



Androgen Interpretation

Developing Proficiency Using the DUTCH Dozen

Jaclyn Smeaton, ND



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Dr. Jaclyn Smeaton, ND, is the Chief Medical Officer (CMO) at Precision Analytical and a naturopathic physician focused on infertility, reproductive, and genitourinary health. Alongside her work at Hello Fertility, she is a prolific teacher in the field of reproductive endocrinology and hormones and has trained thousands of clinicians on her treatment methodology. Dr. Smeaton has extensive leadership experience in integrative medicine including as president of the American Association of Naturopathic Physicians, as an ambassador for the Academy of Integrative Health and Medicine, and a board member of the Integrative Health Policy Consortium.

Learning Objectives



Understand the purpose and clinical application of the four **androgen-related** key elements of the DUTCH Dozen.



Evaluate whether adrenal production of androgens (**Total DHEA Production**) is normal and recognize its impact on downstream metabolites and health.



Assess **testosterone** production and identify associated signs and symptoms of high and low levels.



Understand if **5a-androstanediol** production is normal and how it gives insight into **intracellular** production and activity of 5a-DHT.



Analyze the preference for **5a-metabolism in androgen pathways** and identify how it can affect androgen activity in the body.



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

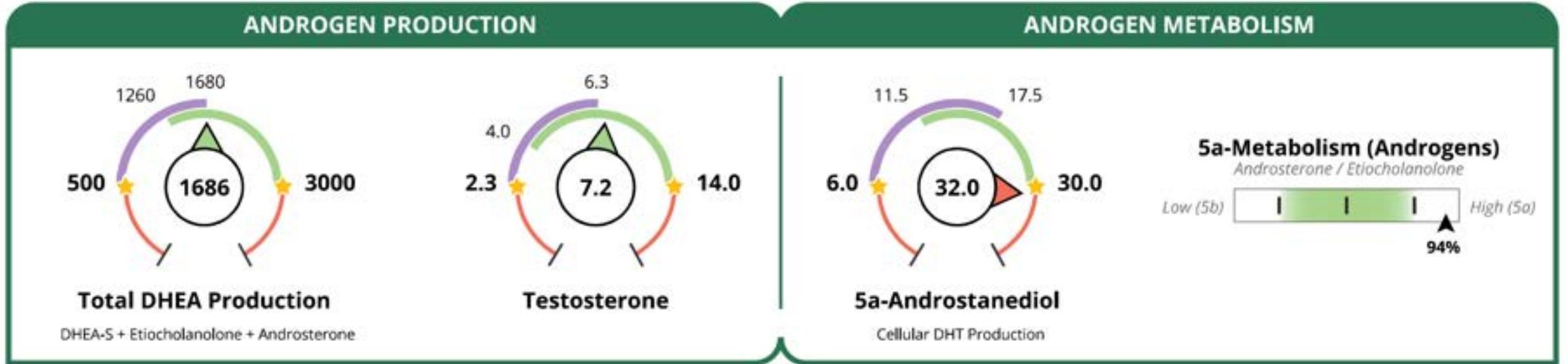
- 5 Assess adrenal androgen levels (Total DHEA)
- 6 Assess testosterone levels
- 7 Assess cellular production of 5a-DHT via 5a-androstane-3β-diol
- 8 Assess if there is a preference for the more potent alpha metabolism of the androgens

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



The DUTCH Dozen: Androgens

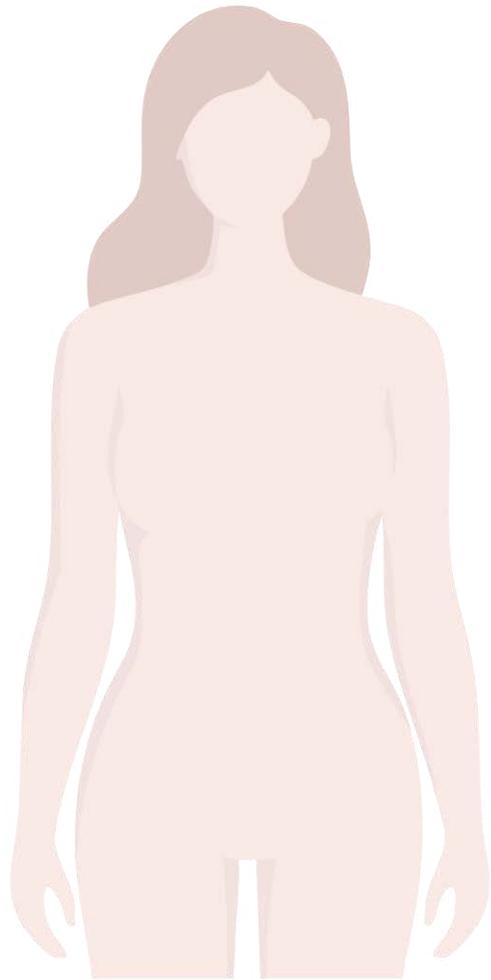


Androgens



What are “Androgens”?

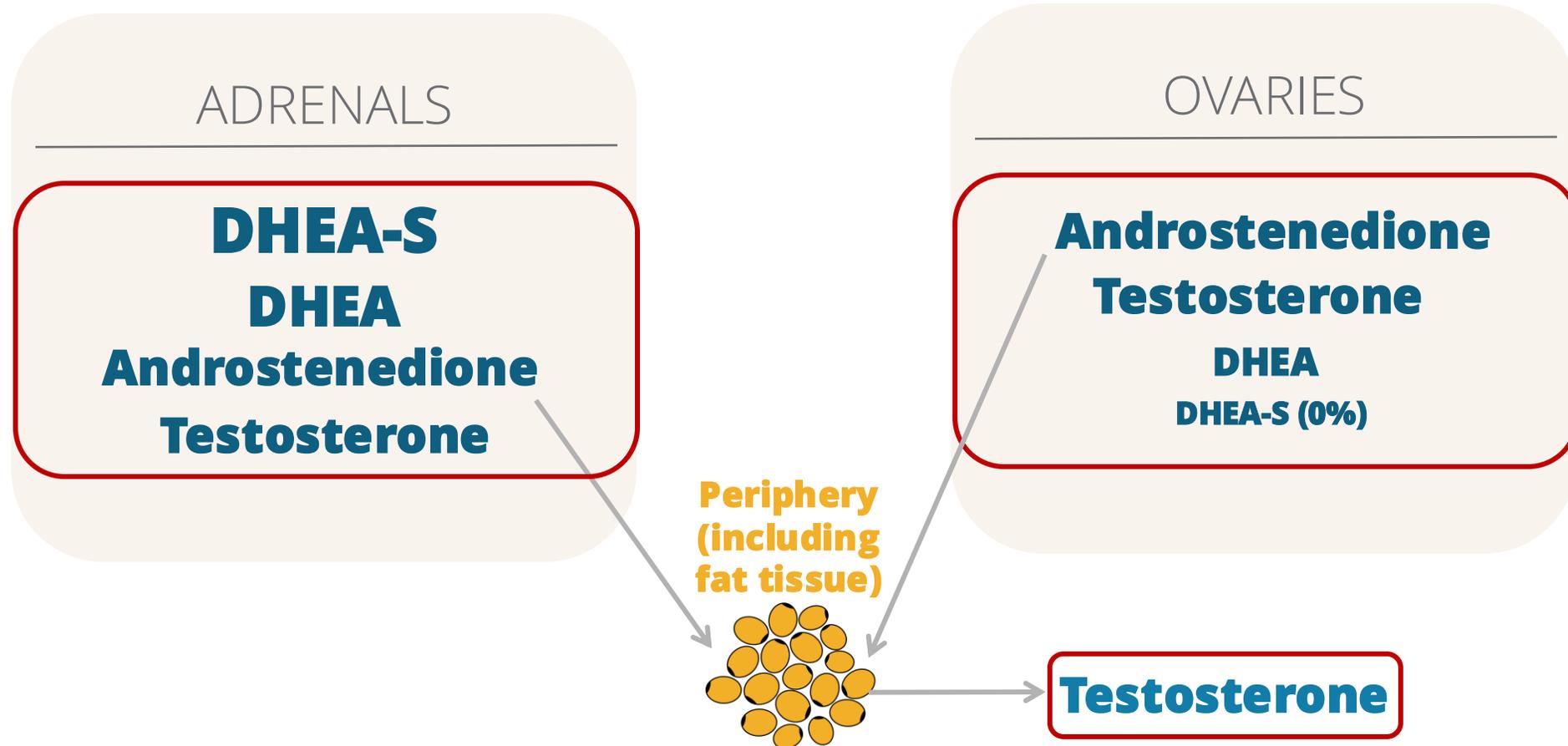
- A class of hormones and metabolites that are classically thought of as the “male” hormones as they are responsible in males to drive development of secondary sex characteristics.
- They also have critical function in females!
 - Precursors to production of estrogen & progesterone.
 - Critical for follicular development and egg quality.
- Commonly known androgens include **testosterone** and **DHEA**. Some people have heard of testosterone’s potent metabolite, **5a-DHT**.



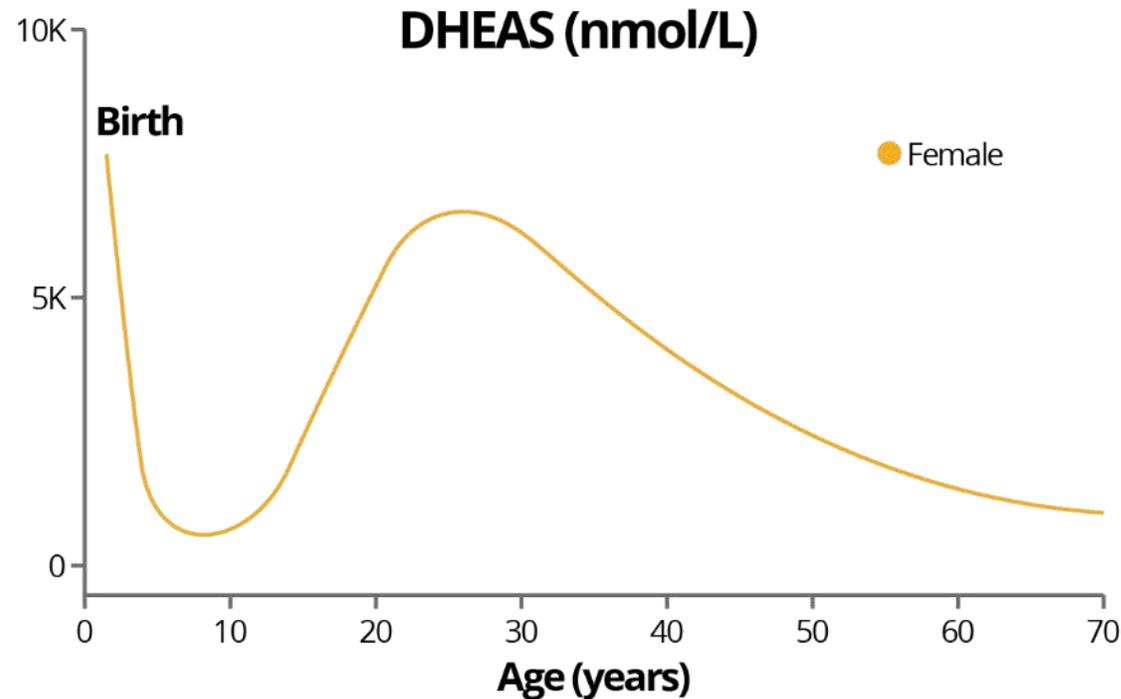
Androgen's Actions

- **Brain:** Mood, motivation, energy, sex drive, focus, sense of well-being
- **Bone density**
- **Insulin secretion**
- **Hair (body) growth**
- **Skin:** Moisture, elasticity, sebum production
- **Muscle mass:** Strength, Stamina, Recovery
- **Cardiovascular Health**
- **Immune function**
- **Sexual function:** Vasodilation, tissue elasticity, moisture
- **Fertility:** At optimal levels helps follicle growth

Where **Androgens** are Made in Women



- Androgens **peak in our 20's and 30's** and then decline thereafter.



Labrie F, et al. Front Neuroendocrinol. 2001;22(3):185-212

On the DUTCH Test, we measure the following **eight** androgen metabolites:

Testosterone Metabolites

- Testosterone
- 5a-DHT
- 5a-androstenediol
- 5b-androstenediol

DHEA Metabolites

- DHEA-S
 - Androsterone
 - Etiocholanolone
-
- Epi-testosterone (not an active androgen; measured to double check urine testosterone levels – ***more on this tomorrow!***)

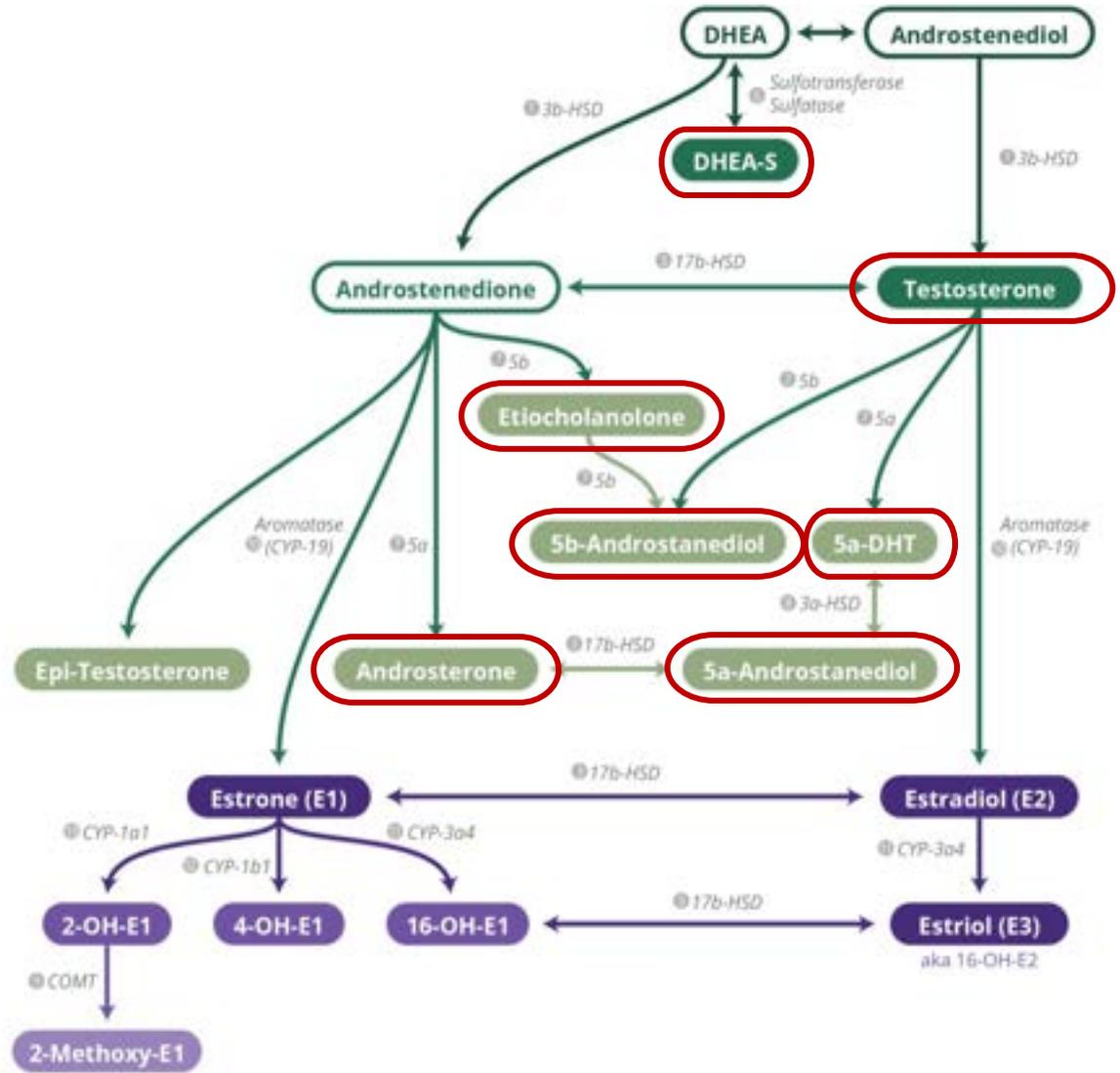
The DUTCH Dozen: Androgens

- DHEA-S is the bound-up sulfated form of DHEA.
- Etiocholanolone is a *beta* DHEA metabolite.
- Androsterone* is an *alpha* DHEA metabolite.

Alpha metabolites are made in target tissues and are active on the androgen receptors.

Beta metabolites are made in the liver and are NOT active on the androgen receptors.

- Testosterone is converted into:
- *Alpha* metabolites in the tissues:
 - 5a-DHT
 - 5a-Androstanediol
- *Beta* metabolites in the liver:
 - 5b-Androstanediol



We are primarily interested in these androgens:

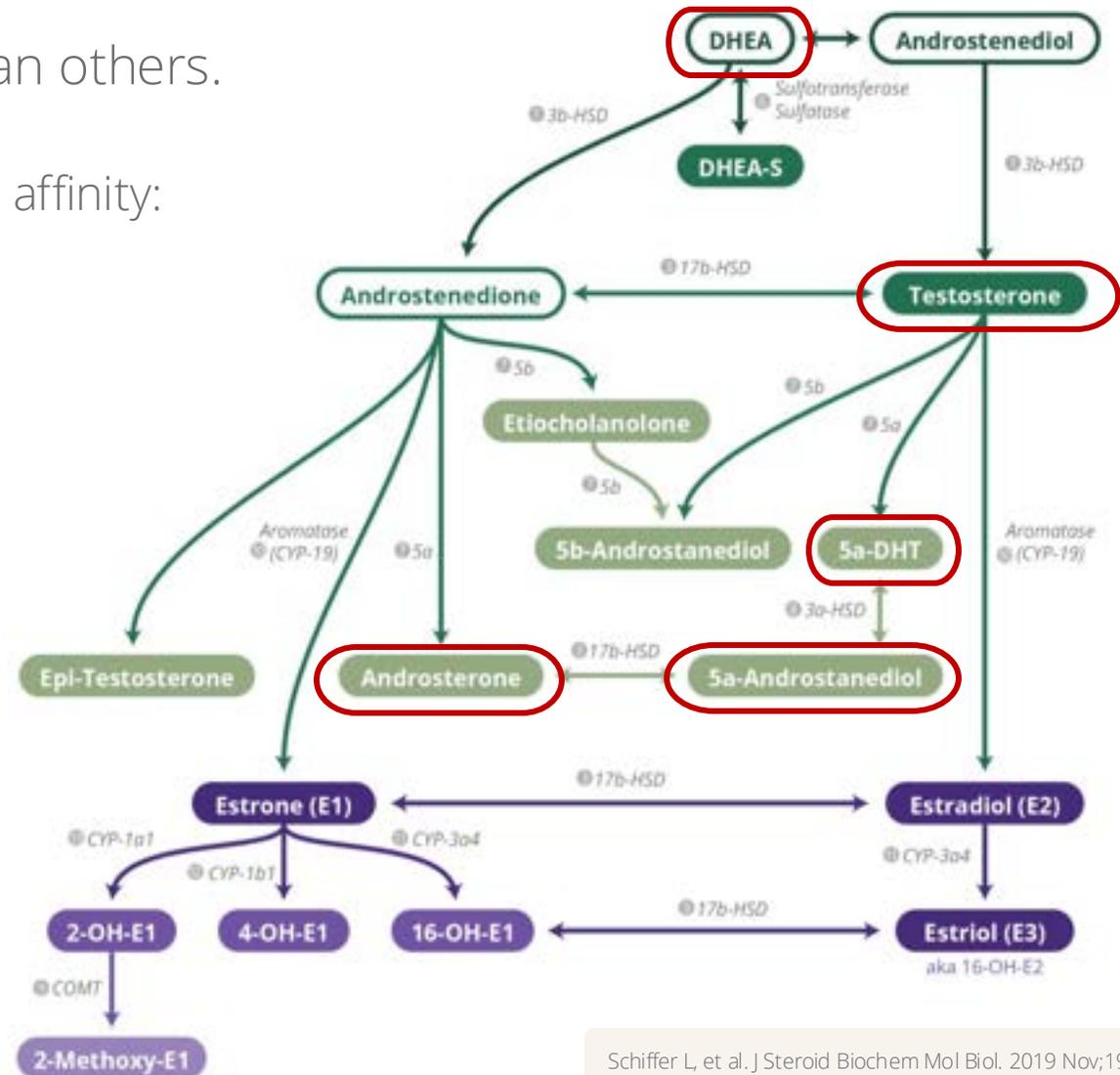
- Parent androgens
 - **DHEA** (not biologically active on its own but can convert down into testosterone, other active androgens, and estrogens)
 - **Testosterone**
- *Alpha* androgen metabolites:
 - 5a-DHT
 - 5a-androstanediol
 - Androsterone

The DUTCH Dozen: Androgens

Some of these androgens are more potent than others.

- In order of strongest to weakest receptor binding affinity:
 - **5a-DHT (strongest)**
 - **Testosterone**
 - **5a-Androstanediol**
 - **Androsterone (weakest)**
 - **DHEA (not biologically active)**

Keep in mind, however, we must also consider hormone concentration. For example, in female urine, Aldosterone can be 3x higher than DHEA, and DHEA can be 10x higher than testosterone!



Schiffer L, et al. J Steroid Biochem Mol Biol. 2019 Nov;194:105439.

The DUTCH Dozen

Total DHEA Production



Androgens

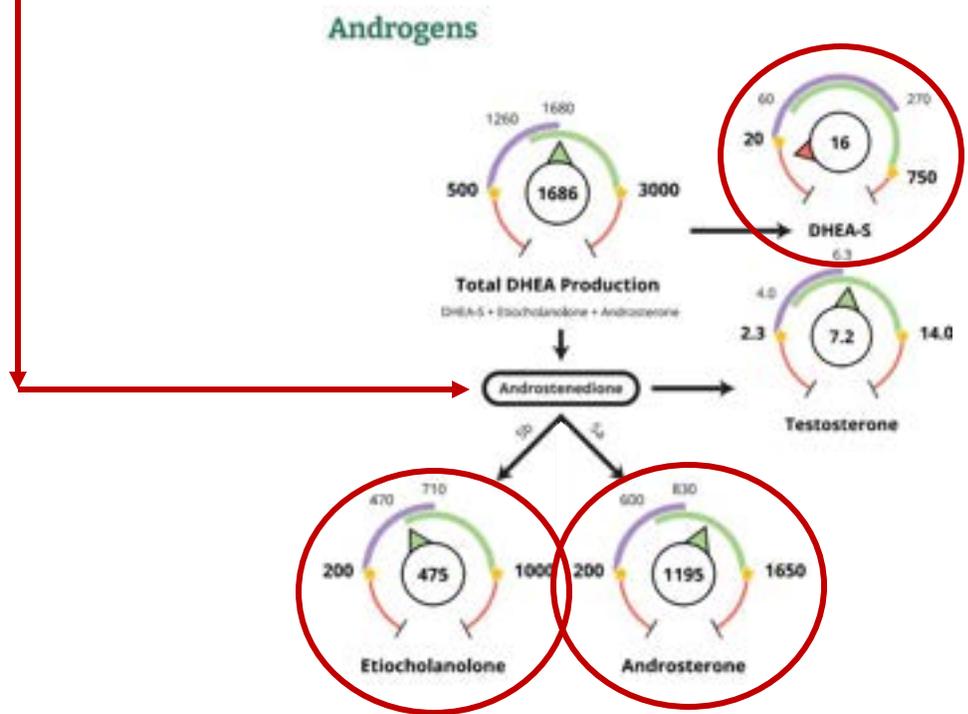
- 5** Assess adrenal androgen levels (Total DHEA)

- The **fifth assessment** measures **Total DHEA Production**, which reflects the adrenal glands' overall androgen production: *DHEA + Androstenedione (A4)*.

The DUTCH Dozen: 5 Total DHEA Production

- **Total DHEA Production** is calculated as the sum of three urinary androgen metabolites: **DHEA-S**, **etiocholanolone**, and **androsterone**.

Note that the adrenals make DHEA but also make Androstenedione (A4) which converts down into Etiocholanolone and Androsterone.

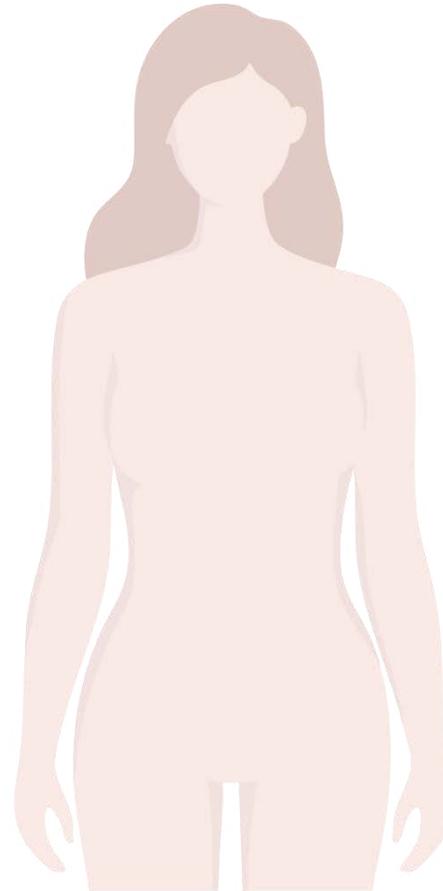


The DUTCH Dozen: 5 Total DHEA Production

Because DHEA can be converted into androgens and estrogens it can affect both androgen and estrogen activity in the body!

Estrogen's Actions

- **Brain:** Mood, cognition, memory, and focus, thermoregulation, sleep, energy
- **Hair (scalp) growth**
- **Skin:** Elasticity, collagen, repair, moisture
- **Muscle mass**
- **Nervous system:** Parasympathetic balance
- **Joint health & Bone density**
- **Breast health**
- **Liver function:** healthy cholesterol
- **Insulin sensitivity**
- **Weight management**
- **Uterine health**
- **Genitourinary system:** Elasticity, microflora, moisture
- **Fertility**
- **Cardiovascular:** endothelial function, etc.



Androgen Actions

- **Brain:** Mood, motivation, energy, sex drive, focus, sense of well-being
- **Bone density**
- **Insulin secretion**
- **Hair (body) growth**
- **Skin:** Moisture, elasticity, sebum production
- **Muscle mass:** Strength, Stamina, Recovery
- **Cardiovascular Health**
- **Immune function**
- **Sexual function:** Vasodilation, tissue elasticity, moisture
- **Fertility:** At optimal levels helps follicle growth

DHEA levels are dependent on:

Age

- DHEA declines gradually after our 20's and 30's.

ACTH secretion through the HPA axis

- Like cortisol, DHEA has a diurnal pattern because it is secreted in response to ACTH signaling from the brain.
- DHEA is also involved in the stress response.

Zona reticularis of the adrenal gland

- Function, hypertrophy, atrophy, etc.

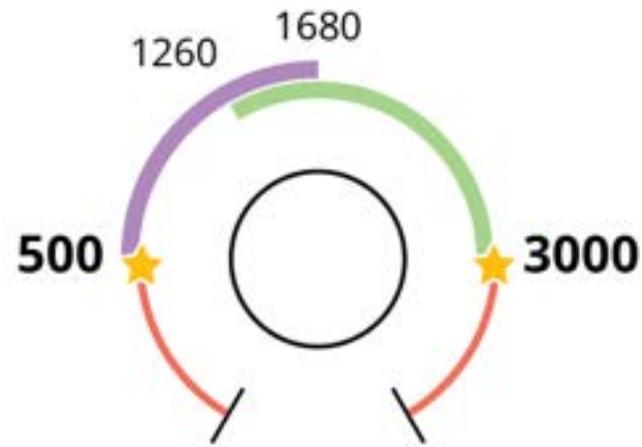
Labrie F, et al. Front Neuroendocrinol. 2001;22(3):185-212.
Schiffer L, et al. Mol Cell Endocrinol. 2018;465:4-26.

- **Menopause does not have a significant effect on DHEA levels**, but DHEA levels can have a significant effect on menopausal symptoms and hormone levels.
- At menopause, **adrenal DHEA becomes the major source of estrogens in circulation.**
 - Low DHEA in menopause can lead to lower-than-average menopausal estrogens, resulting in more severe menopause symptoms and outcomes.
 - Therefore, **healthy DHEA levels are important!**

Masjoudi M, et al. J Clin Diagn Res. 2017;11(8):Qc17-qc21.

The DUTCH Dozen: 5 Total DHEA Production

- Female androgen dials have reproductive stage-related reference ranges.
- “Optimal Premenopausal” is regarding women **age 20+**.
- **Women aged 41-55 may fall within or below the optimal pre-menopausal androgen range.**



Key to Reading the Dial

- Optimal Premenopausal
- Postmenopausal Range
- Out of Range
- ★ Edge of Range

Total DHEA Production

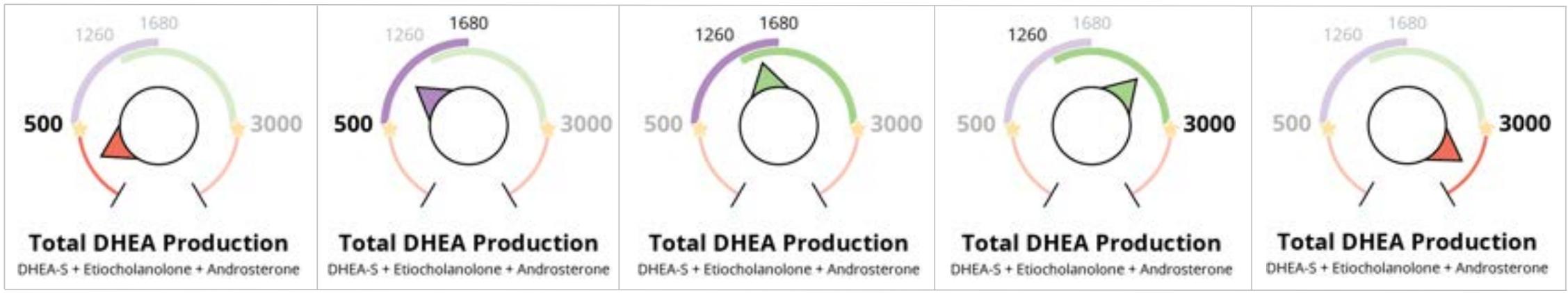
DHEA-S + Etiocholanolone + Androsterone

The DUTCH Dozen: 5 Total DHEA Production

The patient's DHEA result will be within **one of these 5 areas on the DUTCH dial**:

Key to Reading the Dial

- Optimal Premenopausal
- Postmenopausal Range



- Below the postmenopausal range
(Low for *any* age!)
- Within the postmenopausal range
- Within both the PMP and premenopausal range
- Within the premenopausal range
- Above the premenopausal range
(High for *any* age!)

DHEA in Women: Causes



Low
<500 ng/mg

Low DHEA Levels Due To:

- Accelerated age-related decline in DHEA production from the zona reticularis
- Significant chronic HPA axis **dysfunction** (e.g., prolonged stress, sleep deprivation, chronic inflammation, etc.) (8)
- Medications that **impair** (but do not fully suppress) the HPA axis (e.g., lower-dose glucocorticoids, opioids, etc.) (9)
- Conditions that slow the cortisol clearance rate (CCR), including hypothyroidism (10)
- Pituitary or hypothalamic **dysfunction**



Postmenopausal (PMP)
500-1680 ng/mg

PMP DHEA Levels:

- Common and expected with aging, particularly in women over age 40
- Women aged 41-55 may fall within or below the optimal pre-menopausal androgen range

Lower than Expected DHEA (e.g., women under age 40 or not PMP) Due To:

- Mild chronic HPA axis **dysfunction** (8)
- Medications that **mildly impair** (but do not fully suppress) the HPA axis (e.g., lower-dose glucocorticoids, opioids, etc.) (9)
- Accelerated age-related decline in DHEA production from the zona reticularis
- Conditions that slow the cortisol clearance rate (CCR), including hypothyroidism (10)



High
>3000 ng/mg

High DHEA Levels Due To:

- Significant acute HPA axis activation or dysfunction (21)
- Hyperprolactinemia
- Adrenal-driven PCOS
- Conditions that increase the cortisol clearance rate (CCR) such as obesity or metabolic disease (22)
- CAH/NCCAH (23)
- Cushing's Syndrome (not due to exogenous glucocorticoid use) (25)



Very Low

Subphysiologic DHEA Levels Due To:

- Pituitary or hypothalamic **suppression**
- Medications that **suppress** the HPA axis (e.g., higher-dose or prolonged glucocorticoids, opioids, etc.) (9)
- Adrenal insufficiency, including Addison's disease
- Adrenalectomy



Optimal Pre-Menopausal
1260-3000 ng/mg

Premenopausal DHEA Levels:

- Expected in women age 40 and younger
- Associated with normal adrenal androgen production
- Women aged 41-55 may fall within or below the optimal pre-menopausal androgen range



Very High

Supraphysiologic DHEA Levels Due To:

- Oral or sublingual DHEA or T therapy (1st pass increases urine metabolites only, not serum) (24)
- DHEA secreting neoplasms (rare)

DHEA in Women: Effects



Low
<500 ng/mg

Low DHEA Signs & Symptoms:

- Impaired fertility in premenopausal women
- Hypoactive sexual desire disorder (HSDD) or low libido
- Increased risk of metabolic or cardiovascular disease
- Fatigue and brain fog
- Cognitive decline or memory difficulties
- Reduced psychological well-being
- Mood issues, including low mood or anxiety
- Immune dysregulation



PMP
500-1260 ng/mg

Low(er) DHEA:

Some women – particularly younger, cycling women under age 40 - may be more likely to experience symptoms of low DHEA.



Optimal Pre-Menopausal
1260-3000 ng/mg

Healthy DHEA Levels Support:

- Healthy estrogen levels
- Maintenance of the majority of female testosterone
- Maintenance of muscle mass, if exercising
- Preservation of bone mineral density
- Maintenance of insulin sensitivity
- Psychological well-being and mood stability

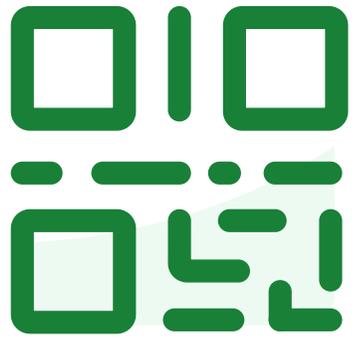


High
>3000 ng/mg

High DHEA Signs & Symptoms:*

- Mild androgen excess may present as acne, hirsutism, scalp hair thinning
- Menstrual irregularities
- Impaired fertility (in premenopausal women)
- In severe cases, virilization (e.g., voice deepening, clitoral enlargement)
- May contribute to elevated estradiol (E2) and testosterone (T) levels

*An appropriate dose of oral or sublingual DHEA or T taken near the time of testing may increase urinary DHEA metabolites due to first-pass metabolism, without reflecting serum DHEA levels or causing symptoms of androgen excess.



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#DUTCHFEST2**

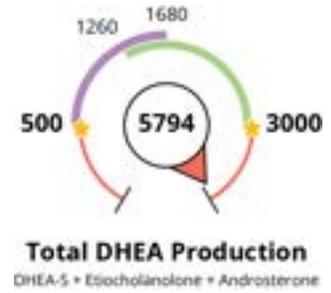


Game time!

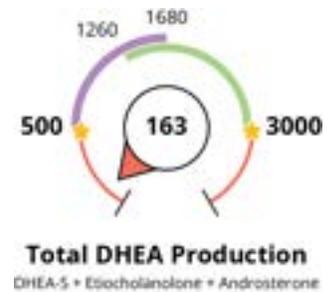
Match the description to the dial:

1 51-year-old female
PMP
Took oral DHEA on day of collection

2 58-year-old female
PMP
Congenital Adrenal Hyperplasia



A



B



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Question 1: Match the description to the correct Total DHEA Production dial



Game time!

Match the description to the dial:

1 51-year-old female
PMP
Took oral DHEA on day of collection

2 58-year-old female
PMP
Congenital Adrenal Hyperplasia

A

B

Total DHEA Production
DHEA-S + Epiandrosterone + Androsterone

Total DHEA Production
DHEA-S + Epiandrosterone + Androsterone



Game time!

Match the description to the dial:

1

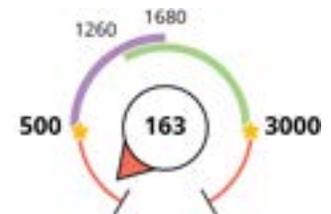
25-year-old female
PCOS
High cortisol

2

36-year-old female
Long-term use of opioids
for pain

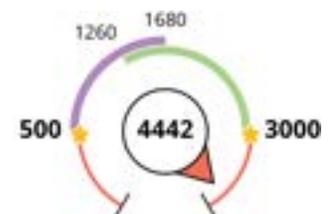
3

55-year-old female
PMP
Addison's Disease



Total DHEA Production
DHEA-5 + Epiandrosterone + Androsterone

A



Total DHEA Production
DHEA-5 + Epiandrosterone + Androsterone

B



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Question 2: Match the description to the correct Total DHEA Production dial



Game time!

Match the description to the dial:

1

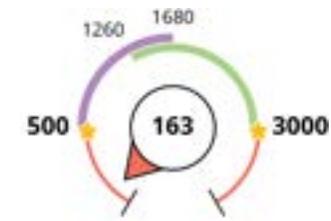
25-year-old female
PCOS
High cortisol

2

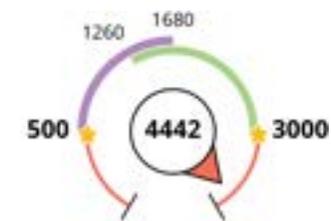
36-year-old female
Long-term use of opioids
for pain

3

55-year-old female
PMP
Addison's Disease



A



B

The DUTCH Dozen

Testosterone

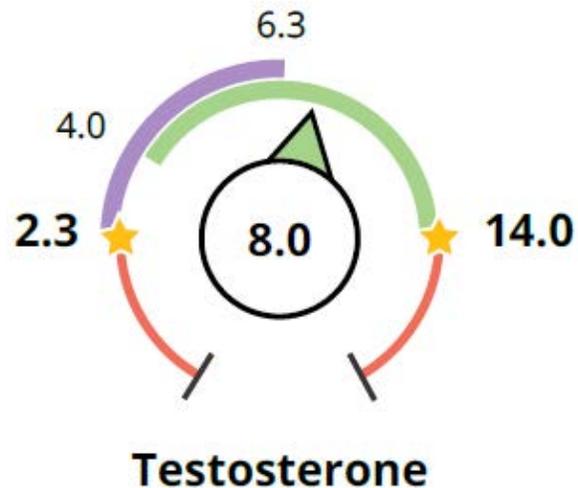


Androgens

6 Assess testosterone levels

- The sixth assessment looks at testosterone levels.
- The DUTCH **Testosterone** represents the bioavailable conjugated testosterone in urine, which typically correlates most closely with serum free testosterone.

- The Testosterone DUTCH dial is read in the same manner as the DHEA dial.
- **Women aged 41-55 may fall within or below the optimal pre-menopausal androgen range.**



Key to Reading the Dial

- Optimal Premenopausal
- Postmenopausal Range
- Out of Range
- ★ Edge of Range

Though ovarian production of estrogen and progesterone stops after menopause, **testosterone production does not**.

- In fact, postmenopausal women showed a 40% decline in testosterone after oophorectomy.

Remember, testosterone is made in the **ovaries** (25%), **adrenals** (25%), and **periphery** (50% converted from androstenedione).

Testosterone is an active androgen but also converts to other **active androgens** (e.g., 5a-DHT) and to **estrogens** in the peripheral tissues.

Davey DA. Womens Health. 2012;8(4):437-446.
Schiffer L, et al. Mol Cell Endocrinol. 2018;465:4-26.

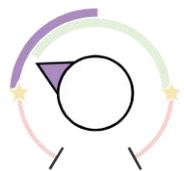
Testosterone in Women: Causes



Low
<2.3 ng/mg

Low T Levels Due To:

- Conditions & medications that suppress the HPO axis, including combo OCPs (1)
- Diminished ovarian reserve, POI, perimenopause
- Low adrenal androgens that are precursors to T (e.g., DHEA, A4)
- Accelerated age-related decline in T production from the adrenals and ovaries
- Medically induced, such as in oophorectomy (3)
- High SHBG (as seen with combo OCPs or oral estrogens) (11)
- Hypogonadism
- Hypopituitarism
- Medications that suppress the HPA axis (e.g., higher-dose or prolonged glucocorticoids, opioids, etc.) (9)



Postmenopausal (PMP)
2.3-6.3 ng/mg

PMP T Levels:

- Common and expected with aging, particularly in women over age 40
- Women aged 41-55 may fall within or below the optimal premenopausal androgen range

Lower than Expected T (e.g., women under age 40) Due To:

- Conditions that impair (but do not fully suppress) the HPO axis (2)
- High SHBG (as seen with combo OCPs or oral estrogens) (11)
- Low adrenal androgens that are precursors to T (e.g., DHEA, A4)
- Mild chronic HPA axis dysfunction (8)
- Medically induced, such as in oophorectomy (3)
- Accelerated age-related decline in T production from the adrenals and ovaries
- High aromatase activity (more T → E), typically obesity-related (12)
- Medications that mildly impair (but do not fully suppress) the HPA axis (e.g., lower-dose glucocorticoids, opioids, etc.) (9)



High
>14 ng/mg

High T Levels Due To:

- Metabolic issues as seen with PCOS and obesity
- Low SHBG (as seen with PCOS and insulin resistance) (26)
- High adrenal androgens that are precursors to T (e.g., DHEA, A4)
- Suboptimal T detoxification adding to the high T levels
- Low aromatase activity (less T → E) (4)
- Hormone therapy is increasing T on top of high endogenous T production
- CAH/NCCAH (23)



Very Low

Very Low T Levels (in urine):

- Confirm with serum testing. A genetic deletion polymorphism in the UGT2B17 gene can lead to very low urinary excretion of testosterone even when serum levels are normal
- If accurate, refer to the possible contributors seen under "Low"



Optimal Pre-Menopausal
4.0-14 ng/mg

Premenopausal T Levels:

- Expected in women age 40 and younger
- Associated with normal adrenal and ovarian androgen production
- Women aged 41-55 may fall within or below the optimal pre-menopausal androgen range



Very High

Supraphysiologic T Levels Due To:

- Oral or sublingual DHEA or T therapy (1st pass increases urine metabolites only, not serum) (24)
- CAH/NCCAH (23)
- Androgen-secreting neoplasms (rare)

Testosterone in Women: Effects



Low
<2.3 ng/mg

Low T Signs & Symptoms:

- Impaired fertility in premenopausal women
- Increased pregnancy loss
- Reduced psychological well-being
- Mood issues, including low mood
- Fatigue
- Reduced bone mineral density and muscle mass
- Hypoactive sexual desire disorder (HSDD) or low libido



Post-Menopausal
2.3-6.3 ng/mg

Low(er) T:

- Some women – particularly younger, cycling women under age 40 - may be more likely to experience symptoms of low T
- Reduced psychological well-being
- Mood issues, including low mood
- Fatigue
- Reduced bone mineral density and muscle mass
- Hypoactive sexual desire disorder (HSDD) or low libido



Pre-Menopausal
4.0-14 ng/mg

Healthy T Levels Support:

- Normal sexual function
- Maintenance of muscle mass, if exercising
- Preservation bone mineral density
- Maintenance of insulin sensitivity
- Psychological well-being and mood stability

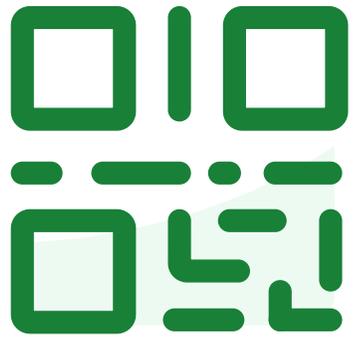


High
>14 ng/mg

High T Signs & Symptoms:*

- Hirsutism (body and facial hair growth)
- Androgenic alopecia (scalp hair loss)
- Acne
- Menstrual irregularities or no cycles (amenorrhea)
- Impaired fertility in premenopausal women
- In severe cases, virilization (e.g., voice deepening, clitoral enlargement)
- May contribute to elevated estradiol (E2) levels

*An appropriate dose of oral or sublingual T or DHEA therapy taken near the time of testing may increase urinary T metabolites due to first-pass metabolism, without reflecting serum T levels or causing symptoms of androgen excess.



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Game time!

Match the description to the dial:

1

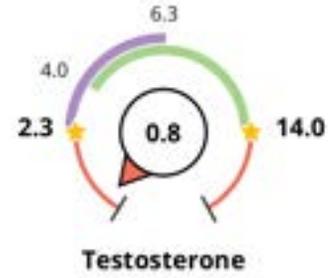
31-year-old female
PCOS

2

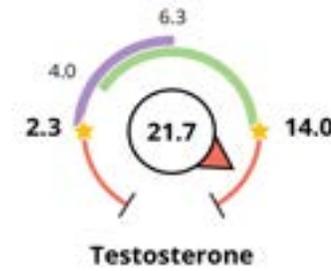
55-year-old female
PMP
Addison's Disease

3

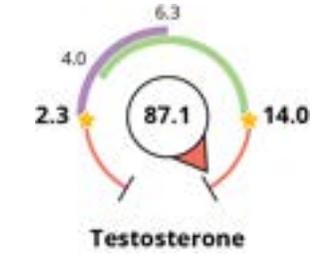
67-year-old female
PMP
Took 2 mg oral T
during testing



A



B



C



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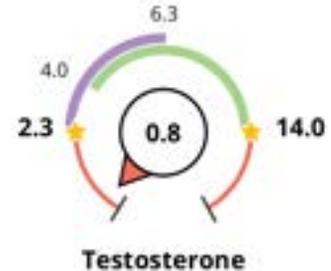
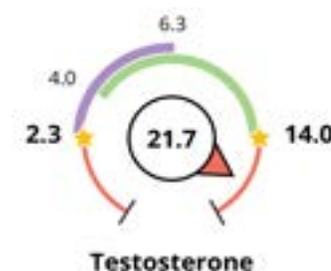
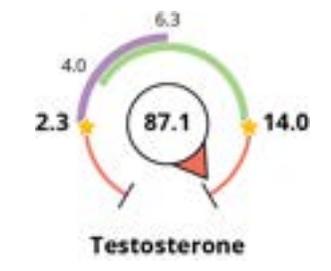


Question 3: Match the description to the correct Testosterone dial



Game time!

Match the description to the dial:

1	31-year-old female PCOS	→	 <p>A</p>
2	55-year-old female PMP Addison's Disease	→	 <p>B</p>
3	67-year-old female PMP Took 2 mg oral T during testing	→	 <p>C</p>



Game time!

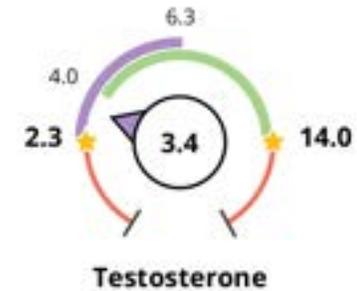
Match the description to the dial:

1

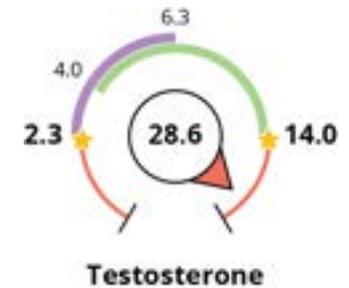
60-year-old female
PMP
Took 60 mg oral DHEA
during testing

2

44-year-old female
Bilateral oophorectomy
year prior
Normal DHEA



A



B



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Question 4: Match the description to the correct Testosterone dial



Game time!

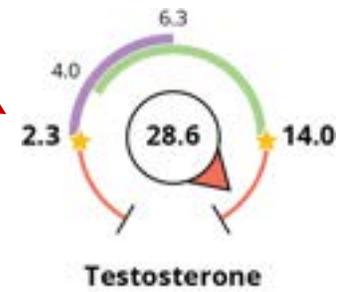
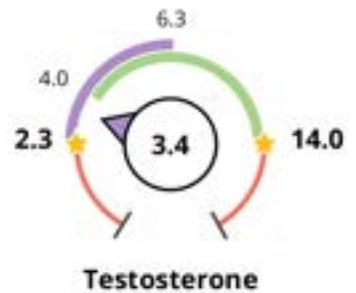
Match the description to the dial:

1

60-year-old female
PMP
Took 60 mg oral DHEA
during testing

2

44-year-old female
Bilateral oophorectomy
year prior
Normal DHEA



A

B

Does this T result reflect what's in circulation?

Would you lower her oral DHEA dose based on this result?

Androgen Treatments

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

The DUTCH Treatment Guide: **Low Androgens**

*And additionally, HPG axis and gonadal support in females and males, respectively (pages 10 and 18)

<p>HPA Axis Support* <i>Pages 24, 34, 36</i></p>	<p>Hypothyroidism Support <i>Page 52</i></p>	<p>Mitochondrial Support <i>Page 56</i></p>	<p>(Chronic) Insulin Resistance Support <i>Page 54</i></p>
<p>Slow CCR Support <i>Page 39</i></p>	<p>DHEA & Testosterone Therapy <i>Page 72</i></p>	<p>(Chronic) Stress Support <i>Page 63</i></p>	<p>(Chronic) Obesity (Weight Loss) Support <i>Page 58</i></p>
<p>Low CAR Support <i>Page 41</i></p>	<p>Androgen-Supportive Herbs <i>Page 36</i></p>	<p>(Chronic) Sleep/Circadian Support <i>Page 60</i></p>	<p>(Chronic) Inflammation Support <i>Page 53</i></p>
<p>5a-Reductase Activity Support <i>Page 25</i></p>	<p>DHEA, T & E Support if Low <i>Pages 24, 16, 10</i></p>	<p>Mood & Cognition Support <i>Page 57</i></p>	<p>Hyperprolactinemia Support, if Contributing to Low T <i>Page 52</i></p>

-  HPO Axis Support
-  HPA Axis Support
-  Other Hormone support
-  OATs Support
-  Symptom Support
-  Detox Support
-  Lifestyle Support
-  Other Support

The DUTCH Treatment Guide: High Androgens

*And additionally, calming HPG axis support in females and males, respectively (pages 10 and 18)

<p>HPA Axis Support* <i>Pages 14, 34, 36</i></p>	<p>Lower DHEA, T, & E if High <i>Pages 22, 20, 14</i></p>	<p>Insulin Resistance Support <i>Page 54</i></p>
<p>Fast CCR Support <i>Page 39</i> High CAR Support <i>Page 40</i></p>	<p>Support Aromatase if Low E <i>Page 21</i></p>	<p>Obesity (Weight Loss) Support <i>Page 58</i></p>
<p>Anti-Androgens to Improve Symptoms <i>Page 23</i></p>	<p>Stress Support <i>Page 63</i></p>	<p>Inflammation Support <i>Page 53</i></p>
<p>Decrease 5a-Reductase Activity <i>Page 25</i></p>	<p>Sleep/Circadian Rhythm Support <i>Page 60</i></p>	<p>Hyperprolactinemia Support** <i>Page 52</i></p>

**To reduce adrenal DHEA production

- HPO Axis Support
- HPA Axis Support
- Other Hormone support
- OATs Support
- Symptom Support
- Detox Support
- Lifestyle Support
- Other Support

The DUTCH Dozen

5 α -Androstane-3 β -diol



Androgens

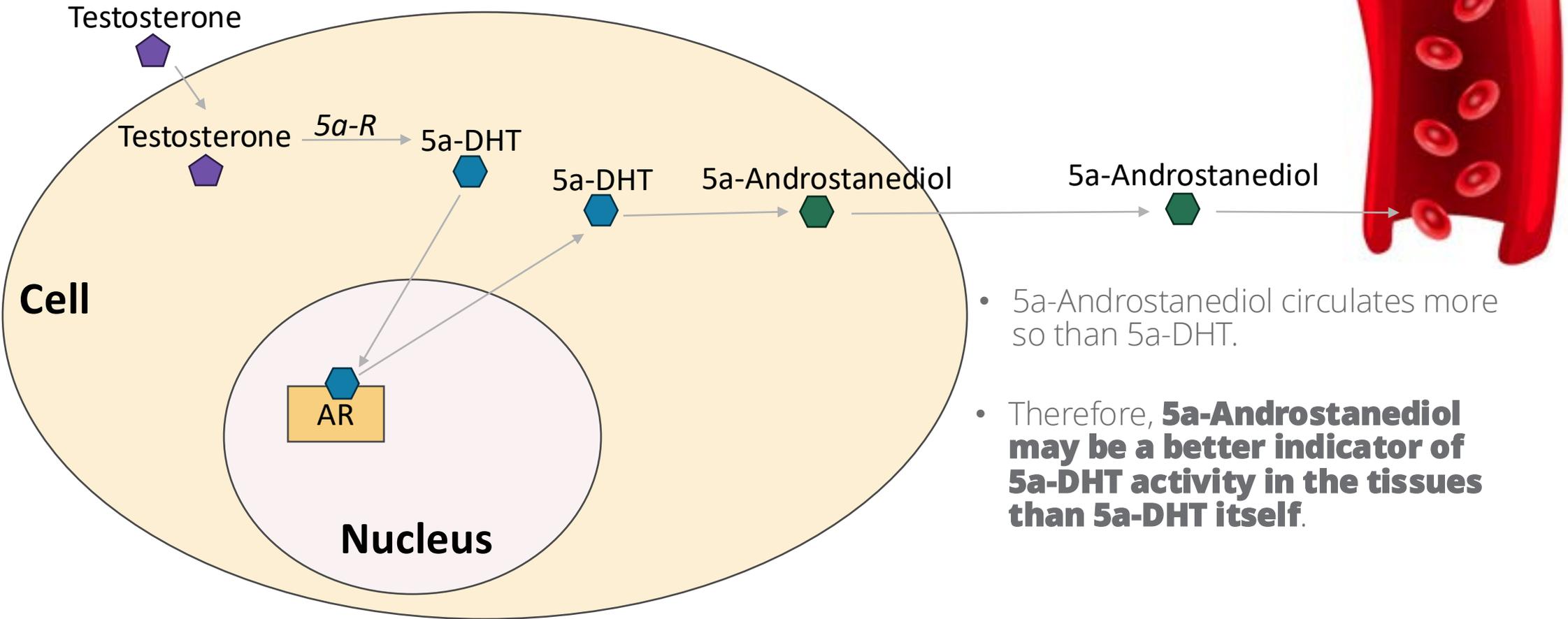
7 Assess cellular production of 5a-DHT via 5a-androstenediol

- The **seventh assessment** examines cellular 5a-DHT formation and activity by looking at **5a-androstenediol** levels.

- **5α-DHT** is our most **potent** androgen.
- 5α-DHT is **4x** more androgenic than testosterone!
- However, 5α-DHT is considered a “**peripheral hormone**”, meaning that it is **primarily made and metabolized in the tissues**.
- In other words, 5α-DHT is more concentrated in the **tissues (peripherally)** than in the **blood or urine (centrally)**.

The DUTCH Dozen: 7 5 α -Androstane-3 β -diol

- 5 α -DHT is used in the tissues and **converted to 5 α -Androstane-3 β -diol**.



- 5 α -Androstane-3 β -diol circulates more so than 5 α -DHT.
- Therefore, **5 α -Androstane-3 β -diol may be a better indicator of 5 α -DHT activity in the tissues than 5 α -DHT itself.**

Extracellular Matrix (ECM)

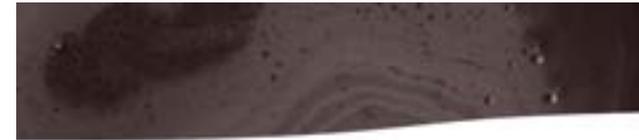
Precision Analytical published a white paper "**5 α -Androstenediol: A Marker of Androgen Status in Women**"

CONCLUDING REMARKS

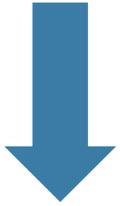
Summary of key research findings

Based on the research reviewed here on 5 α -androstenediol in women's health, the evidence suggests that:

1. 5 α -androstenediol levels reflect intracellular DHT activity and androgen metabolism in peripheral tissues.
2. 5 α -androstenediol levels are abnormally elevated in women with androgen excess symptoms, including male-pattern hair growth, scalp hair loss, acne, menstrual irregularities, and PCOS.
3. 5 α -androstenediol levels can be elevated even when testosterone levels are within normal range, as in the case of idiopathic hirsutism in women.
4. Elevations in 5 α -androstenediol levels resolve along with symptom improvement following treatment of androgen excess symptoms in women.



<https://dutchtest.com/research/5-a-androstenediol-a-marker-of-androgen-status-in-women>



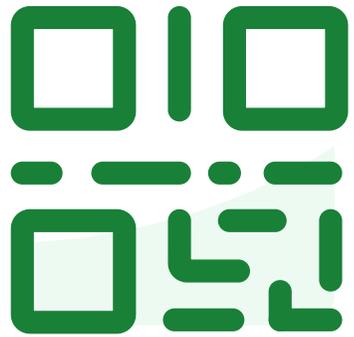
What contributes to **low(er)** 5a-Androstenediol?

- **Low parent upstream androgens**
 - E.g., testosterone, DHEA - see low T and DHEA contributors
- **Low 5a-reductase (5a-R) activity**
 - Natural and Pharmaceutical 5a-reductase inhibitors (saw palmetto, finasteride), etc.
 - *More on this in the next section!*
- **Other: Progesterone**
 - Progesterone directly competes with testosterone for 5a-R's active site, blocking the conversion of these substrates into more potent androgens like DHT.
 - If supplementing with progesterone, **ROA matters!** For example, with OMP most 5a-R metabolism occurs in the gut/liver, and less in the target tissue.



What contributes to **high(er)** 5a-Androstanediol?

- **High parent upstream androgens**
 - E.g., testosterone, DHEA - see high T and DHEA contributors
- **High 5a-reductase activity**
 - Insulin resistance, obesity, PCOS, etc.
 - *More on this in the next section!*



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Game time!

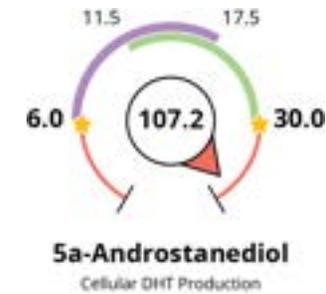
Match the description to the dial:

1

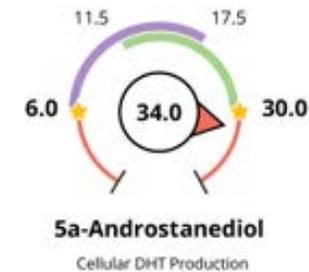
21-year-old female
Normal T
Strong 5a Preference

2

28-year-old female
High T PCOS
Strong 5a Preference



A



B



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#DUTCHFEST2



Question 5: Match the description to the correct 5 α -Androstane-3 β -diol



Game time!

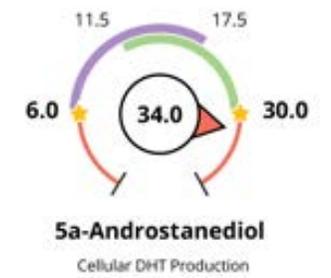
Match the description to the dial:

1
 21-year-old female
 Normal T
 Strong 5a Preference

2
 28-year-old female
 High T PCOS
 Strong 5a Preference



A



B



Game time!

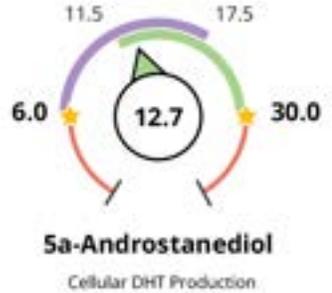
Match the description to the dial:

1

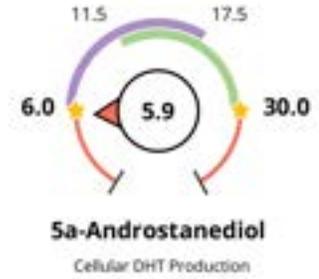
52-year-old female
PMP
Using a Well-Dosed
Transdermal Testosterone

2

52-year-old female
Low T
Low 5a Preference



A



B



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Question 6: Match the description to the correct 5 α -Androstane diol dial



Game time!

Match the description to the dial:

1 52-year-old female
PMP
Using a Well-Dosed
Transdermal Testosterone

2 52-year-old female
Low T
Low 5a Preference

A

B

The DUTCH Dozen

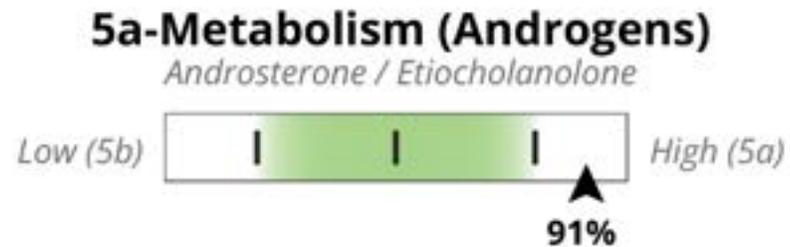
5a-Metabolism



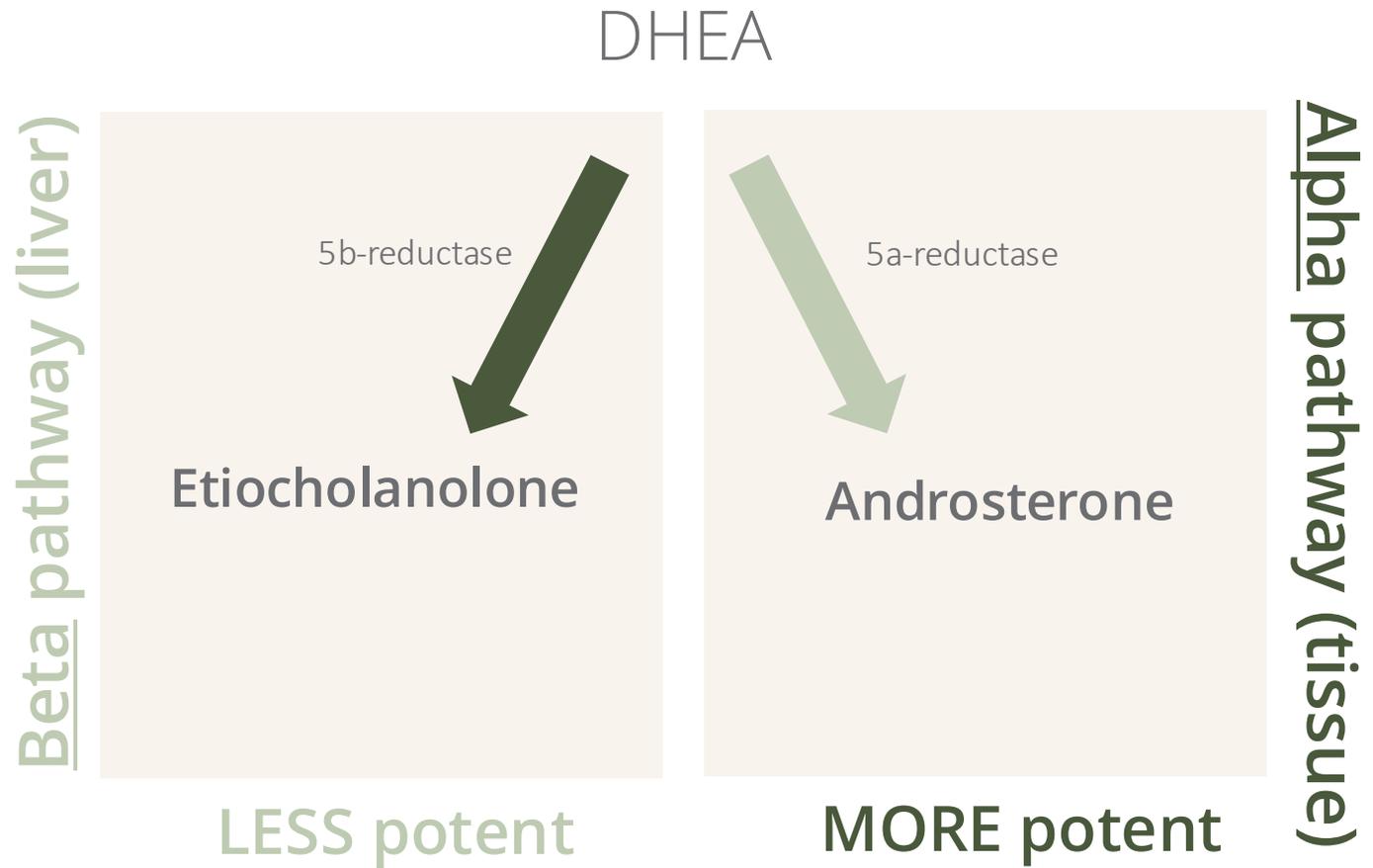
Androgens

8 Assess if there is a preference for the more potent alpha metabolism of the androgens

- The **eighth assessment** evaluates the preference for **5a-reductase metabolism**, which produces more potent androgens.
- The 5a-Metabolism slider result is a population percentile based off the ratio of two DHEA metabolites, Androsterone (**alpha**) to Etiocholanolone (**beta**).

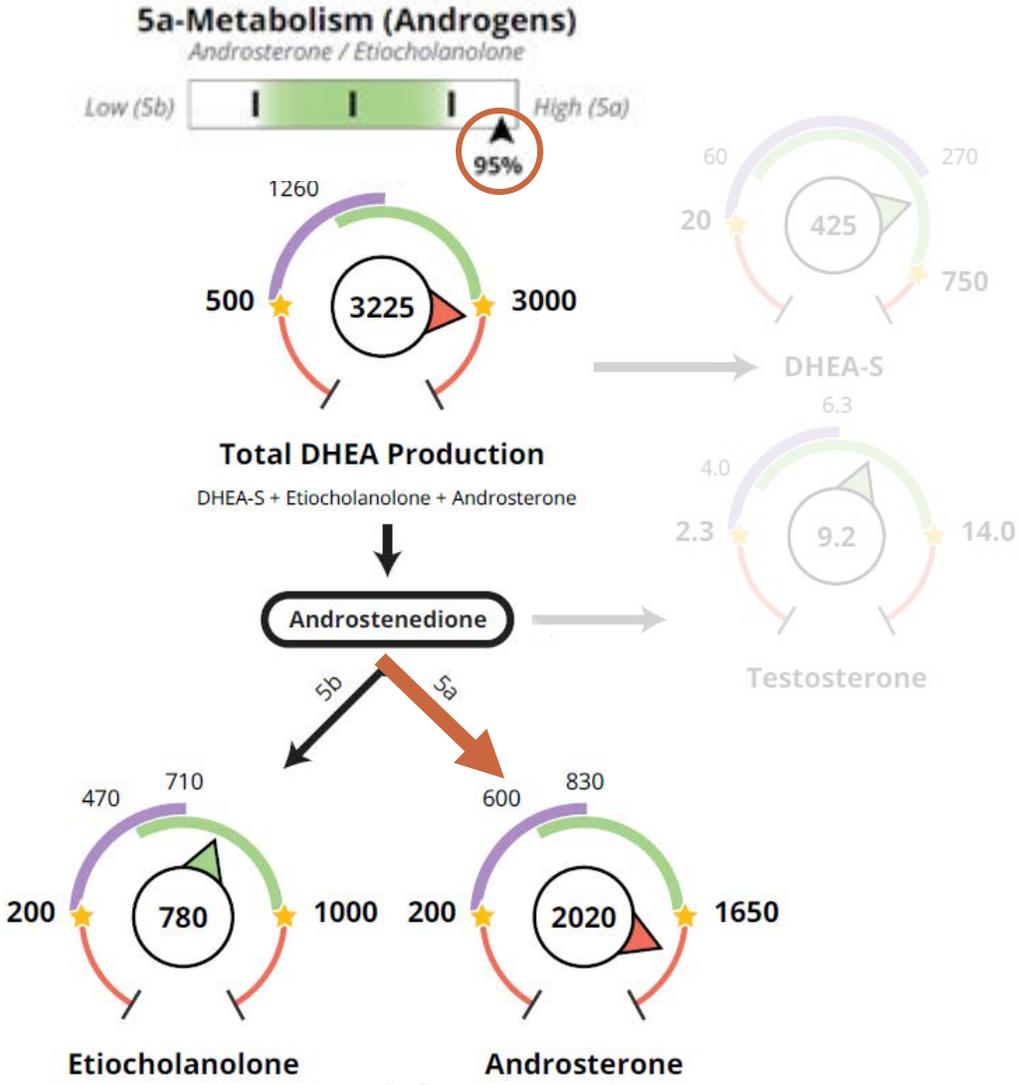


- For example, this patient has a higher 5a preference than 91% of the population.

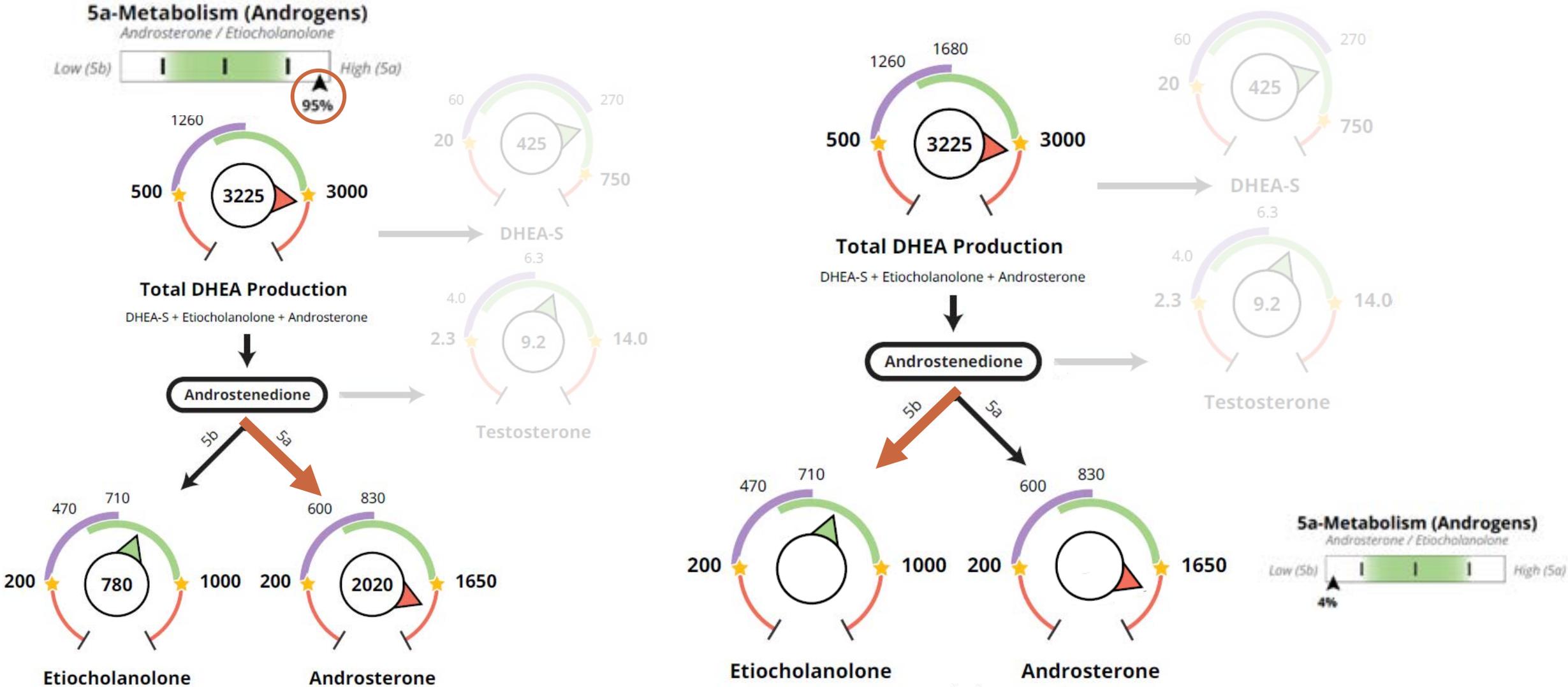


“alpha male”

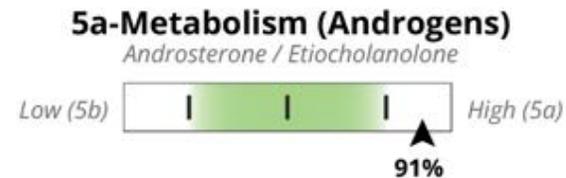
Patient Results



Patient Results



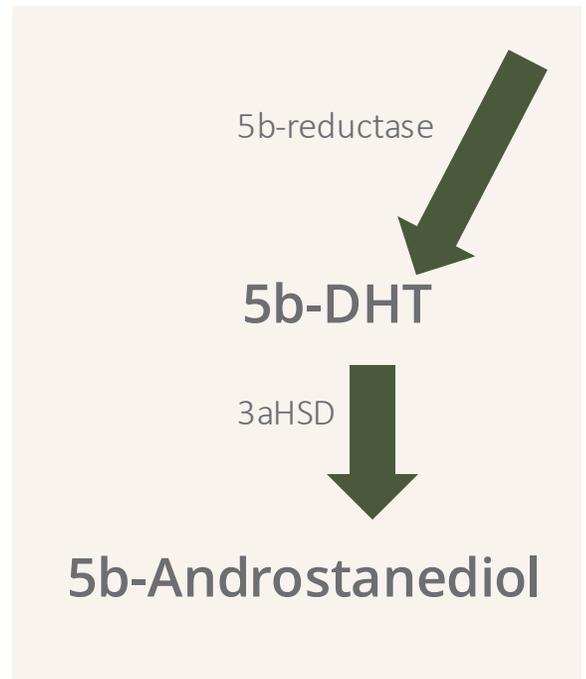
- Again, the **5a-Metabolism (Androgens)** slider compares androsterone (5a) to etiocholanolone (5b).
- A **shift toward 5a metabolites indicates higher androgenic activity**, which may contribute to symptoms like oily skin, acne, or hair loss.



- However, an alpha preference may not require intervention if androgen excess symptoms are absent.

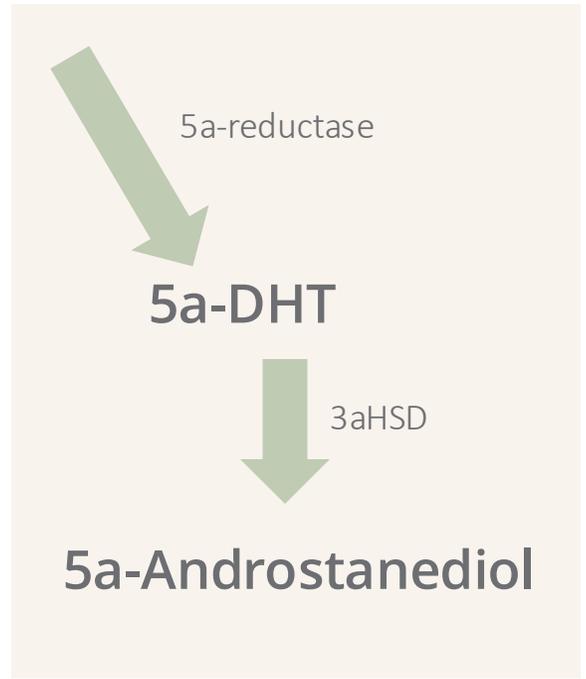
Testosterone

Beta pathway (liver)



LESS potent

Alpha pathway (tissue)

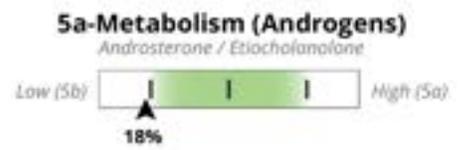
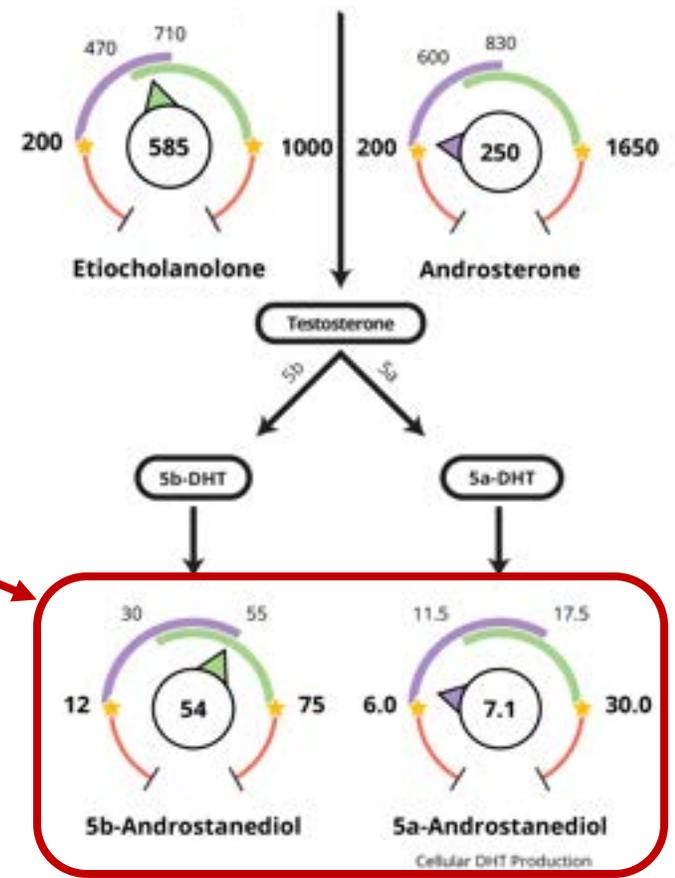


MORE potent



“alpha male”

- The Androgen 5a-Metabolism slider is based off the ratio of Androsterone: Etiocholanolone because these metabolites are best-represented in the research and most reliable.
- However, you can confirm an alpha or beta preference by comparing 5b-Androstanediol and 5a-Androstanediol.
- You can also compare the (alpha and beta) progesterone and cortisol metabolites to check for an overall body/tissue preference for alpha vs beta. **More on this tomorrow!**





What contributes to **Low(er)** 5a-Reductase activity?

- **Natural 5a-reductase inhibitors**
 - Saw palmetto, stinging nettle root, reishi, EGCG, Beta-sitosterol, polyunsaturated fats, Pygeum (***threatened/vulnerable species***) and zinc
- **Pharmaceutical 5a-reductase inhibitors**
 - Finasteride, Dutasteride, etc.
- Hypothyroidism
- Genetic SNPs in SRD5A2* that ***downregulate*** 5a-R activity
- **High 5b-reductase activity**
 - Fatty liver disease

Effects of Lower 5a-R Activity:

- Androgens are ***deactivated***

* SRD5A2 gene encodes the steroid 5a-reductase type 2 enzyme that converts testosterone to DHT.

Westerbacka J, et al. J Clin Endocrinol Metab. 2003;88(10):4924-4931.



What contributes to **high(er)** 5a-Reductase activity?

- **Metabolic issues:**
 - Insulin resistance
 - Obesity
 - PCOS
- Bodybuilding
- Pine Pollen
- Genetic SNPs in SRD5A2* that **upregulate** 5a-R activity
- Low 5b-reductase activity

Effects of Higher 5a-R Activity

- Androgens are **activated!**

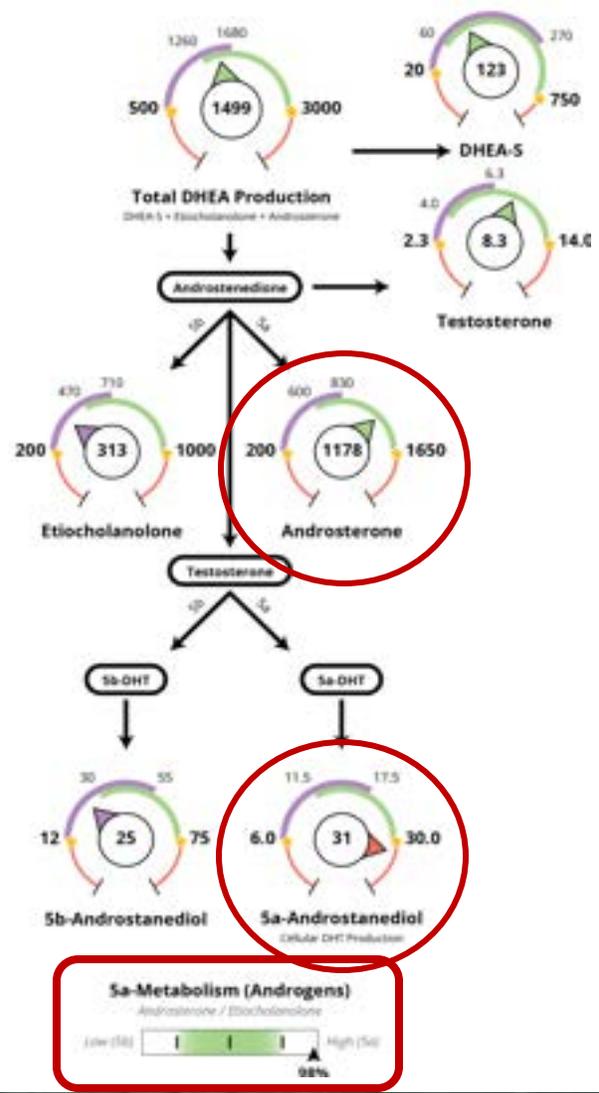
* SRD5A2 gene encodes the steroid 5a-reductase type 2 enzyme that converts testosterone to DHT.

Tomlinson JW, et al. Diabetes. 2008;57(10):2652-2660.
Tsilchorozidou T, et al. J Clin Endocrinol Metab. 2003;88(12):5907-5913.

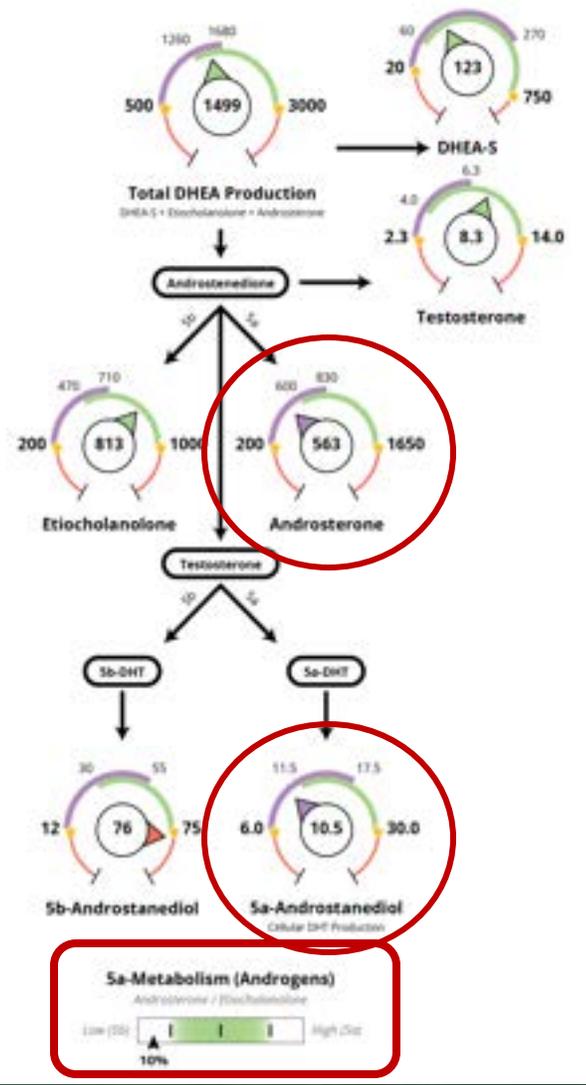
If parent androgens are normal:

- 5a-Preference increases alpha metabolite levels and may contribute to androgen excess symptoms.
- 5b-Preference lowers alpha metabolite levels and may reduce the likelihood of androgen excess symptoms (**may contribute to androgen deficiency symptoms**).

Androgens

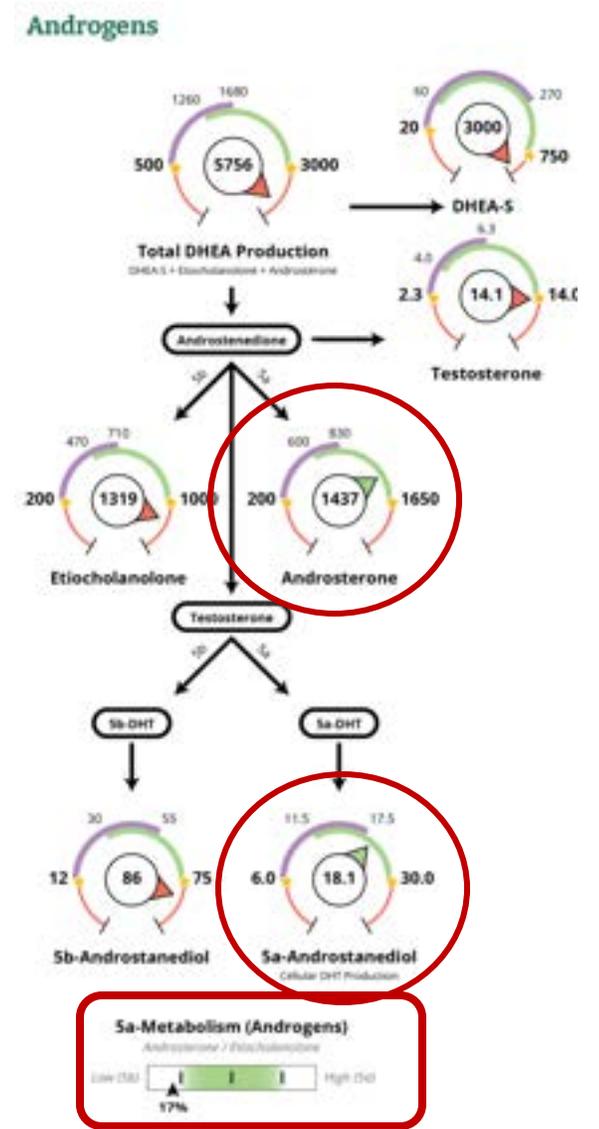
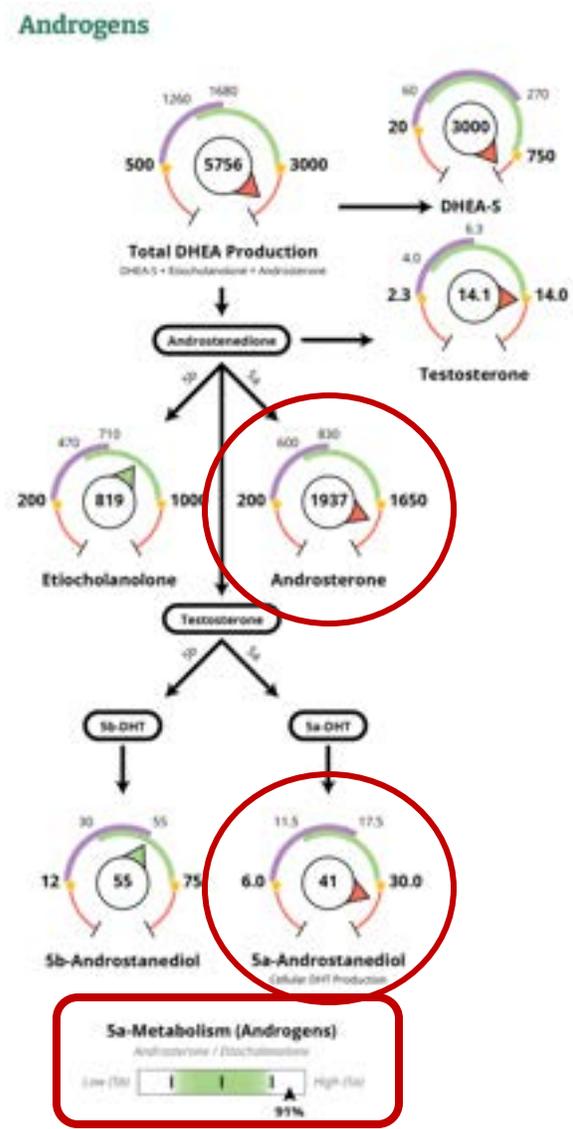


Androgens



If parent androgens are elevated:

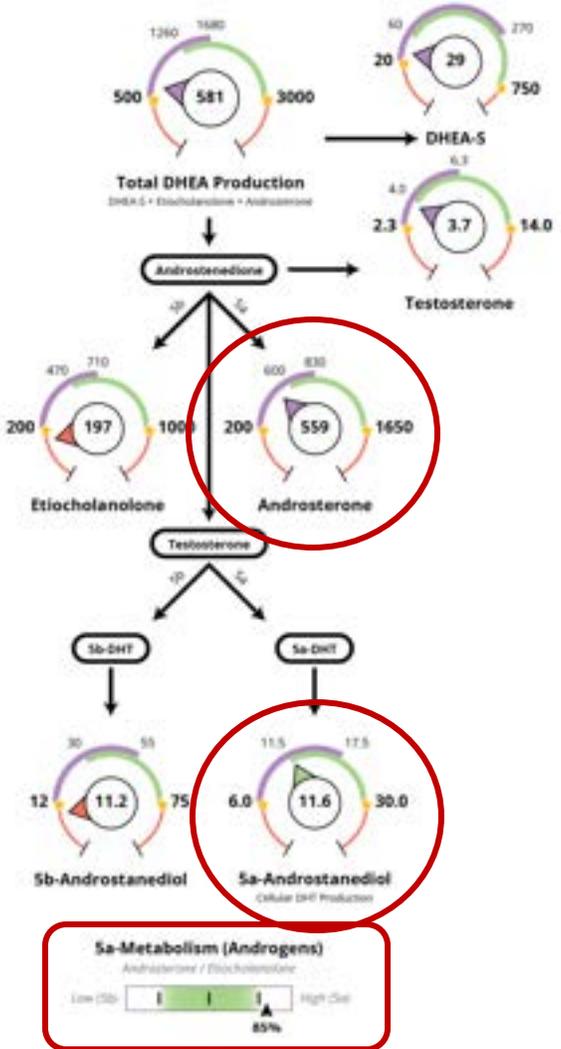
- 5a-Preference increases alpha metabolite levels and may worsen androgen excess symptoms.
- 5b-Preference lowers alpha metabolite levels and may reduce the likelihood/severity of androgen excess symptoms.



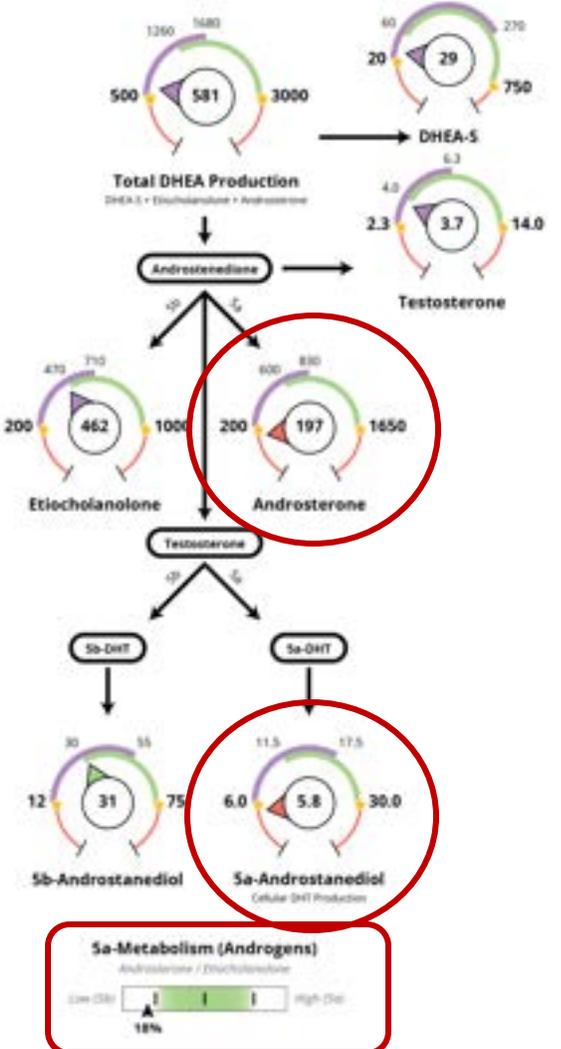
If parent androgens are low:

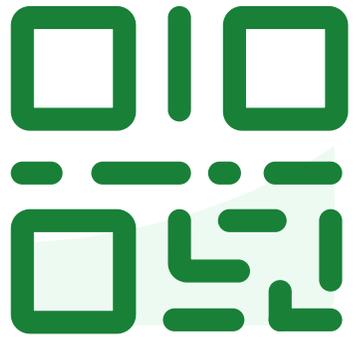
- 5a-Preference increases alpha metabolite levels and may help mitigate low androgen symptoms.
- 5b-Preference lowers alpha metabolite levels and can worsen low androgen symptoms.

Androgens



Androgens



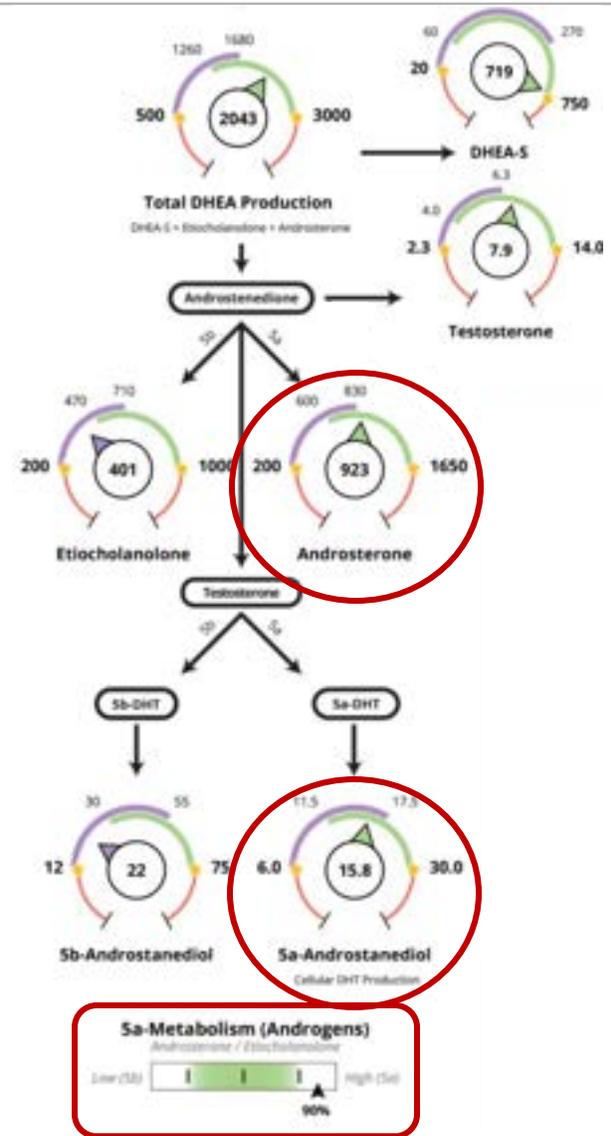


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Game time!

- What if a patient strongly favors the alpha pathway but their androgens are within range.
- **Could the androgens be contributing to the patient's acne and hair loss?**



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Question 7: What if a patient strongly favors the alpha pathway but their androgens are within range. Could the androgens be contributing to the patient's acne and hair loss?



Game time!

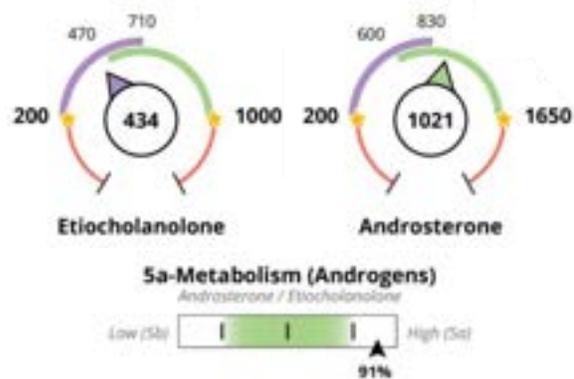
Match the description to the pattern:

1

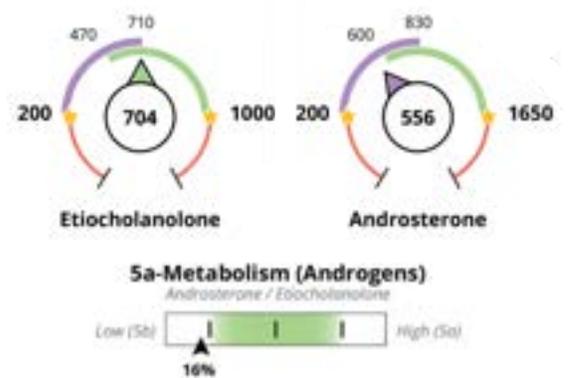
50-year-old female
PMP
Oily skin, hair loss

2

36-year-old female
Saw Palmetto
Spironolactone



A



B



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Question 8: Match the description to the correct Androgen 5 α -Metabolisms slider



Game time!

Match the description to the pattern:

1 50-year-old female
PMP
Oily skin, hair loss

2 **36-year-old female**
Saw Palmetto
Spironolactone

A

B

5a-Metabolism (Androgens)
Androsterone / Etiocholanolone

Low (5%) | High (5%)

91%

5a-Metabolism (Androgens)
Androsterone / Etiocholanolone

Low (5%) | High (5%)

16%



Game time!

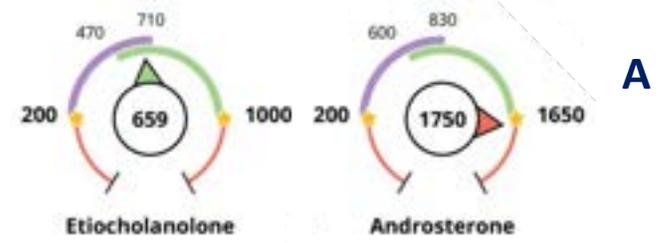
Match the description to the pattern:

1

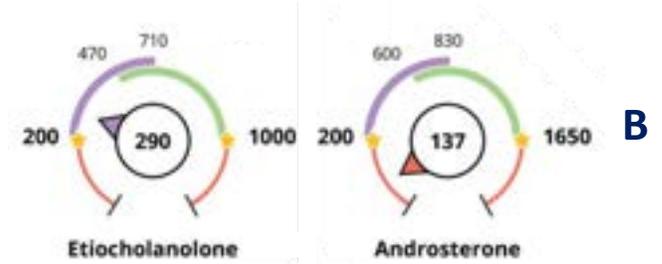
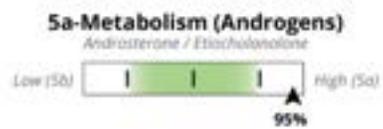
48-year-old female
Oral Minoxidil 1.25 mg
Finasteride 1 mg
Mild scalp hair loss

2

63-year-old female
Obesity (BMI 39.5)
Fasting glucose 118



A



B



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#DUTCHFEST2



Question 9: Match the description to the correct Androgen 5 α -Metabolisms slider

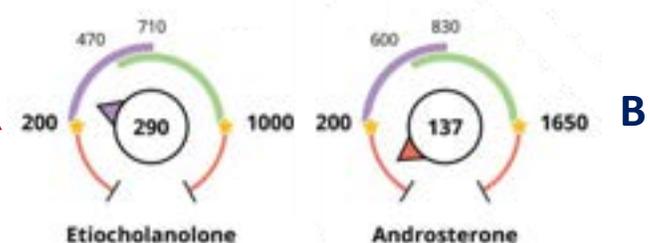
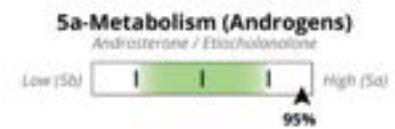
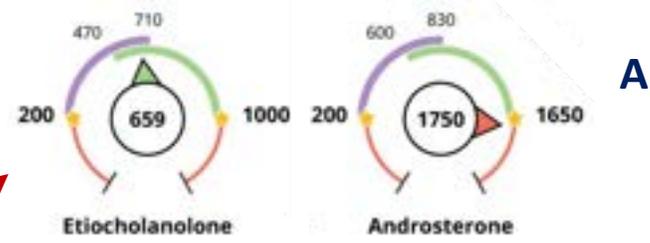


Game time!

Match the description to the pattern:

1
 48-year-old female
 Oral Minoxidil 1.25 mg
 Finasteride 1 mg
 Mild scalp hair loss

2
63-year-old female
 Obesity (BMI 39.5)
 Fasting glucose 118



The DUTCH Treatment Guide: 5a-Metabolism

Lower an ALPHA Preference:

5a-Reductase Inhibitors <i>Page 25</i>	Insulin Resistance Support <i>Page 54</i>
Support Progesterone if Low <i>Page 8</i>	Obesity (<i>Weight Loss</i>) Support <i>Page 58</i>
Stress Support <i>Page 63</i>	Inflammation Support <i>Page 53</i>

"Encourage" an ALPHA Preference:

Treat Hypothyroidism <i>Page 52</i>
Avoid 5a-Reductase Inhibitors <i>Page 25</i>
Strength Training Pine Pollen

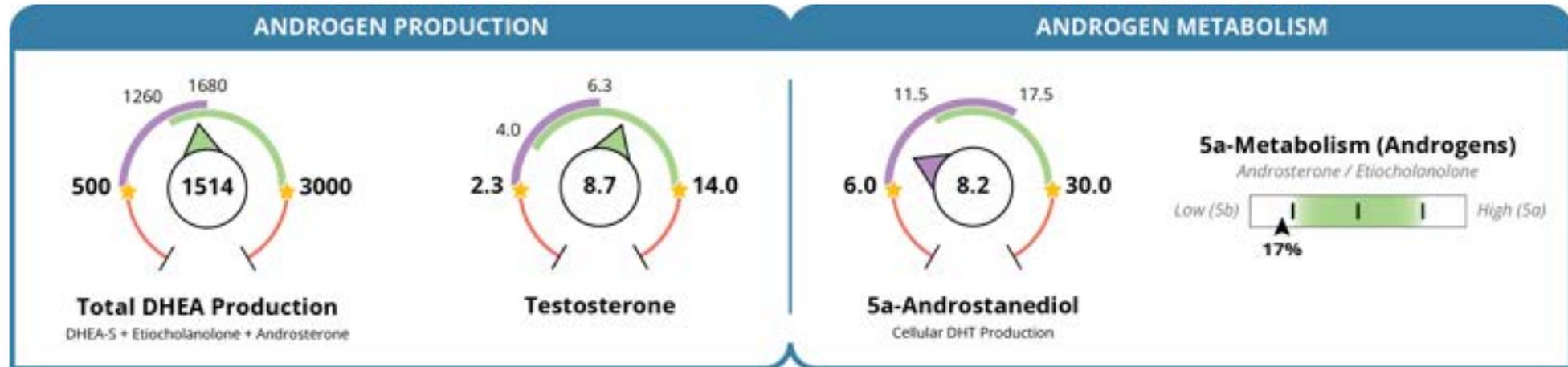
- HPO Axis Support ● HPA Axis Support ● Other Hormone support ● OATs Support ● Symptom Support ● Detox Support ● Lifestyle Support ● Other Support



Putting it *All* Together!

The DUTCH Dozen: 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.



- Her testosterone is within range for her age. Besides stress, what might be contributing to her low libido?
- She adds a reishi mushroom powder (5a-R blocker) to her coffee every morning. How might this be affecting her DUTCH test results and symptoms?

The DUTCH Dozen: Putting it all together!

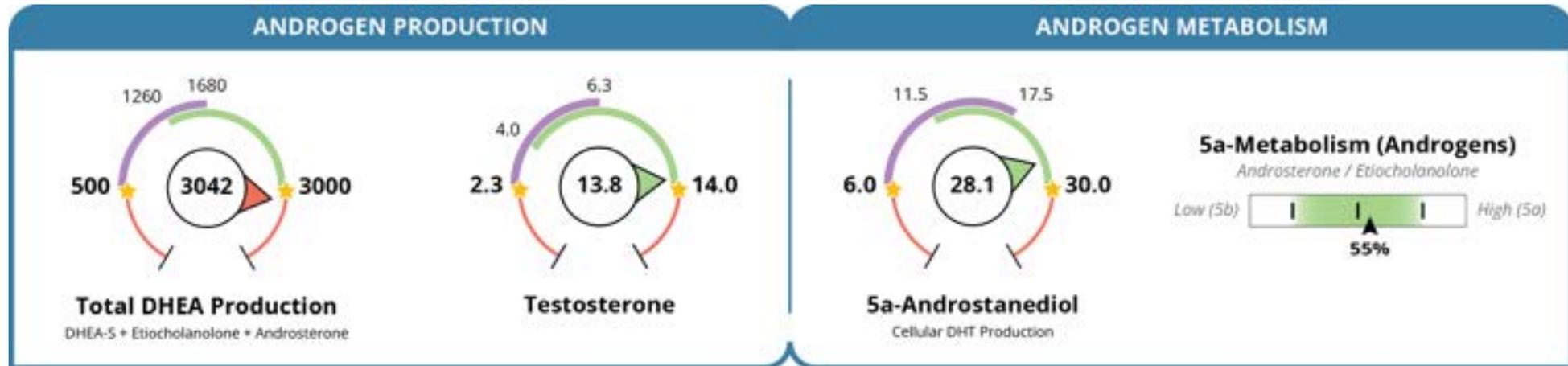
- 29-year-old female diagnosed with PCOS. Complains of irregular cycles, high stress, facial hair, and breast tenderness. BMI 29.3.



- What serum labs might you order after seeing her high 5a-metabolism (94%)?
- She collected during ovulation. Does this change your assessment or treatment plan?

The DUTCH Dozen: Putting it all together!

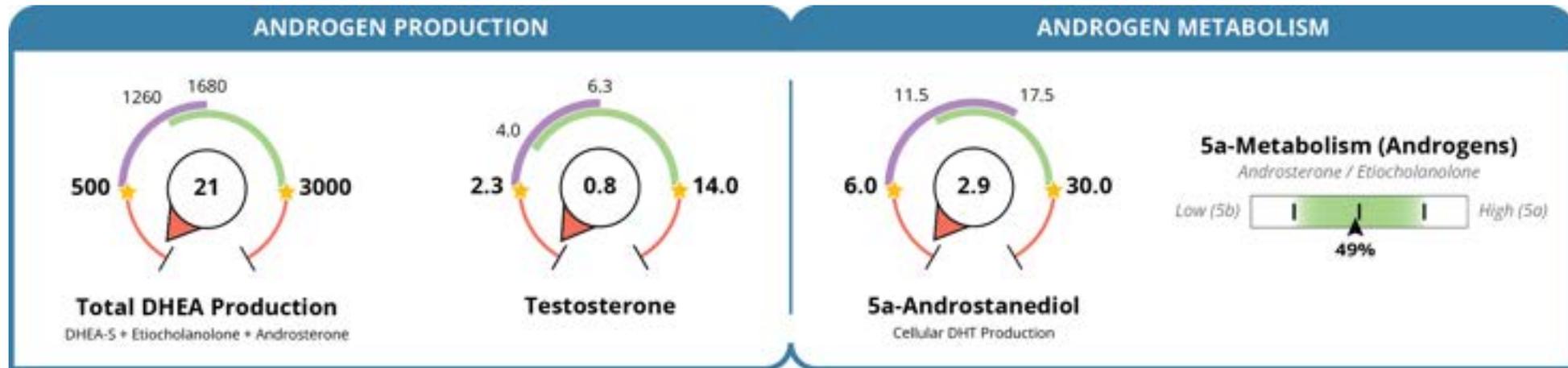
- 39-year-old female with suspected endometriosis. Complains of dysmenorrhea, heavy bleeding, and frequent night wakings. BMI 26.6.



- How might high DHEA be contributing to her high estrogen levels and symptoms?
- What if she collected on an extremely stressful day, which is unusual for her. Would that change your assessment and treatment plan?

The DUTCH Dozen: Putting it all together!

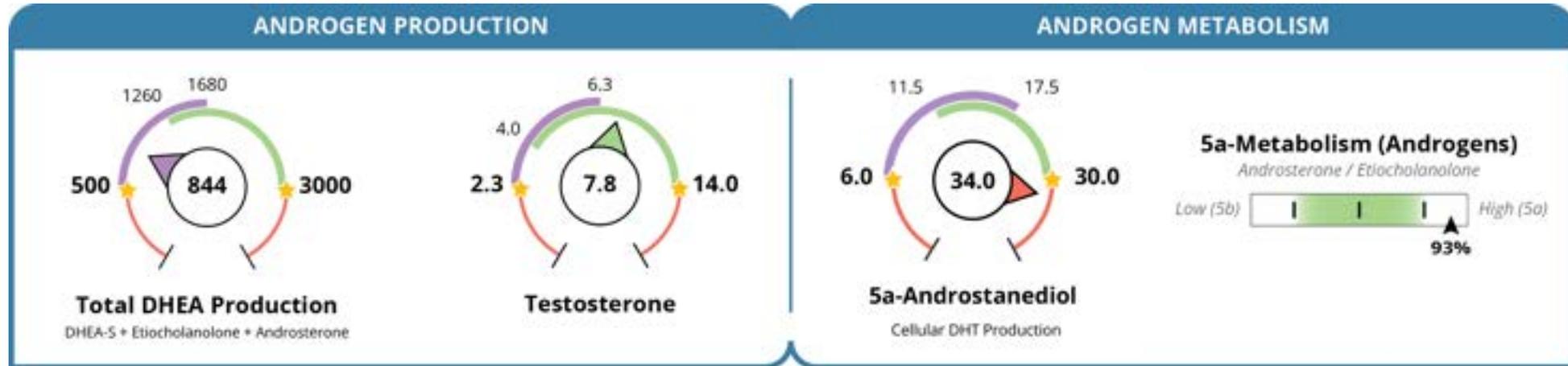
- 55-year-old PMP female on 15 mg prednisone for the past month. She has not been able to taper below 15 mg without her ulcerative colitis flaring up. Complains of hair loss, hot flashes, irritability, and sleep issues. BMI 28.1.



- Why is her testosterone and 5a-Androstanediol lower than expected for a woman her age?
- Would you prescribe this patient DHEA and/or T therapy?

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- **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.



- Why might she be getting acne with a normal dose of transdermal T cream (5 mg)?
- What if the patient lost weight and decreased her BMI to 25. How might this change her DUTCH Test results?

References

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Thank You!

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