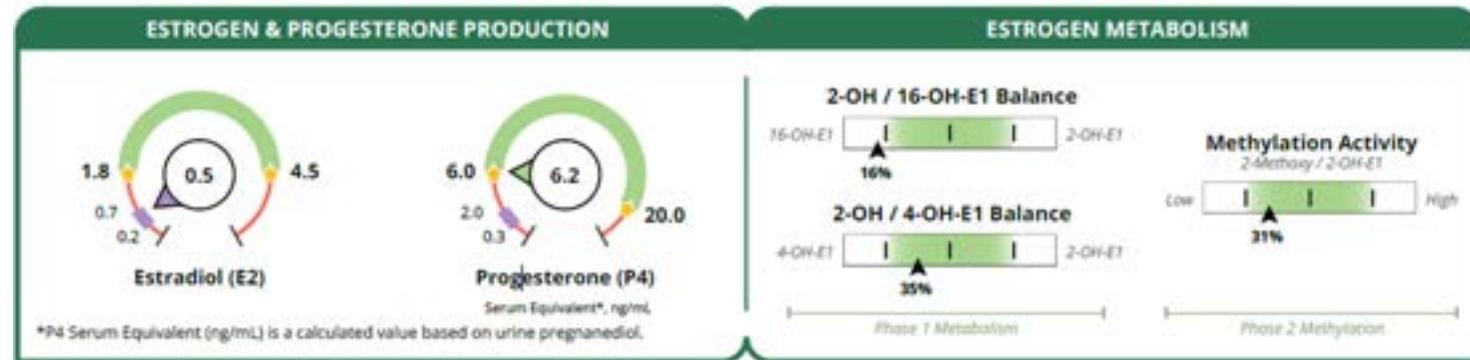
# OMP DUTCH Case Studies



# OMP DUTCH Case Studies



- Summary Page P4 Value
- Does NOT correlate with serum with OMP
- Ignore (mostly)



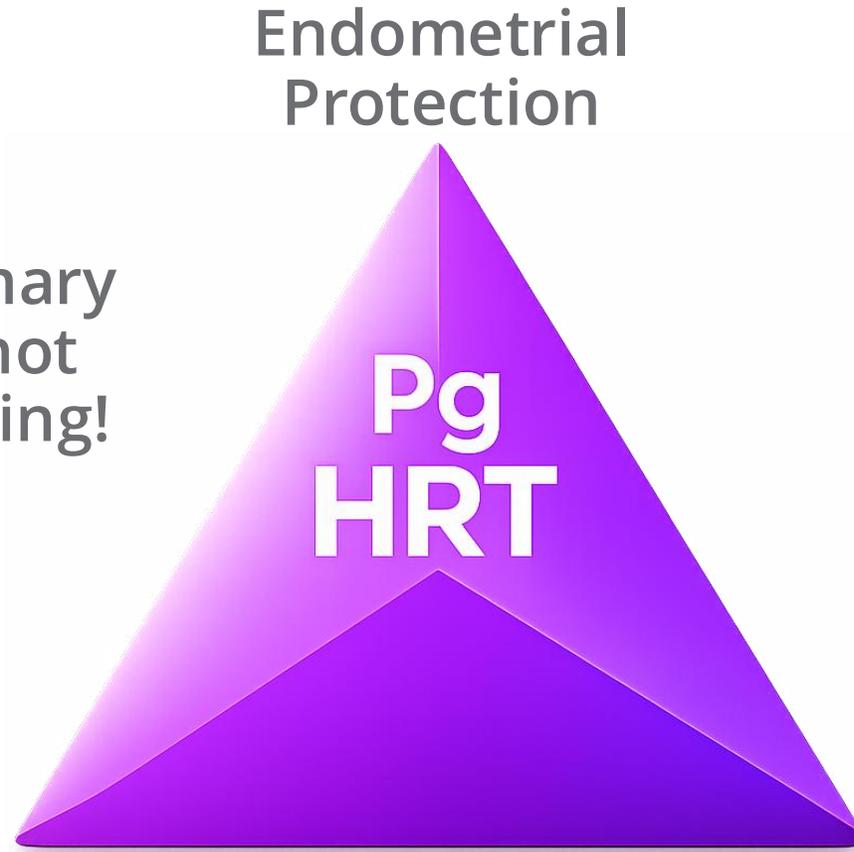
5b-Metabolism means she does not make typical amounts of sedating metabolites from her OMP

# Testing Options with HRT – Can you triangulate testing with treatment?

As it relates to P4's primary role, lab testing does not help in dosage monitoring!

~~Serum~~  
~~Saliva~~  
~~Urine~~

Lab Results 



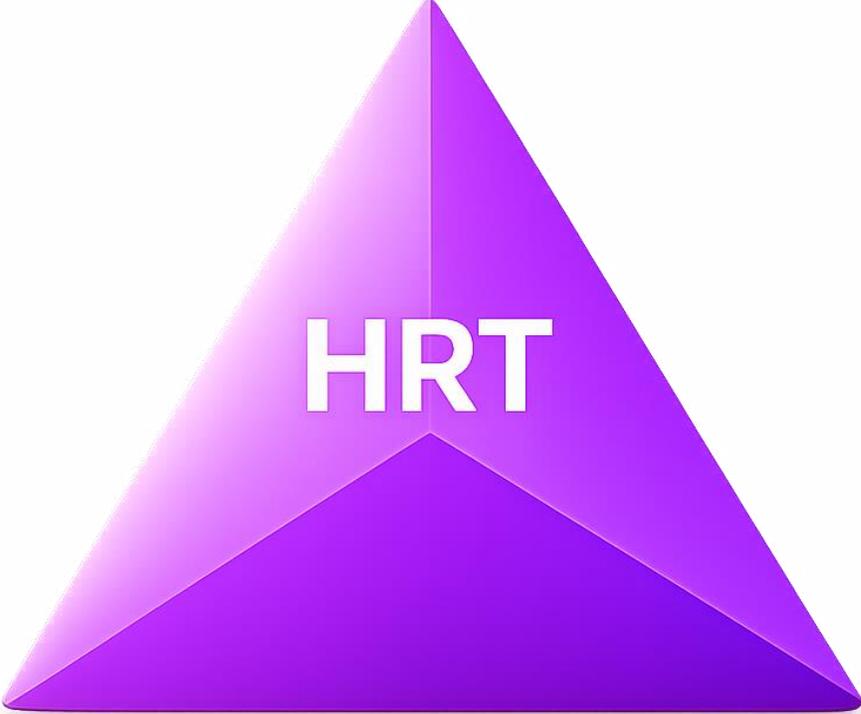
# Testing Options with HRT – Can you triangulate testing with treatment?

---

What about  
Transdermal E2?

Clinical Outcome

What about  
TRT?



HRT

Lab Results

Hormone Dose

# Testing Options with HRT – Can you triangulate testing with treatment?

Clinical Outcomes

ERT

E2  
Patches

(published E2 patch data?)



Serum  
Saliva  
Urine



(published TRT Injection data?)

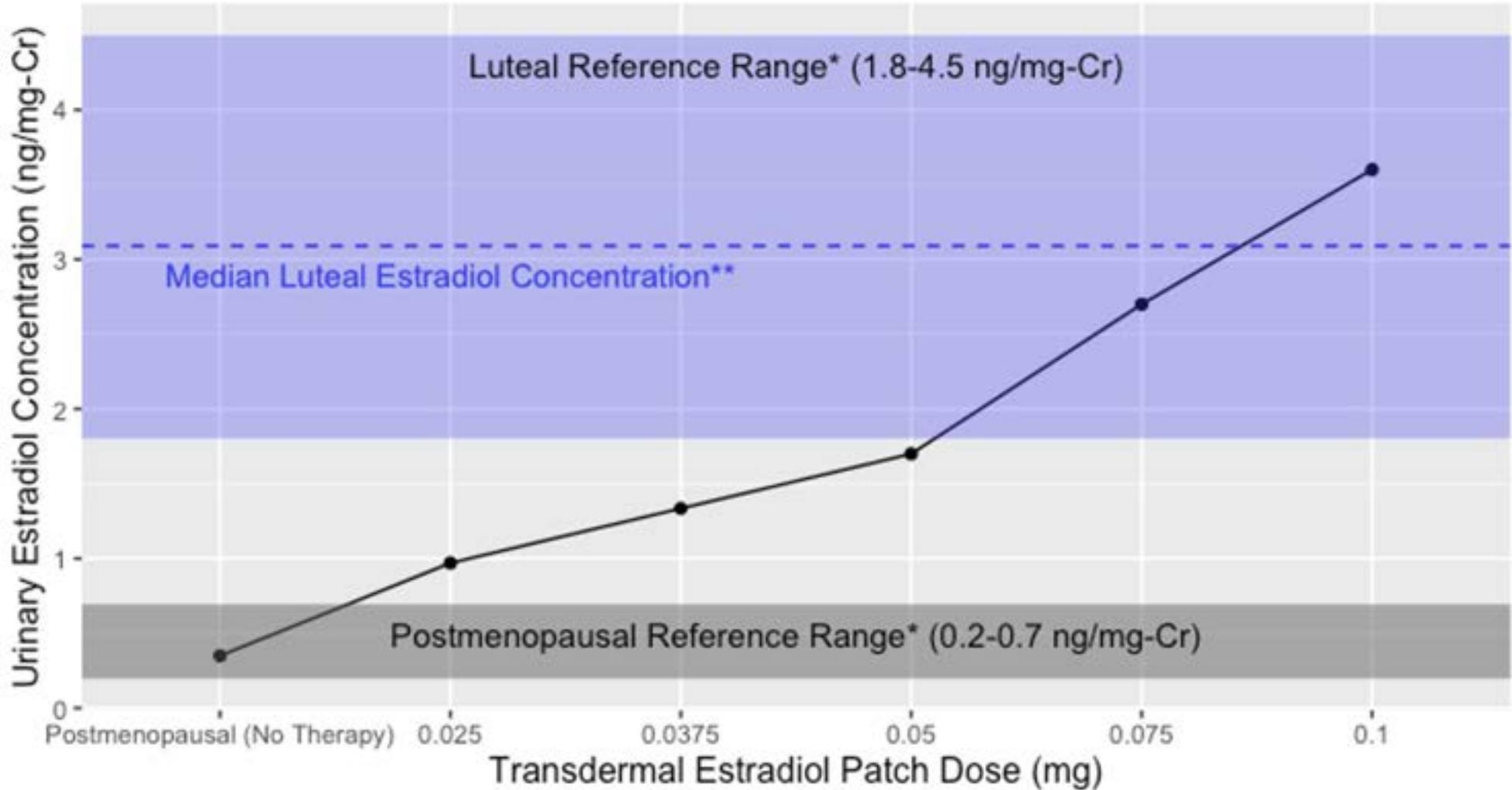
Clinical Outcomes

TRT

TRT  
Injections

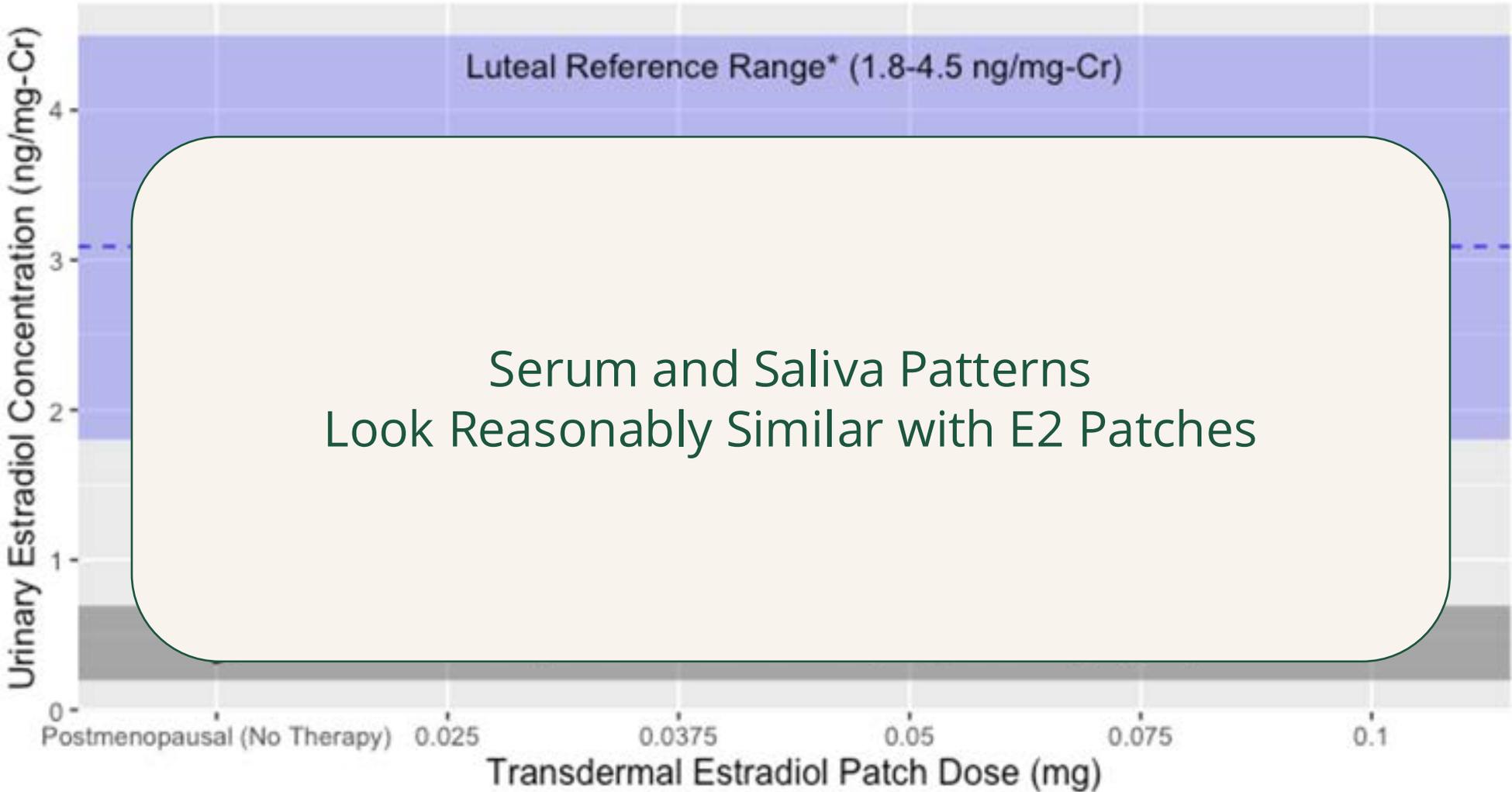
# E2 Patch Data from DUTCH Test (with Concurrent DIM Use)

## Median Estradiol Concentrations by Dose

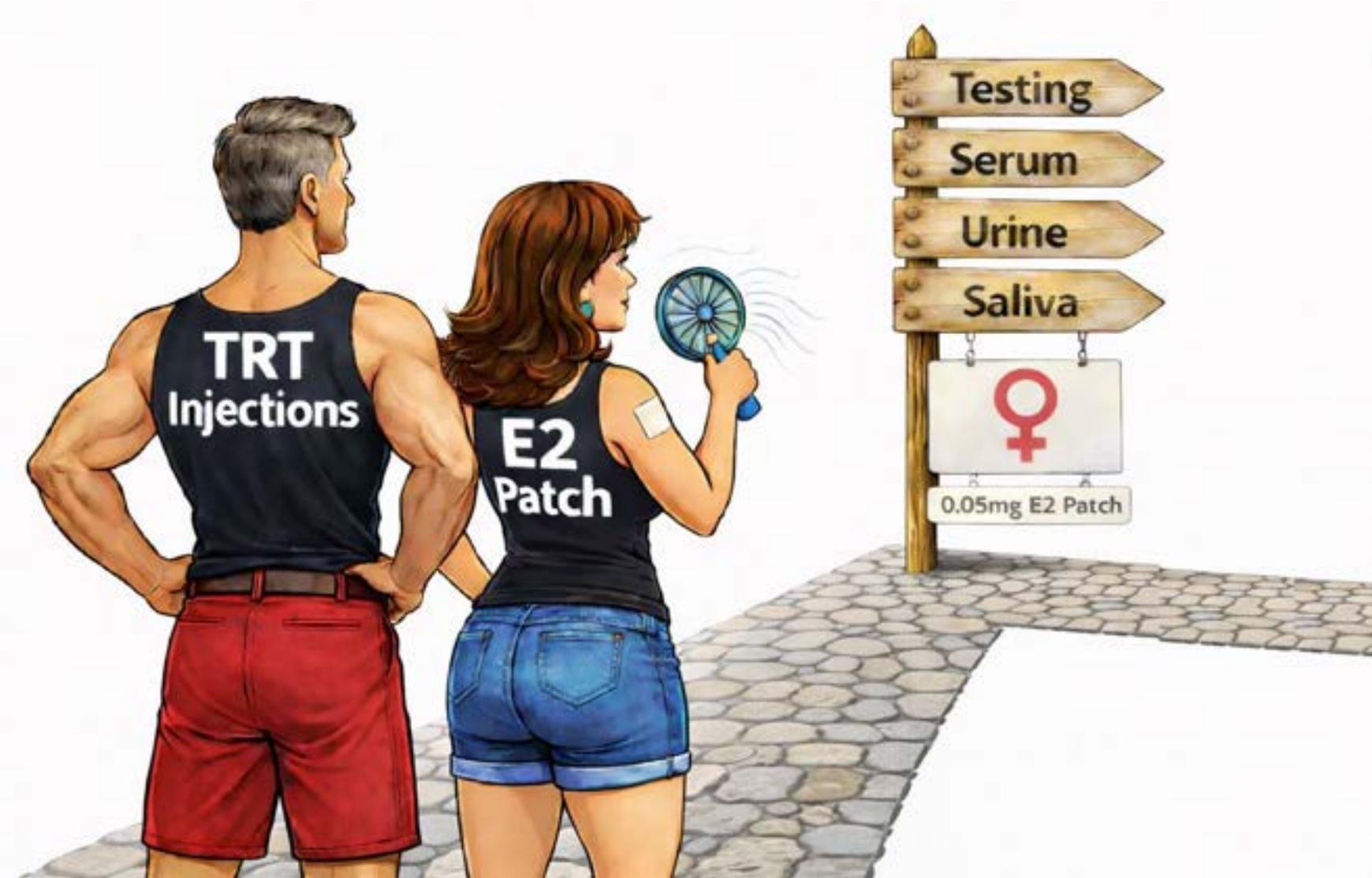


# E2 Patch Data from DUTCH Test (with Concurrent DIM Use)

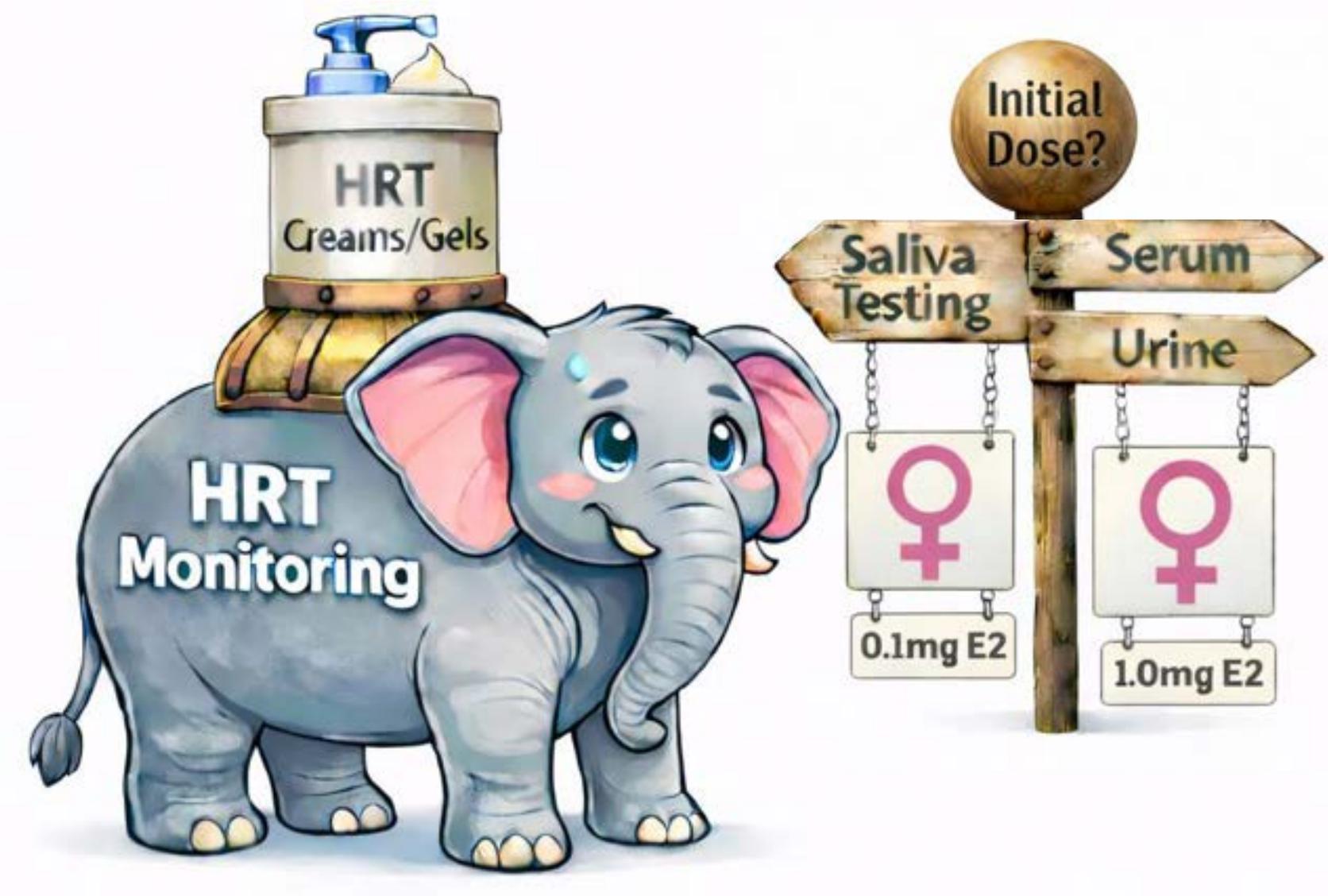
## Median Estradiol Concentrations by Dose



# Hormone Injections and Patches Show Similar Patterns Across All Tests



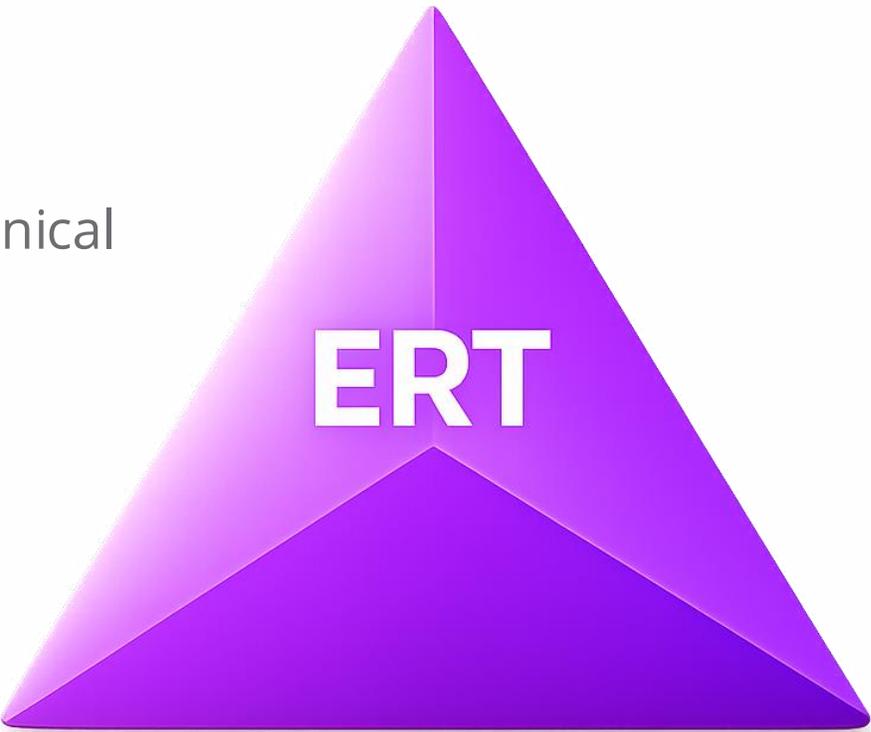
# The Elephant in the room – Transdermal Hormone Creams and Gels



# Testing Options with HRT – Can you triangulate testing with treatment?

E2 0.05mg Patch

What gel dose gives similar clinical outcomes to E2 patch?



Clinical Outcome  
(hot flashes, vaginal atrophy, bone)

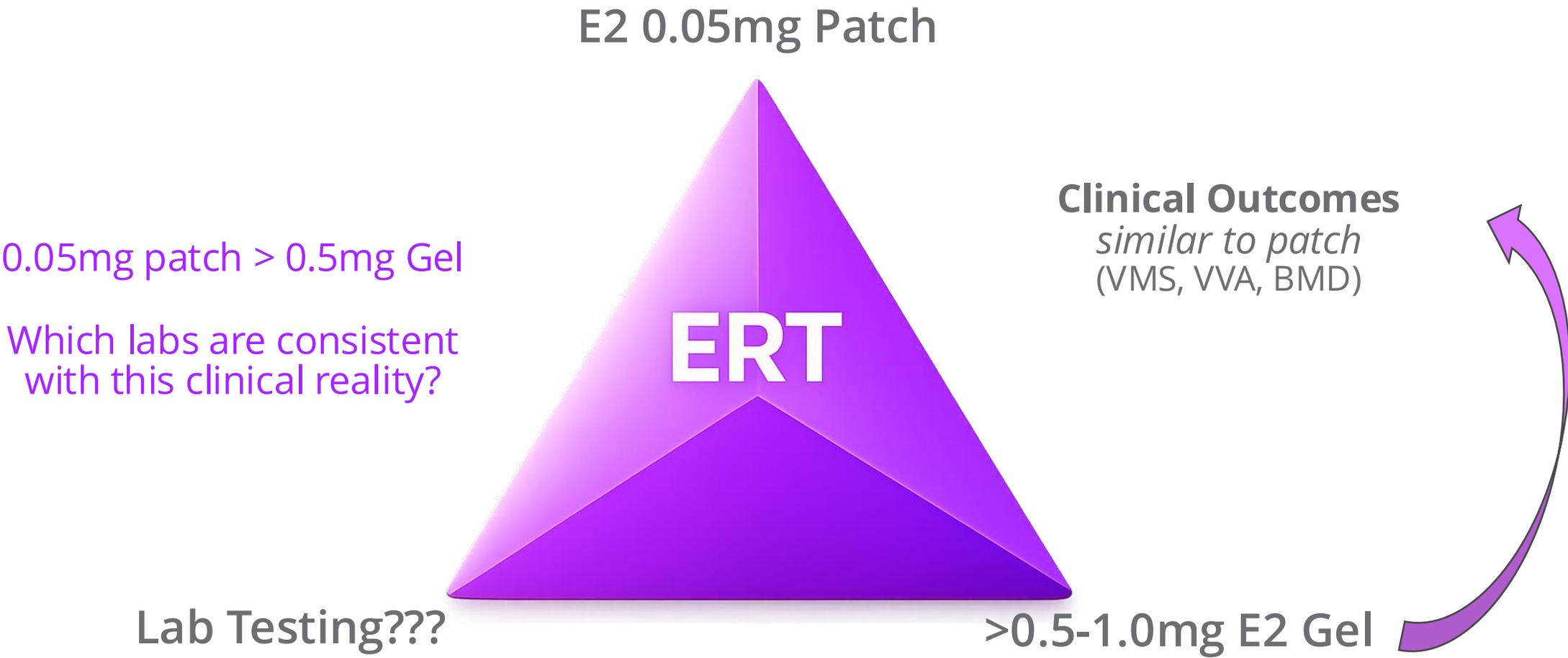
E2 Gel Dose?

# Studies Showing E2 Gel Clinical Impact

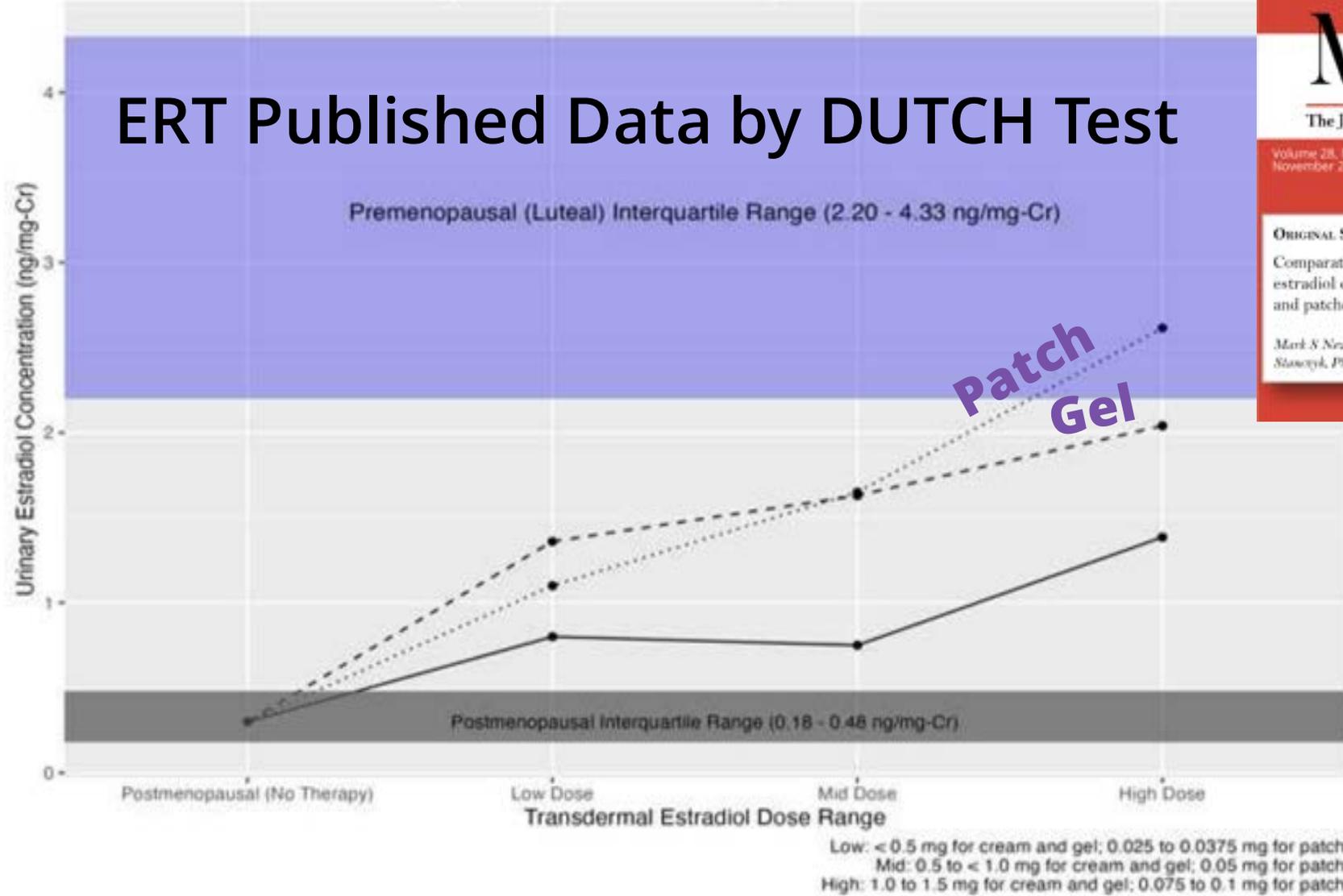
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- Archer DF, for the EstroGel Study Group. Percutaneous 17b-estradiol gel for the treatment of vasomotor symptoms in postmenopausal women. *Menopause*. 2003; 10(6): 516-521.
- Yang TS, et al. A Clinical Trial of 3 Doses of Transdermal 17b-estradiol for Preventing Postmenopausal Bone Loss: A Preliminary Study. *J Chin Med Assoc*. 2007; 70(5): 200-206.
- Brennan JJ, Lu Z, Whitman M, Stafiniak P, van der Hoop RG. Serum concentrations of 17beta-estradiol and estrone after multiple-dose administration of percutaneous estradiol gel in symptomatic menopausal women. *Ther Drug Monit*. 2001;23:134-8.
- Newman MS, Smeaton J. The impact of 3,3'-diindolylmethane on estradiol and estrogen metabolism in postmenopausal women using a transdermal estradiol patch. *Menopause*. 2025 Jul 1;32(7):630-639.
- Newman MS, Saltiel D, Smeaton J, Stanczyk FZ. Comparative estrogen exposure from compounded transdermal estradiol creams and Food and Drug Administration-approved transdermal estradiol gels and patches. *Menopause*. 2023 Nov 1;30(11):1098-1105.

# Testing Options with HRT – Can you triangulate testing with treatment?



**Figure 2.**  
**Median Estradiol Concentrations by Formulation and Dose Range**



**NAMS**  
 THE NORTH AMERICAN  
 MENOPAUSE SOCIETY

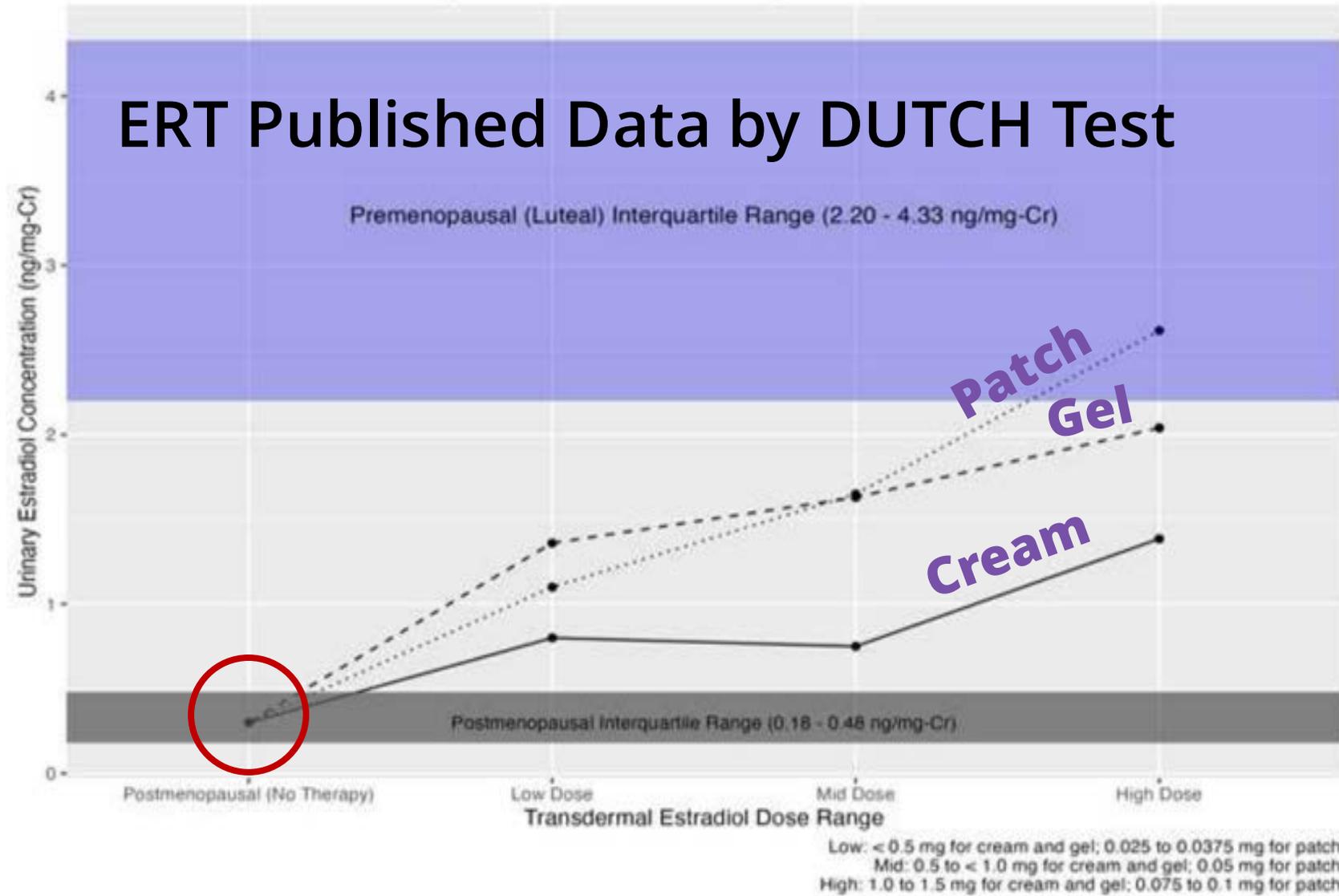
**Menopause**  
 The Journal of The North American Menopause Society

Volume 28, Number 11  
 November 2023

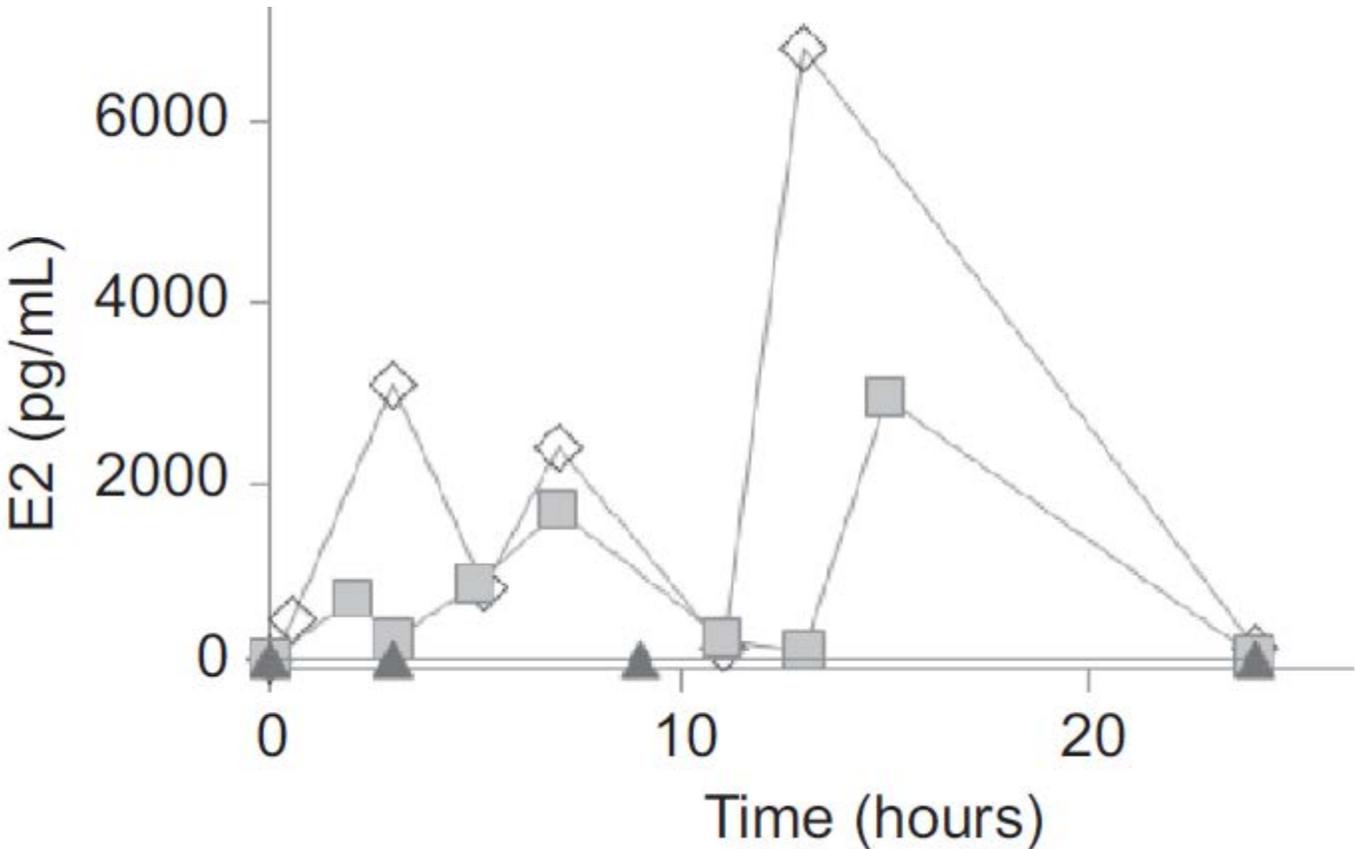
**ORIGINAL STUDY**  
 Comparative estrogen exposure from compounded transdermal estradiol creams and FDA-approved transdermal estradiol gels and patches.

Mari S. Nezman, MD, Dorcas Saltsel, MD, JDR, Jacyln Smolin, ND, Frank Z. Stawczyk, PhD

Figure 2.  
Median Estradiol Concentrations by Formulation and Dose Range



# Transdermal E2 Gel Use VERY High Saliva Values



Endogenous PMP E2 ~ 0.8pg/mL  
0.05mg E2 patch ~1.3  
Pregnancy saliva E2 ~100pg/mL

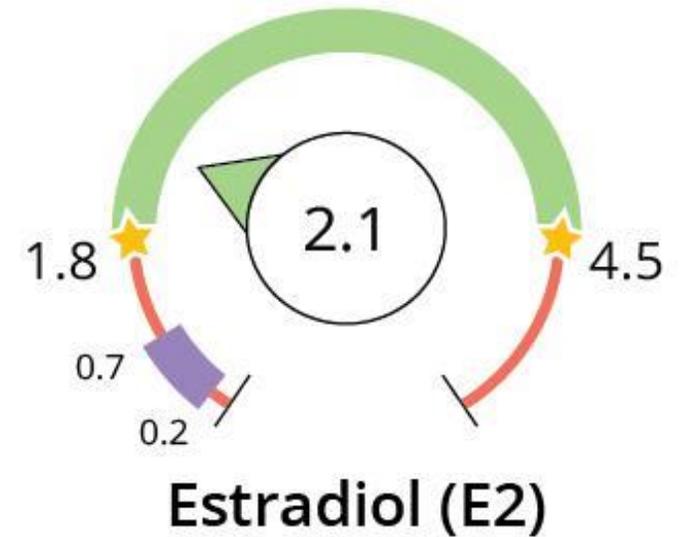
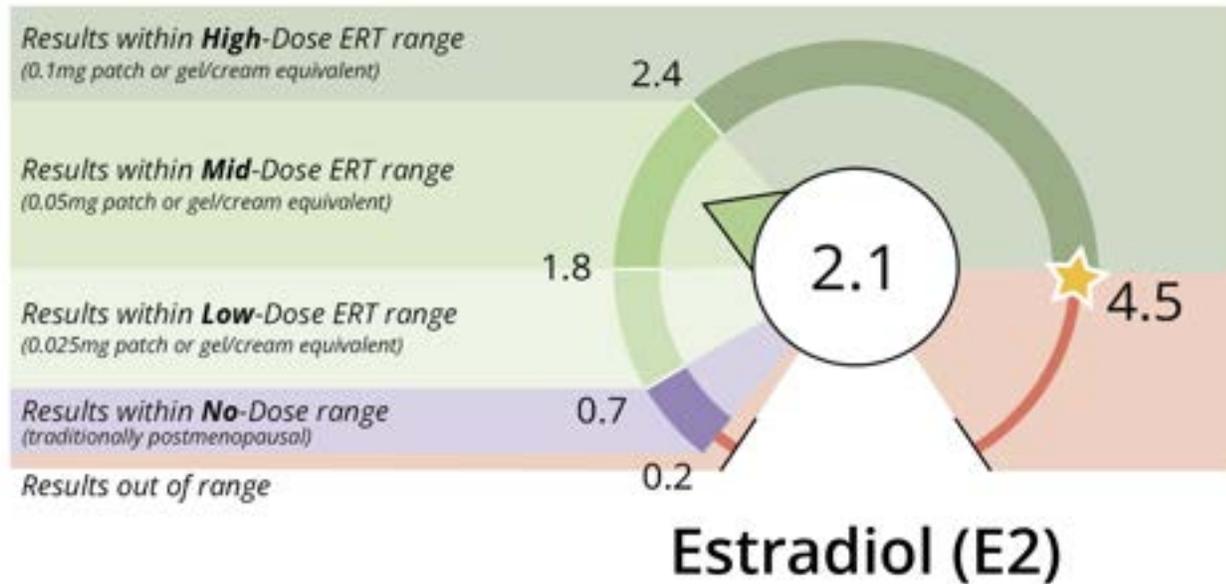
0.75mg E2 Gel (4-12hr) >>100pg/mL

Proven mild clinical impact from this 0.75mg E2 gel product (■).

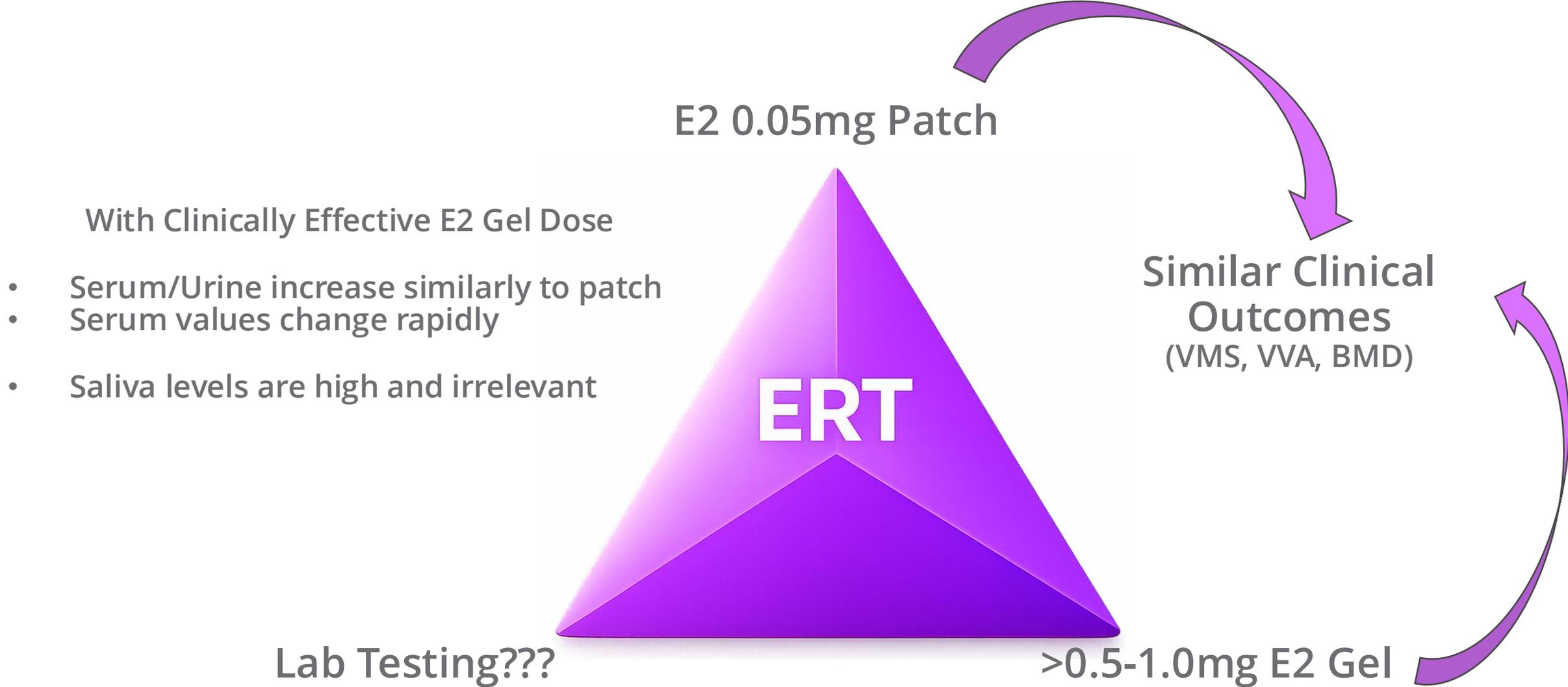
Drug Development and Industrial Pharmacy, 2009; 35(9)

# Observed On-Therapy Ranges from Menopause Publication

## PMP Levels with Estrogen Replacement Therapy (ERT) Observed Ranges



# Testing Options with HRT – Can you triangulate testing with treatment?



# Testing Options with HRT – What does NOT work ?

---

- DUTCH – If hormones are swallowed, gives big, useless numbers
  - Metabolite patterns may still be relevant
- Serum – HRT scenarios with a fast up-and-down pattern
  - Estrogen creams and gels can “disappear” in <12 hours
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# Testing Options with HRT – What DOES work?

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- DUTCH – use as a primary or secondary testing option
  - All estrogen therapy that isn't swallowed (oral, sublingual)
- DUTCH – use complementary option for most androgen therapy
- DUTCH – use metabolite patterns, HPA Axis, OATs in most scenarios
  
- Serum – best primary test for TRT, oral E2, DHEA
  
- DUTCH Fest is NOT addressing “how” to monitor dosing for HRT
  - See our HRT course for more information on how to use HRT

# Agenda for DUTCH Fest

- DUTCH Test and DUTCH Fest follow the same structure
  - Estrogen + Progesterone
  - Androgens
  - Cortisol
- Interpreting each section
  - Identifying Dysfunction
- Cause & Effect of Dysfunction
- Treatment Considerations
- Dig in deeper!



# Thank You!

Mark Newman, DUTCH Founder

For Questions, contact:

[mnewman@dutchtest.com](mailto:mnewman@dutchtest.com)

