

Adrenal PCOS

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Instagram
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Remember

1. The information in this presentation is provided for informational and educational purposes only and is not medical or treatment advice.
2. Any information and statements regarding dietary or herbal supplements have not been evaluated by the Food and Drug Administration and are not intended to diagnose, treat, cure, or prevent any disease.
3. The use of any information provided in this presentation is solely at your own risk.

Objectives

- Review PCOS.
- Learn about androgens in more detail.
- Talk about adrenal involvement in PCOS.
- Go over a few DUTCH Test examples where adrenal involvement is possible.
- Go into potential treatment considerations.

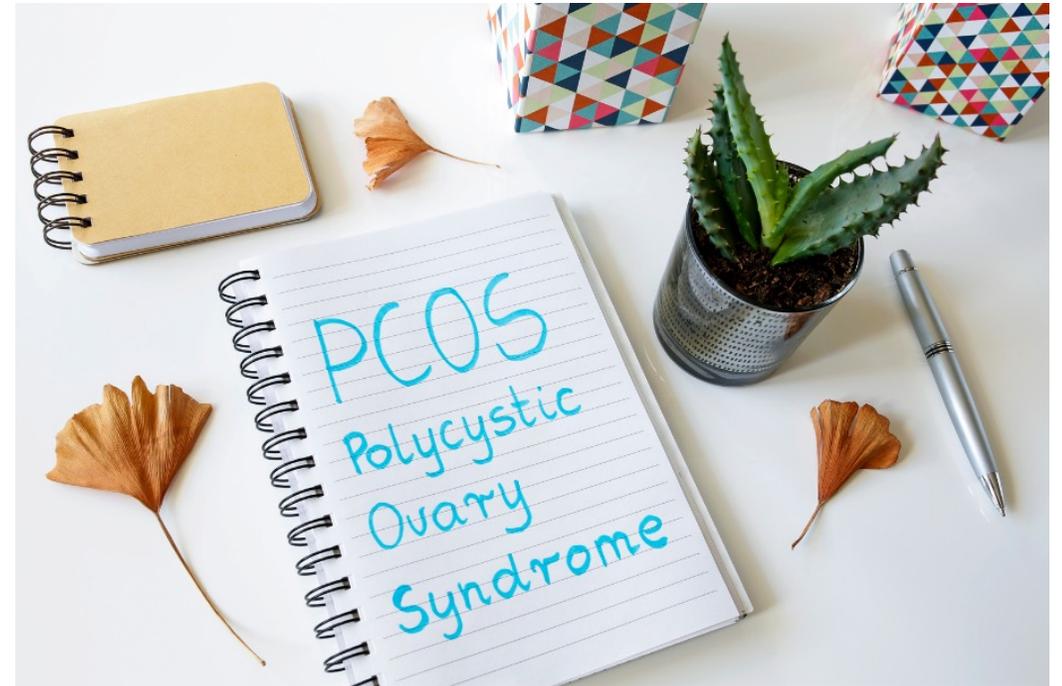


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What is PCOS?

About PCOS

- PCOS stands for “Polycystic Ovary Syndrome.”
- It is one of the most common endocrine disorders in women of reproductive age.
- Women with PCOS can experience irregular or absent cycles, facial and body hair growth, scalp hair loss, acne, anxiety and depression, difficulty conceiving, weight gain, and more.



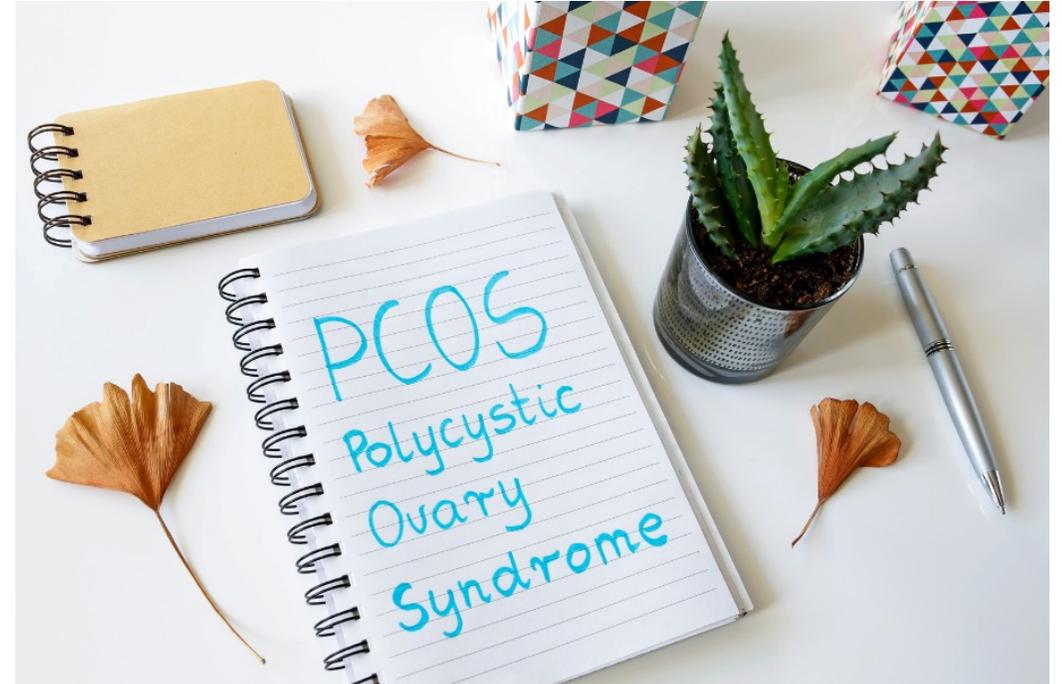
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Barbieri R, et. al. Clinical manifestations of polycystic ovary syndrome in adults. In: UpToDate, Crowley WF (Ed), UpToDate, Waltham, MA. (Accessed on June 28th 2023.)

Che Y, et al. Polycystic Ovary Syndrome: Challenges and Possible Solutions. J Clin Med. 2023 Feb 14;12(4):1500.

PCOS risks

- PCOS increases the risk for infertility, pregnancy complications, obesity, insulin resistance, diabetes, dyslipidemia, NAFLD, metabolic syndrome, cardiovascular disease, sleep apnea, psychological diseases, endometrial hyperplasia & cancer, and more.



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Diagnosis: the Rotterdam Criteria (2003)

According to the Rotterdam Criteria, two out of three of the following criteria are required to make the diagnosis:

- Oligo- and/or anovulation
- Clinical and/or biochemical signs of hyperandrogenism
- Polycystic ovaries ≥ 12 follicles measuring 2-9 mm in diameter and/or an ovarian volume >10 mL in at least one ovary.



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Barbieri R, et. al. Diagnosis of polycystic ovary syndrome in adults. In: UpToDate, Crowley WF (Ed), UpToDate, Waltham, MA. (Accessed on June 28th 2023.)

Yesiladali M, et al. Differentiating Polycystic Ovary Syndrome from Adrenal Disorders. Diagnostics (Basel). 2022;12(9).

Diagnosis: 4 Phenotypes

Adult Diagnostic Criteria (Rotterdam)

Otherwise unexplained alternative phenotypes:

1. Phenotype 1 (classic PCOS)^a
 - a. Clinical and/or biochemical evidence of hyperandrogenism
 - b. Evidence of oligo-anovulation
 - c. Ultrasonographic evidence of a polycystic ovary
2. Phenotype 2 (Essential NIH Criteria)^a
 - a. Clinical and/or biochemical evidence of hyperandrogenism
 - b. Evidence of oligo-anovulation
3. Phenotype 3 (ovulatory PCOS)^a
 - a. Clinical and/or biochemical evidence of hyperandrogenism
 - b. Ultrasonographic evidence of a polycystic ovary
4. Phenotype 4 (nonhyperandrogenic PCOS)
 - a. Evidence of oligo-anovulation
 - b. Ultrasonographic evidence of a polycystic ovary

Ovulatory PCOS comprises 10% of cases.



*Listed in order of decreasing clinical severity

Rosenfield RL, et. al. The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. Endocr Rev. 2016 Oct;37(5):467-520.

Types of PCOS

- Functional **ovarian** hyperandrogenism (FOH)
 - Demonstrable in most cases (87%).
 - Ovary is the source of the disorder.
 - Intrinsic enzyme dysregulation (17,20-lyase and 17-hydroxylase which are two activities of the same enzyme cytochrome P450c17 [CYP17]).
 - Insulin resistance and elevated LH worsen androgen excess.

- Functional **adrenal** hyperandrogenism (FAH)
 - Not as common as FOH.
 - Isolated FAH (no ovary involvement) in 5% of cases.
 - "In general, extra-adrenal factors, including obesity, insulin and glucose levels, and ovarian secretions, play a limited role in the increased APA production observed in PCOS" (Goodarzi).

1. Goodarzi MO, Carmina E, Azziz R. DHEA, DHEAS and PCOS. J Steroid Biochem Mol Biol. 2015 Jan;145:213-25.

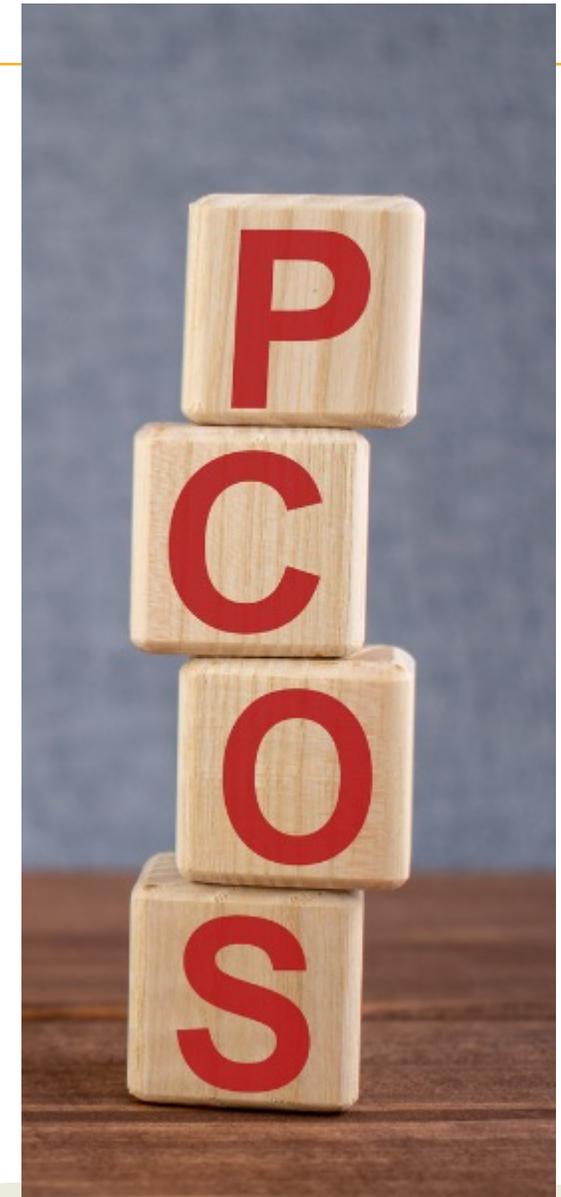
2. Rosenfield RL, et. al. Current concepts of polycystic ovary syndrome pathogenesis. Curr Opin Pediatr. 2020 Oct;32(5):698-706.

3. Rosenfield RL, et. al. The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. Endocr Rev. 2016 Oct;37(5):467-520.

PCOS is a diagnosis of exclusion

PCOS is a diagnosis of exclusion. Providers must rule out other common diseases that could present with similar symptoms:

- Hypothyroidism
- Hyperprolactinemia
- Non-classical congenital adrenal hyperplasia (NCAH)
- Cushing's syndrome
- Hypogonadotropic hypogonadism
- Androgen-secreting tumors



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***These specifically may result in increased adrenal androgen production. If prolactin gets very high, we may see the opposite: lower androgens.



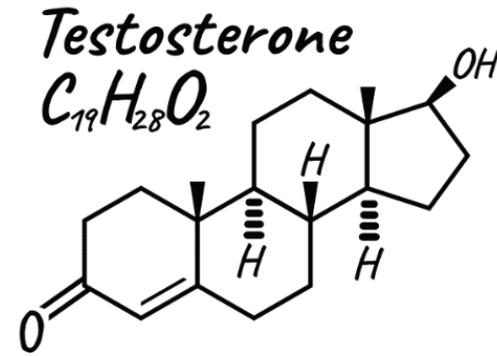
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Androgens

Androgens

From Oxford Languages:

- An “androgen” is a male sex hormone, such as testosterone.



Androgen's role in cycling females

Androgens support:

- Bone
- Skin and hair
- Mood
- Memory
- Fertility
- Sexual function
- Estrogen levels
- Cardiovascular health
- Immune function
- Muscle, strength, stamina, recovery



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Androgen excess

Too many androgens can result in:

- Acne
- Scalp hair loss
- Facial hair growth (hirsutism)
- Body hair growth
- Mood issues, irritability, anger
- Irregular cycles
- Fertility issues
- Weight gain



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Androgen deficiency

Too little androgens can result in:

- Inability to build muscle mass
- Poor strength and stamina
- Poor exercise recovery
- Weight gain
- Osteopenia/osteoporosis
- Memory issues, brain fog
- Mood issues, low mood
- Fatigue
- Low libido
- Infertility
- Cardiovascular disease
- Immune dysregulation



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Androgens on the DUTCH Test

Androgens on the DUTCH Test (urine)



DUTCH Complete

- Signature product
- 4 urine collections over the course of 12-16 hours
- Easy to collect from home!
- Measures androgens, estrogens, progesterone metabolites, cortisol and organic acids.
- Comprehensive!

Androgens measured on the DUTCH Test (urine)

Testosterone metabolites:

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

DHEA metabolites:

- DHEA-S
- Etiocholanolone
- Androsterone

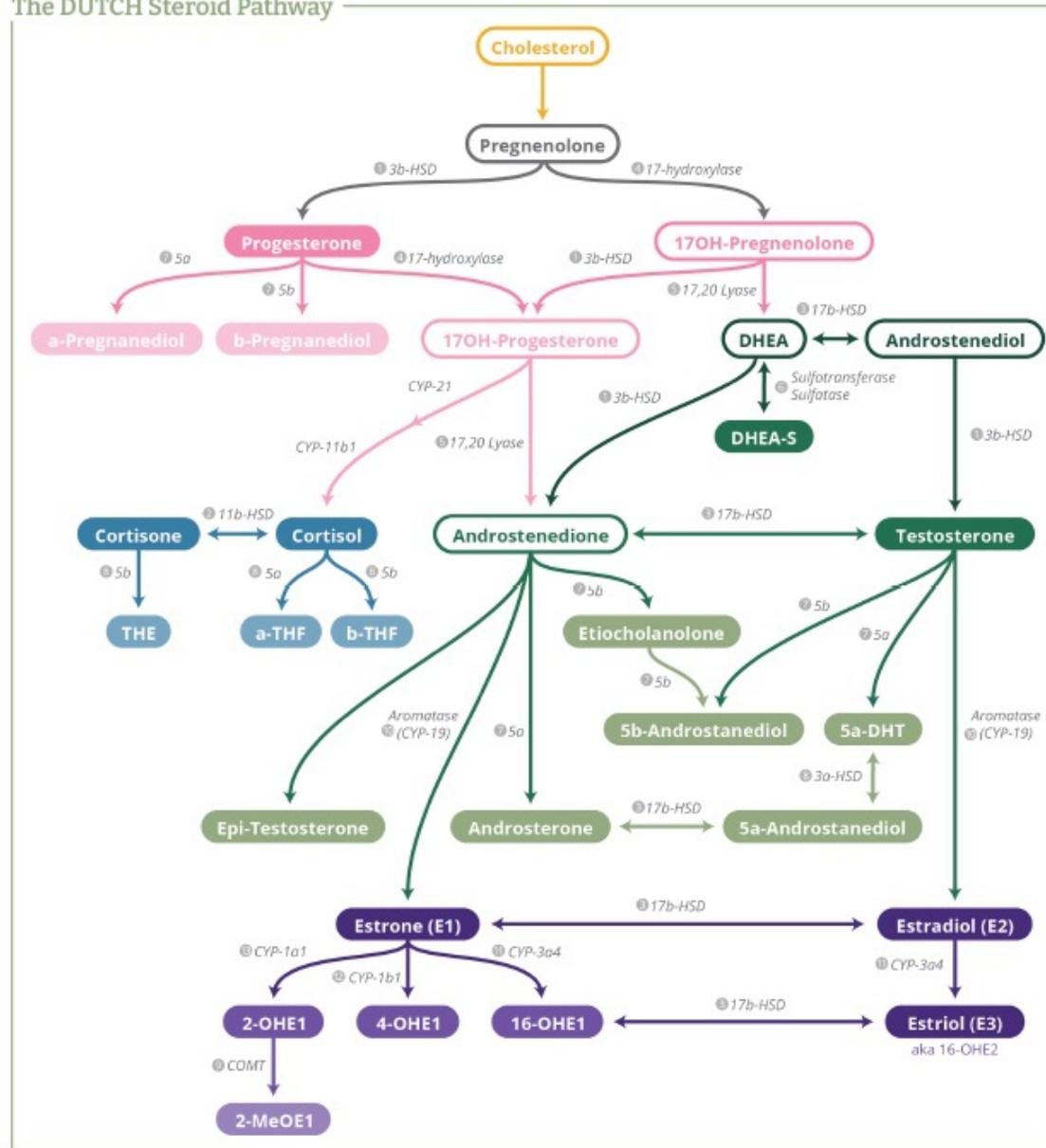


*Note that DHEA can influence testosterone metabolite levels and testosterone can influence etiocholanolone and androsterone levels to some degree.

Androgens



The DUTCH Steroid Pathway



All the markers in **GREEN** are androgens and all the **SOLID** boxes are androgens that are measured on DUTCH Test.

Hormones are color-coded for convenient reading:

- Cholesterol
- Pregnenolone
- Cortisol
- Progesterone
- Androgens
- Estrogen

This is on page 38 of our new DUTCH Interpretive Guide which you can download from your DUTCH provider portal.

Alpha vs Beta

Alpha vs beta metabolites

Alpha metabolites = POTENT

- 5a-DHT
- 5a-androstenediol
- Androsterone



Beta metabolites = weak

- 5b-androstenediol
- Etiocholanolone



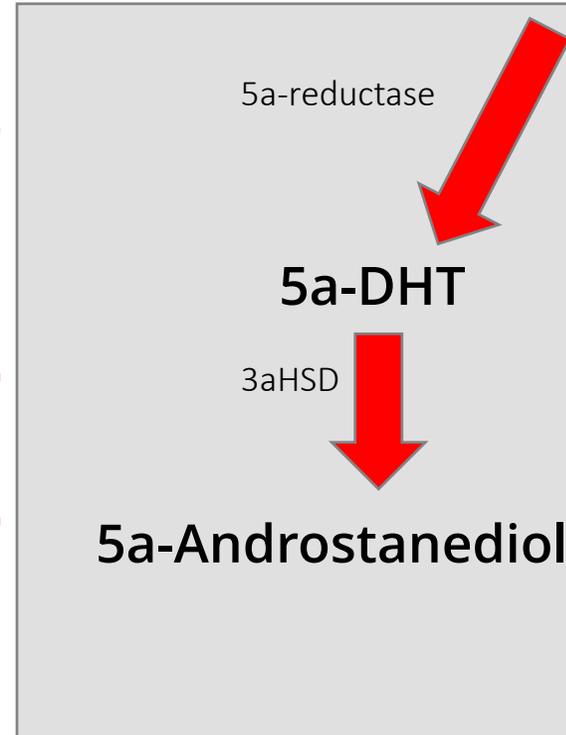
Testosterone metabolites on the DUTCH Test

“alpha male”



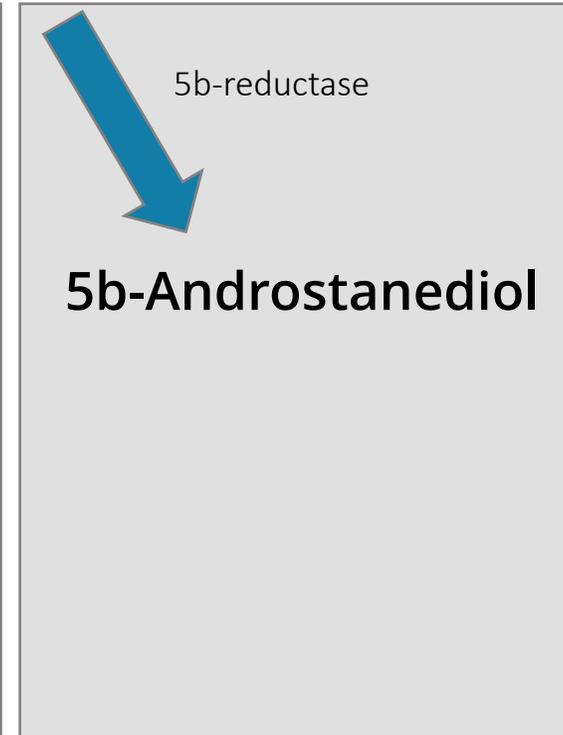
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Alpha pathway



More potent

Testosterone



Beta pathway

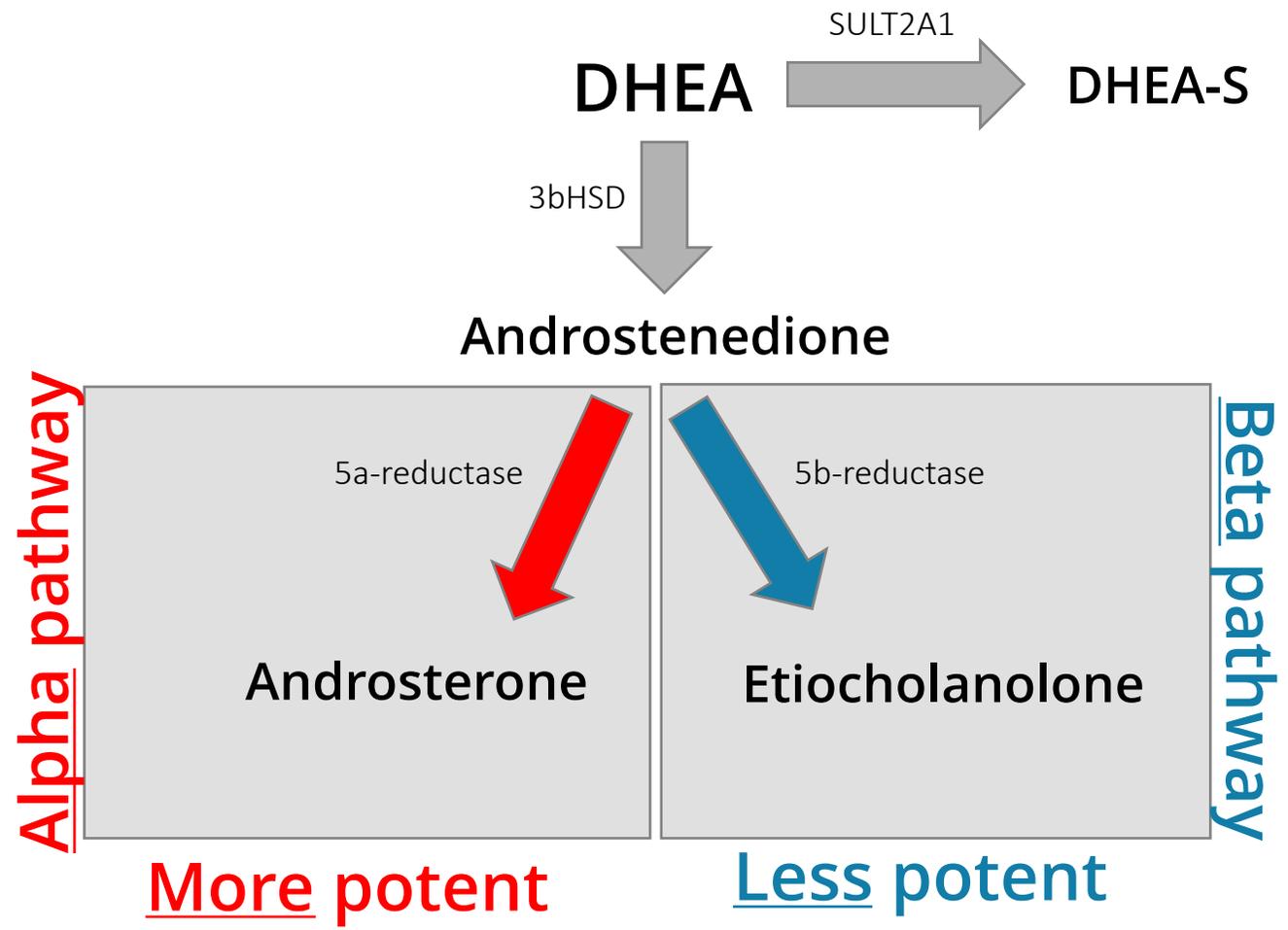
Less potent

DHEA metabolites on the DUTCH Test

"alpha male"



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Androgen activity in target tissues

Since testosterone and the alpha metabolites are the ones acting on the androgen receptors in the target tissues, if you want to get an idea of androgen activity pay special attention to the following markers on the **DUTCH Test**:



- Testosterone
- 5a-DHT
- 5a-androstanediol
- Androsterone

“The amount of local 5-reductase activity and concentration of androgen receptors modulate the extent of the androgenic effects of testosterone in target tissues.”

Yesiladali M, et al. Differentiating Polycystic Ovary Syndrome from Adrenal Disorders. *Diagnostics (Basel)*. 2022;12(9).

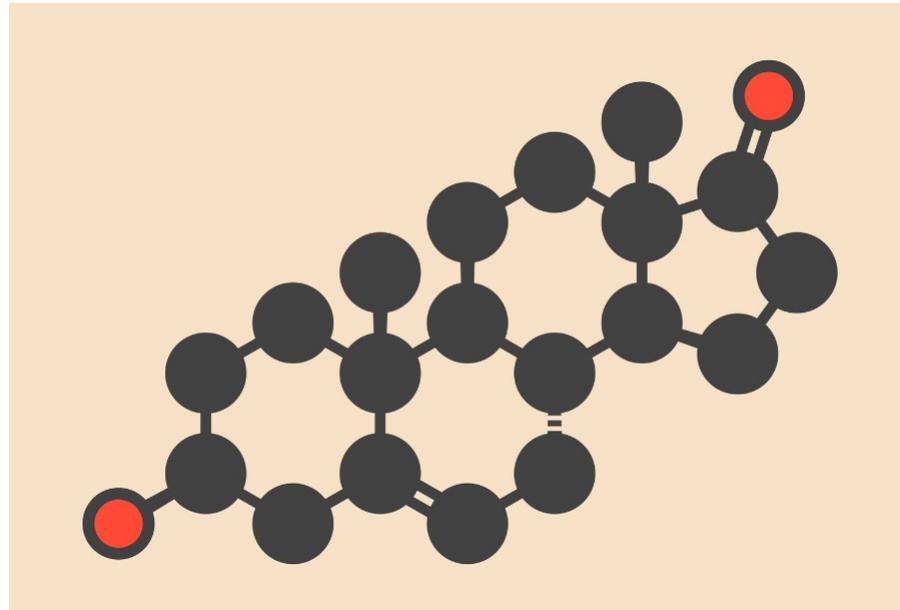
A few more important notes about androgens

- DHEA-S is the sulfated, bound-up form of DHEA. Some people don't sulfate well, so their DHEA-S may be normal/low even if their adrenals are overproducing DHEA.
- DHEA and androstenedione are considered pro-hormones. They need to convert downstream (into testosterone, 5a-DHT, etc.) before they can affect tissues.
- To evaluate androgen activity in the tissues, pay special attention to testosterone, 5a-DHT, 5a-androstenediol, and androsterone.
- Testosterone can act on androgen receptors.
- 5a-DHT, the downstream metabolite of testosterone is about 4x more potent than testosterone.
- 5a-androstenediol may better represent 5a-DHT levels in the tissues.
- Androsterone, the downstream alpha metabolite of DHEA is weaker than testosterone.

Adrenal involvement in PCOS

Adrenal involvement in PCOS

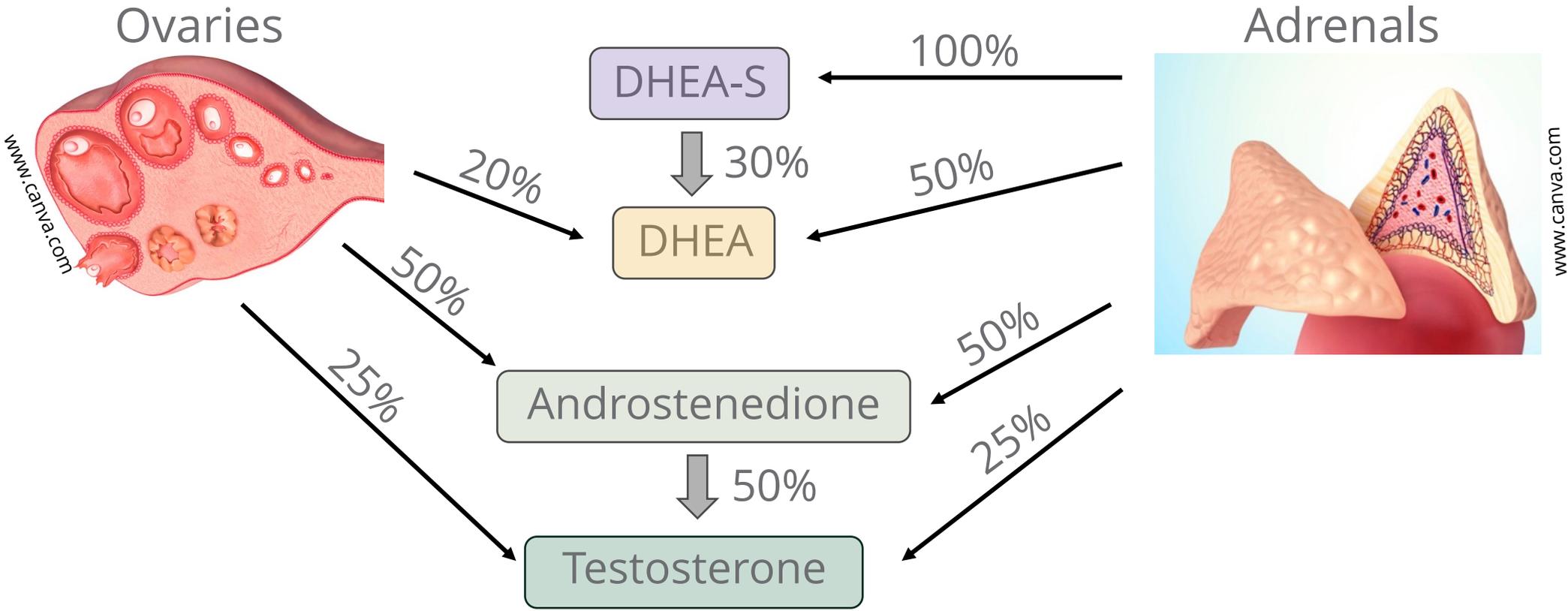
- Between 20% and 30% of women diagnosed with PCOS also have excess DHEAS, indicating hyperfunction of the adrenal cortex (KUMAR, 2005 – 20% white; 30% black).



1. Celik, O.; Yildiz, B.O. Adrenal and Polycystic Ovary Syndrome; Cambridge University Press: Cambridge, UK, 2022; p. 67.
2. Kumar A, et. al. Prevalence of adrenal androgen excess in patients with the polycystic ovary syndrome (PCOS). Clin Endocrinol (Oxf). 2005 Jun;62(6):644-9. Yesiladali M, et al.
3. Differentiating Polycystic Ovary Syndrome from Adrenal Disorders. Diagnostics (Basel). 2022;12(9).

The adrenals make
androgens too!

Where androgens are made in a cycling female



1. Rosenfield RL, et. al. The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. Endocr Rev. 2016 Oct;37(5):467-520.
2. Yesiladali M, et al. Differentiating Polycystic Ovary Syndrome from Adrenal Disorders. Diagnostics (Basel). 2022;12(9).

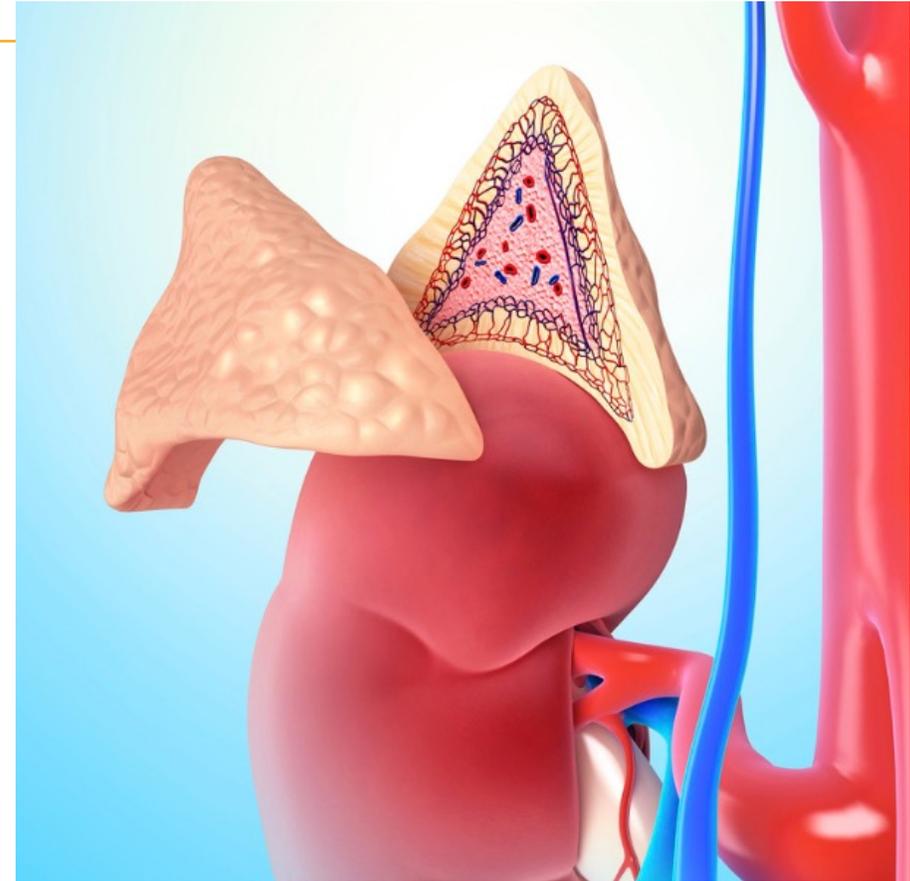
Etiology of Adrenal PCOS

- The etiology behind adrenal PCOS is not 100% clear, but there is some knowledge on the subject that can help a functional medicine approach to care.
- Adrenal PCOS may be due to a combination of factors:
 - Hyperresponsive adrenals
 - Genetic factors
 - Premature adrenarche
 - Stress and higher cortisol in general (perhaps higher ACTH signaling in some individuals)

What signals the
adrenals to make
androgens?

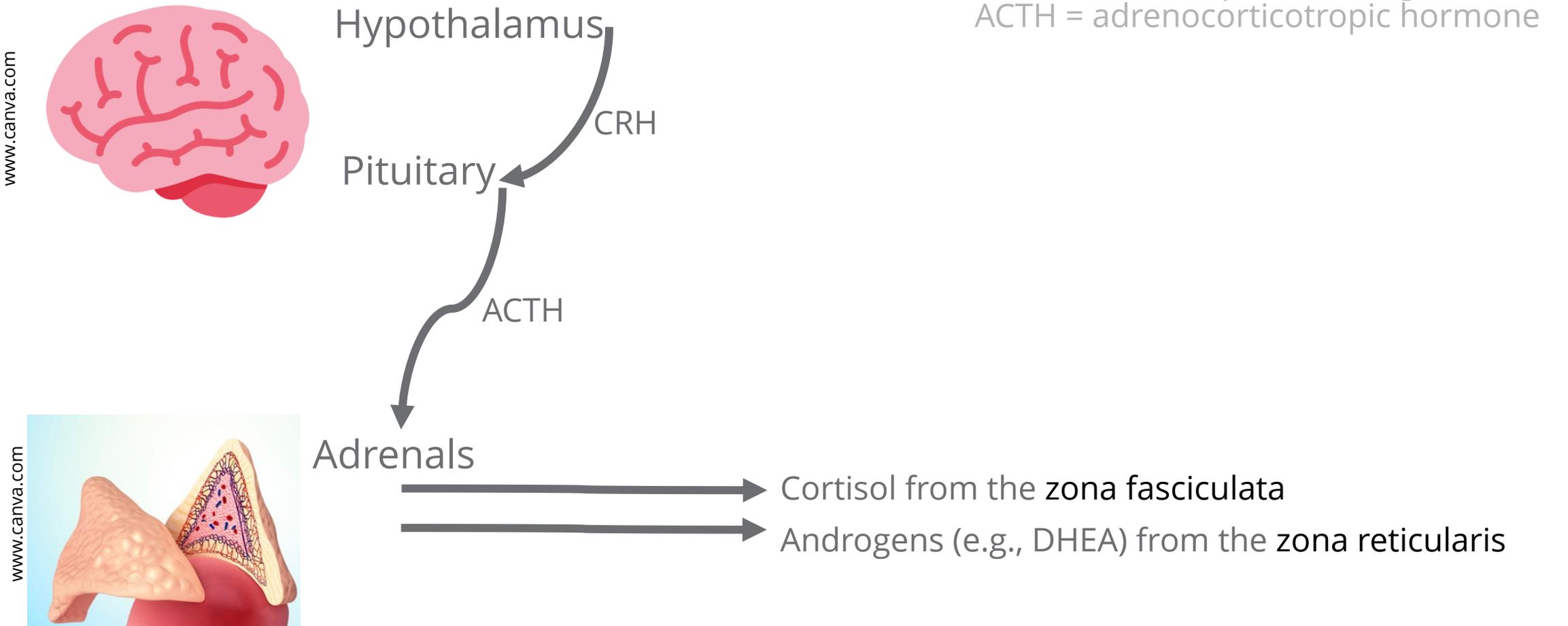
HPA axis

- Adrenocorticotrophic hormone (ACTH) promotes the release of cortisol and androgens from the adrenal cortex.

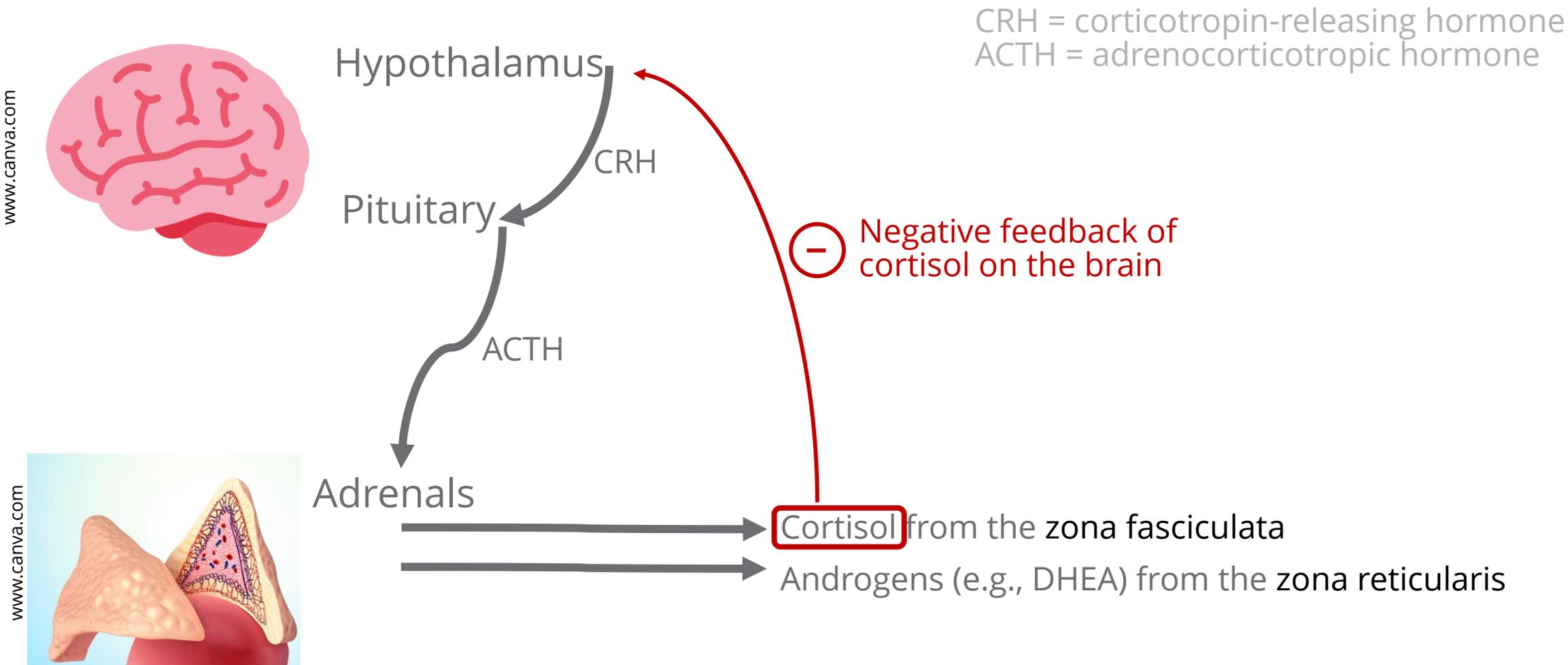


The adrenals sit on top of the kidneys. The outer portion, called the “adrenal cortex” produces androgens, mineralocorticoids, and glucocorticoids (cortisol!).

HPA axis



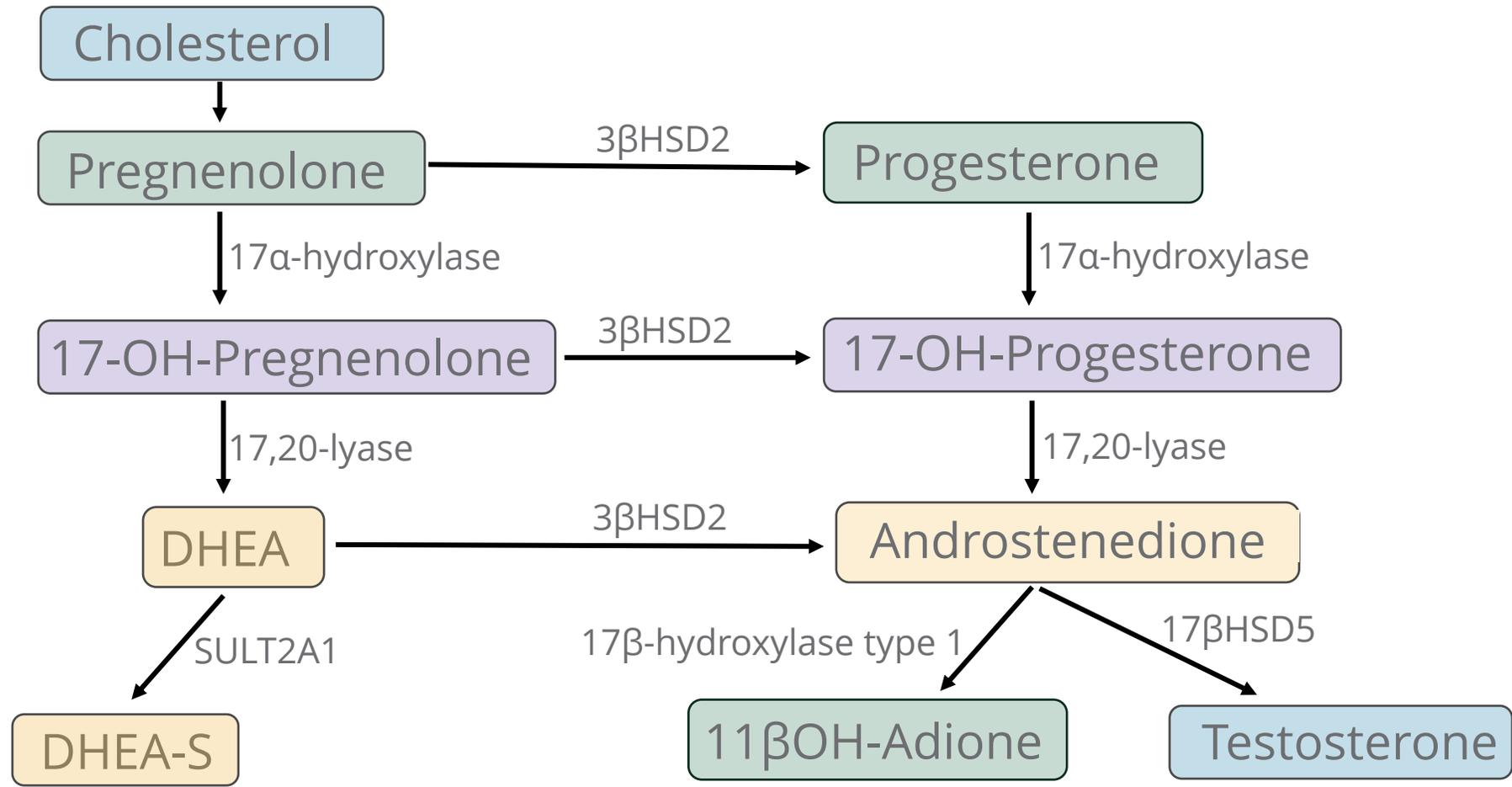
HPA axis



Hyperresponsive adrenals

Etiology: hyperresponsive adrenals

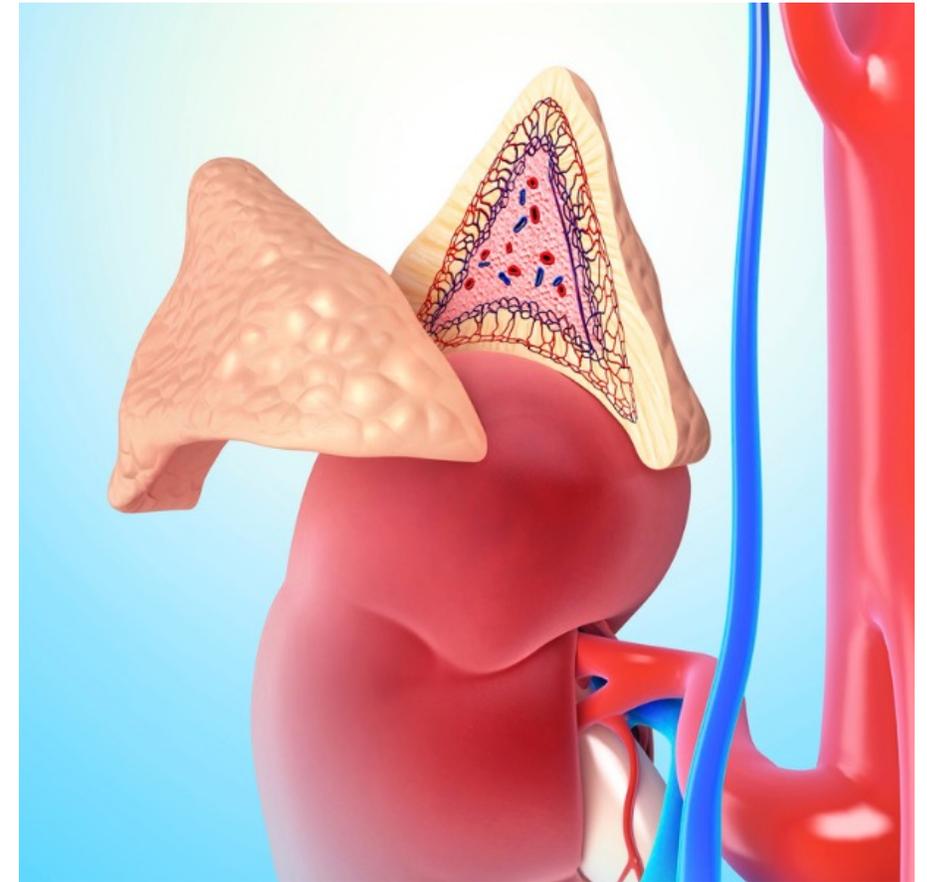
- ACTH promotes the release of adrenal androgens from the zona reticularis.
- In the zona reticularis of the adrenal glands, there is low expression of 3 β HSD, enhancement of 17,20-lyase activity, and expression of (SULT2A).



1. Rosenfield RL, et. al. Current concepts of polycystic ovary syndrome pathogenesis. Curr Opin Pediatr. 2020 Oct;32(5):698-706.
2. Rosenfield RL, et. al. The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. Endocr Rev. 2016 Oct;37(5):467-520.

Etiology: hyperresponsive adrenals

- In women with an adrenal component to their PCOS, their zona reticularis is *hyperresponsive* to the ACTH signal from the pituitary.
- This is significant, because even if they have normal ACTH levels and no HPA-axis dysfunction, their adrenals may *still* overproduce androgens.



1. Goodarzi MO, Carmina E, Azziz R. DHEA, DHEAS and PCOS. J Steroid Biochem Mol Biol. 2015 Jan;145:213-25.
2. Rosenfield RL, et. al. Current concepts of polycystic ovary syndrome pathogenesis. Curr Opin Pediatr. 2020 Oct;32(5):698-706.

Etiology: hyperresponsive adrenals

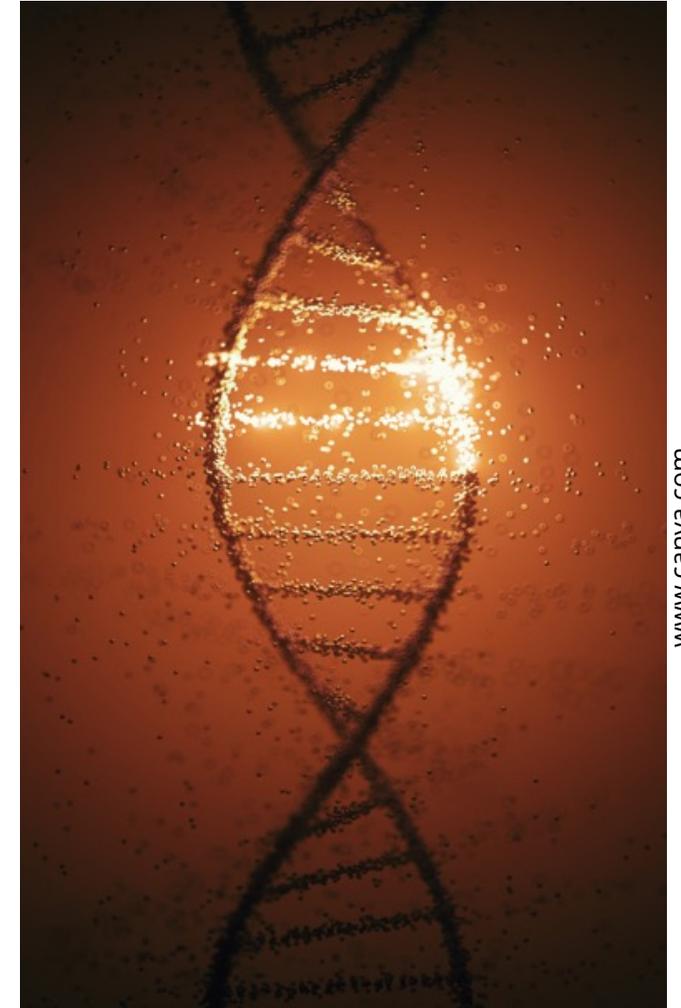
- “In FAH, adrenal androgens are formed in the zona reticularis disproportionately to cortisol formation in the zona fasciculata” (Rosenfield, 2020).
- After age 30, DHEA starts to decline. This is not due to lower ACTH signaling, but instead to a decline in enzymatic activity (especially 17,20-lyase).
- This tells us that enzyme function/activity in the adrenals is just as important/influential on adrenal androgen production as ACTH signaling!

1. Goodarzi MO, Carmina E, Azziz R. DHEA, DHEAS and PCOS. J Steroid Biochem Mol Biol. 2015 Jan;145:213-25.
2. Rosenfield RL, et. al. Current concepts of polycystic ovary syndrome pathogenesis. Curr Opin Pediatr. 2020 Oct;32(5):698-706.

Genetic factors relating to adrenal PCOS

Etiology: genetic factors

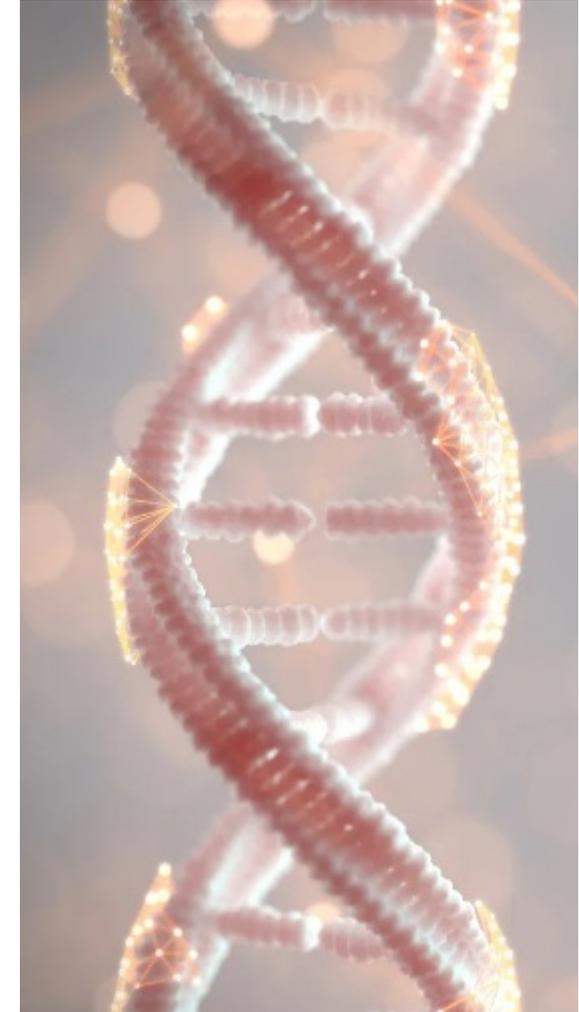
- PAPS synthase 2 (PAPSS2) deficiency results in lower DHEA-S, and possibly more conversion of DHEA to androstenedione, testosterone and 5a-DHT.
 - PAPSS2 provides the universal sulfate donor (PAPS) to all sulfotransferases in the human body, including SULT2A1 which sulfates DHEA to DHEA-S.
- There are also documented genetic variants in SULT2A1 which affects the sulfation of DHEA to DHEA-S (inhibiting it so more DHEA converts to androstenedione/testosterone/5a-DHT).



1. Franks S, et. al. Ovarian morphology is a marker of heritable biochemical traits in sisters with polycystic ovaries. J Clin Endocrinol Metab. 2008 Sep;93(9):3396-402.
2. Goodarzi MO, Carmina E, Azziz R. DHEA, DHEAS and PCOS. J Steroid Biochem Mol Biol. 2015 Jan;145:213-25.

Etiology: genetic factors

- There is likely an interaction of genetic and environmental factors contributing to the etiology and signs/symptoms of PCOS, as there is a high heredity of elevated androgens (such as DHEA-S and androstenedione).



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1. Franks S, et. al. Ovarian morphology is a marker of heritable biochemical traits in sisters with polycystic ovaries. J Clin Endocrinol Metab. 2008 Sep;93(9):3396-402.
2. Goodarzi MO, Carmina E, Azziz R. DHEA, DHEAS and PCOS. J Steroid Biochem Mol Biol. 2015 Jan;145:213-25.

Etiology: genetic factors

- Inherited enzyme defects account for only a very small fraction of women suffering from high adrenal androgens.
- “Rather, women with PCOS and APA excess appear to have a generalized exaggeration in adrenal steroidogenesis in response to ACTH stimulation, although they do not have an overt hypothalamic–pituitary–adrenal axis dysfunction.”



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Premature Adrenarche

Premature adrenarche

- Adrenarche is when the adrenal glands go through puberty!
- Considered premature if it occurs younger than 8 years old in girls or younger than 9 years old in boys.
- The zona reticularis develops. This is the part of the adrenal glands that produces androgens.
- DHEA and DHEA-S levels rise.
- ACTH and cortisol levels do not rise during adrenarche; thus, the increase in DHEA and DHEA-S is not due to a change in ACTH signaling from the brain.



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1. Ibáñez L, Dimartino-Nardi J, Potau N, Saenger P. Premature adrenarche--normal variant or forerunner of adult disease? *Endocr Rev.* 2000 Dec;21(6):671-96.
2. Rosenfield RL, et. al. The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. *Endocr Rev.* 2016 Oct;37(5):467-520.
3. Yesiladali M, et al. Differentiating Polycystic Ovary Syndrome from Adrenal Disorders. *Diagnostics (Basel).* 2022;12(9).

Premature adrenarche

- Premature adrenarche has a 15–20% increased prevalence in PCOS.
- FAH is like an exaggeration of adrenarche
- “...premature adrenarche in childhood may have consequences such as functional ovarian hyperandrogenism, polycystic ovarian syndrome, and insulin resistance in later life, sometimes already recognizable in childhood or adolescence” (Yesiladali, 2022).



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1. Ibáñez L, Dimartino-Nardi J, Potau N, Saenger P. Premature adrenarche--normal variant or forerunner of adult disease? *Endocr Rev.* 2000 Dec;21(6):671-96.
2. Rosenfield RL, et. al. The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. *Endocr Rev.* 2016 Oct;37(5):467-520.
3. Yesiladali M, et al. Differentiating Polycystic Ovary Syndrome from Adrenal Disorders. *Diagnostics (Basel).* 2022;12(9).

Stress

HPA axis



Hypothalamus

Pituitary

Adrenals

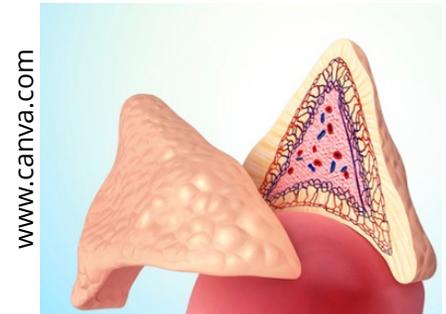
CRH

ACTH

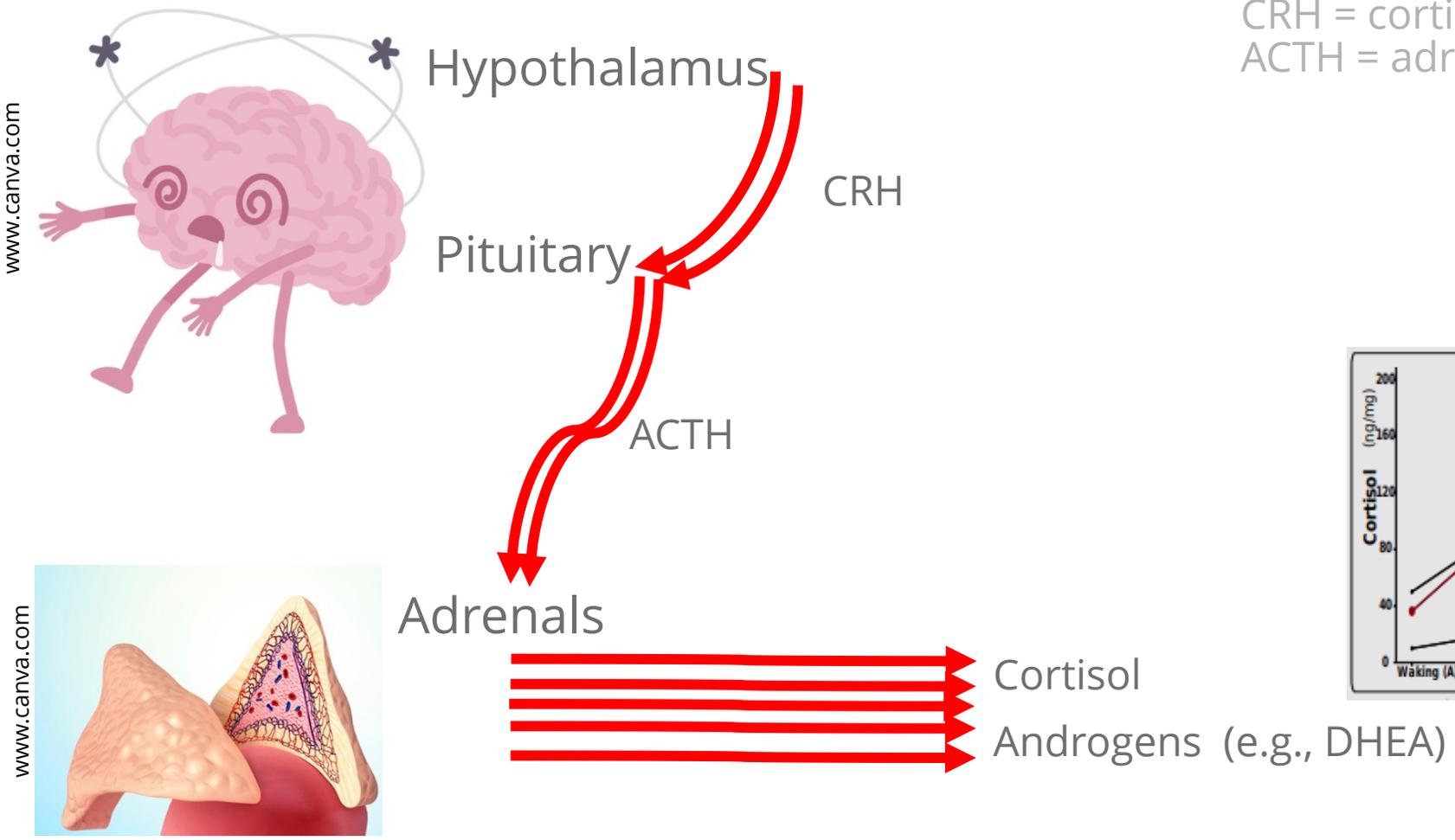
Cortisol from the zona fasciculata

Androgens (e.g., DHEA) from the zona reticularis

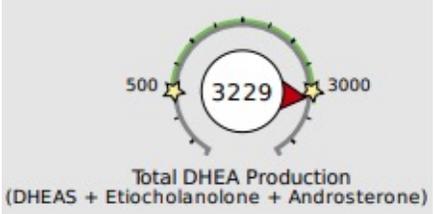
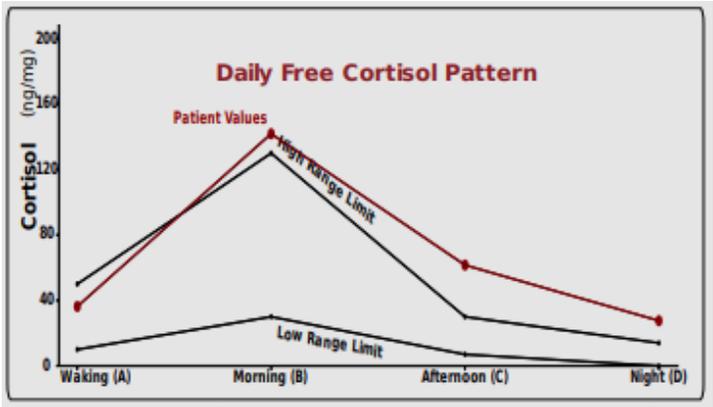
CRH = corticotropin-releasing hormone
ACTH = adrenocorticotrophic hormone



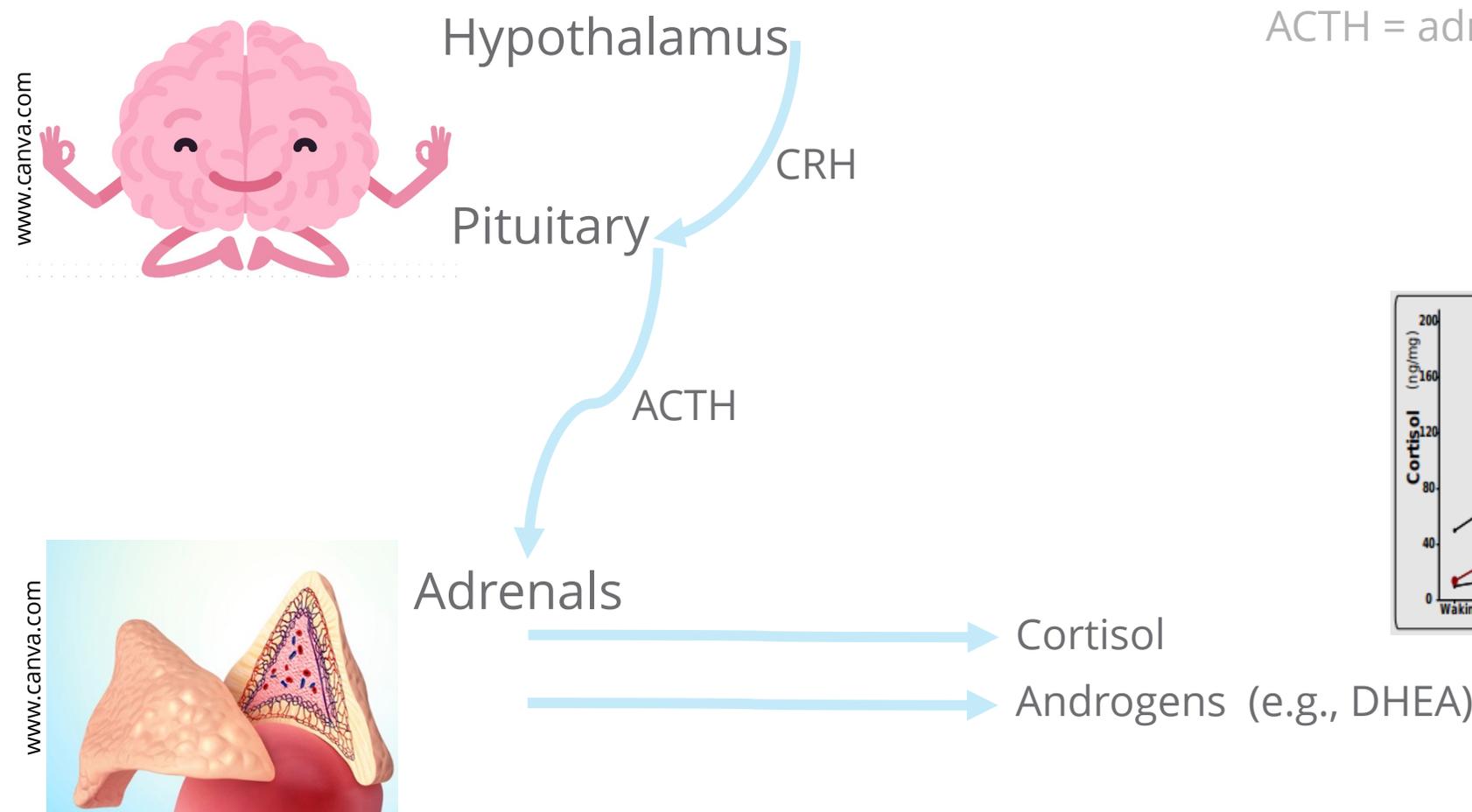
HPA axis: stress!



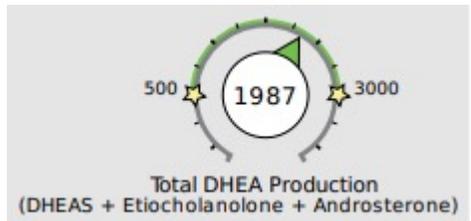
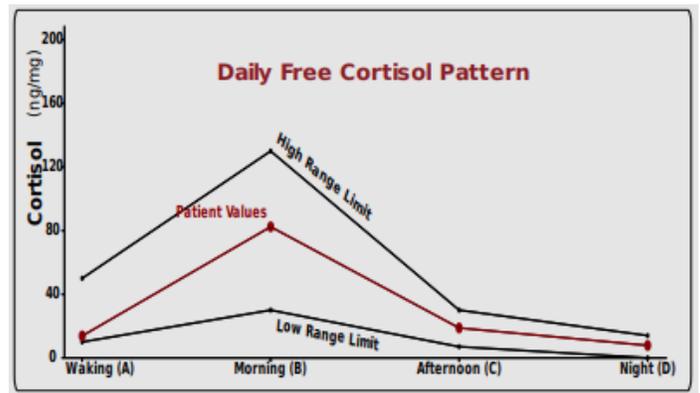
CRH = corticotropin-releasing hormone
ACTH = adrenocorticotrophic hormone



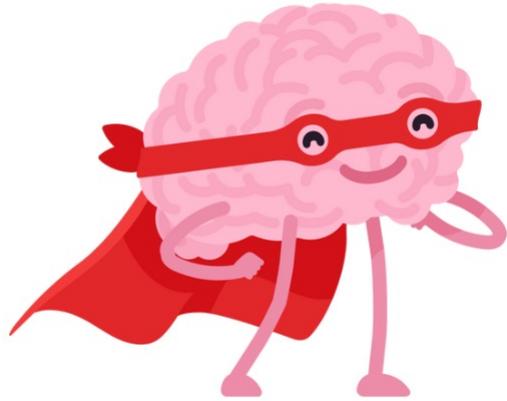
HPA axis: rest and digest



CRH = corticotropin-releasing hormone
ACTH = adrenocorticotrophic hormone



Yet another reason to give your brain some love!

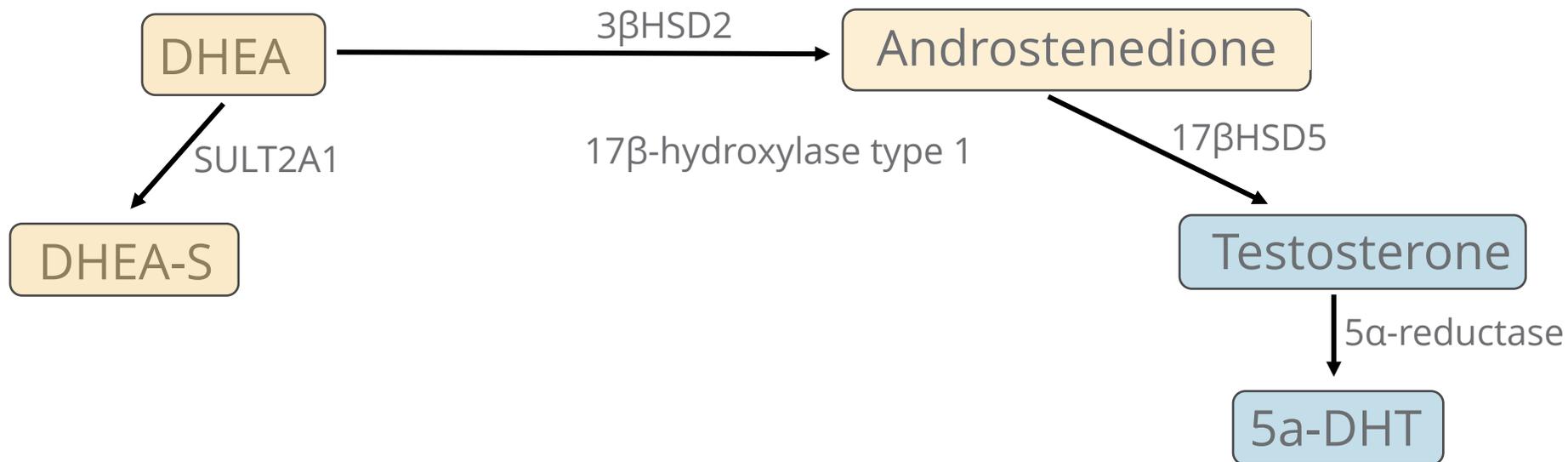


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Evaluating androgens in suspected adrenal PCOS patients

Evaluating androgen: DHEA

- Remember, DHEA can be converted to its inactive form (DHEA-S) or straight over to androstenedione, which is then converted to testosterone and 5 α -DHT. DHEA and androstenedione are pro-hormones (don't act on androgen receptors), whereas testosterone and 5 α -DHT influence androgen receptors in the target tissues.



1. Rosenfield RL, et. al. Current concepts of polycystic ovary syndrome pathogenesis. *Curr Opin Pediatr.* 2020 Oct;32(5):698-706.

2. Rosenfield RL, et. al. The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. *Endocr Rev.* 2016 Oct;37(5):467-520.

Evaluating androgen: DHEA

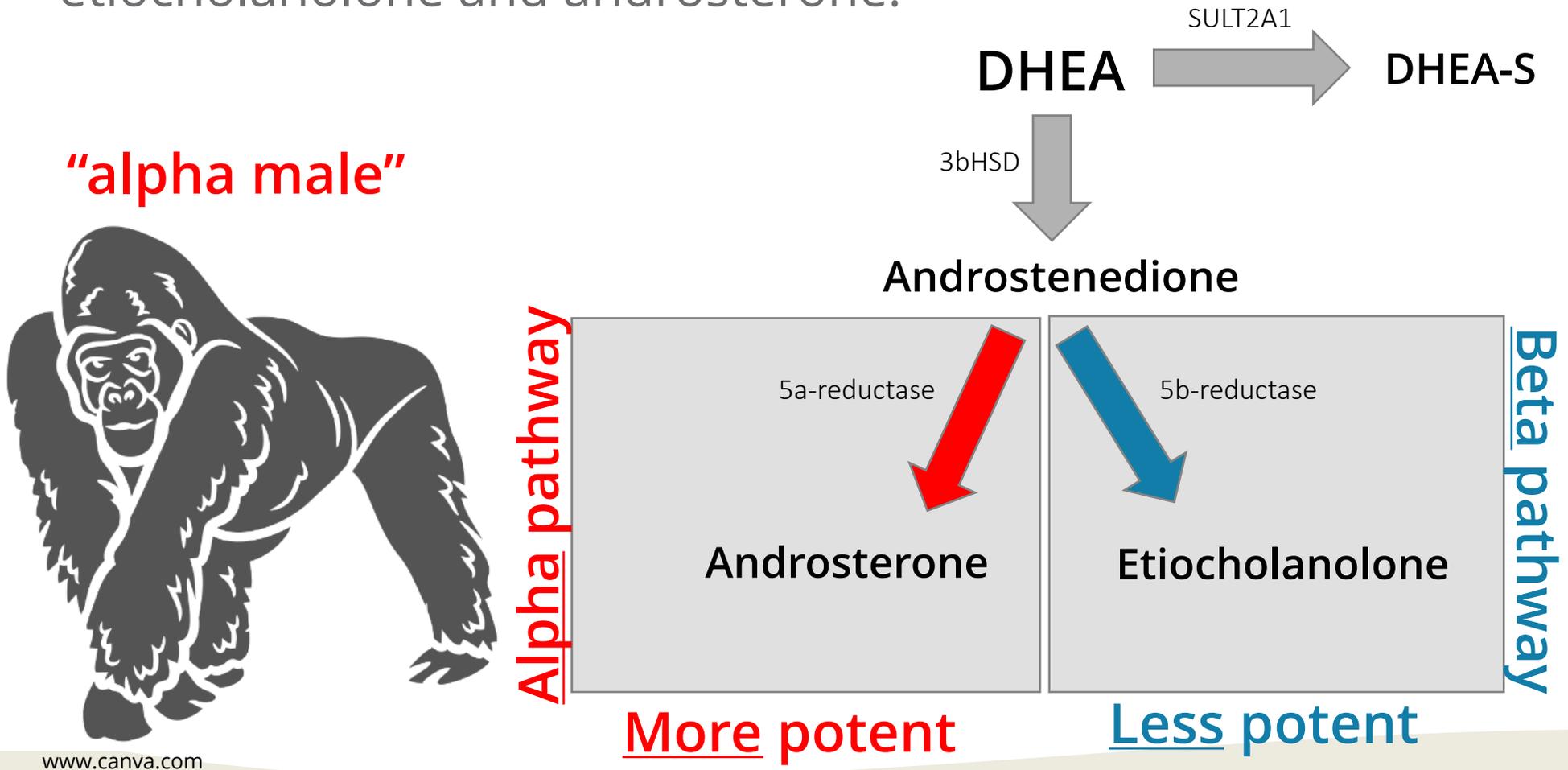
- DHEA-S is not always elevated in adrenal PCOS. This may be because DHEA and DHEA-S do not freely interconvert, and DHEA can directly convert to androstenedione rather than DHEA-S.
- Also, some people have impaired sulfation, and in these individuals, DHEA-S may not estimate DHEA levels well. For example, people with the PAPS synthase 2 (PAPSS2) deficiency and SULT2A1 genetic variants.
- However, measuring DHEA in the blood is not ideal due to its short half-life and diurnal variation.
- Therefore, measuring the downstream DHEA metabolites (etiocholanolone and androsterone) in the urine may provide more insight into the adrenal overproduction of androgens.

1. Goodarzi MO, Carmina E, Azziz R. DHEA, DHEAS and PCOS. J Steroid Biochem Mol Biol. 2015 Jan;145:213-25.

2. Oostdijk W, et. al. PAPSS2 deficiency causes androgen excess via impaired DHEA sulfation--in vitro and in vivo studies in a family harboring two novel PAPSS2 mutations. J Clin Endocrinol Metab. 2015 Apr;100(4):E672-80.

Evaluating androgen: DHEA

- On the DUTCH Test we are measuring urinary DHEA-S, and two downstream metabolites of DHEA and androstenedione: etiocholanolone and androsterone.



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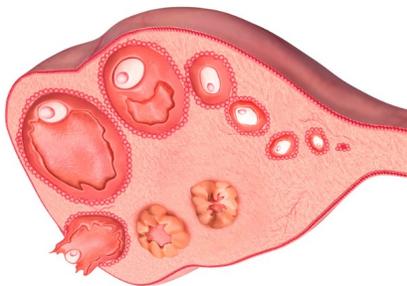
Adrenals or Ovaries?

Wanting to get an idea of where the androgens on the **DUTCH Test** are coming from?



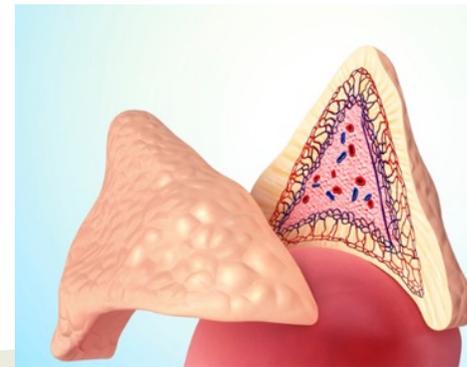
Likely **ovarian** if these are elevated:

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



Likely **adrenal** if these are elevated:

- DHEA-S
- Etiocholanolone
- Androsterone



DUTCH Test Examples

DUTCH Test Example #1:

- 34-year-old female diagnosed with PCOS and struggling with hair loss/thinning, acne, and anxiety. BMI 22, at ideal weight. Irregular cycles.

Hormone Testing Summary

Key (how to read the results):

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

Sex Hormone	Value	Low Limit	High Limit
Estradiol(E2)	3.0	1.8	4.5
Progesterone (Serum Equivalent, ng/mL)	11.3	0.3-2.0	20.0
Testosterone	6.7	2.3	14.0

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

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

Saliva Free Cortisol Pattern

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

Total DHEA Production

Age	Range
20-39	1300-3000
40-59	750-2000
> 60	500-1200

5132 (Total DHEA Production (DHEAS + Etiocholanolone + Androsterone))

9.60 8.89 19.30

Saliva Cortisol Total (Sum of 5 values)

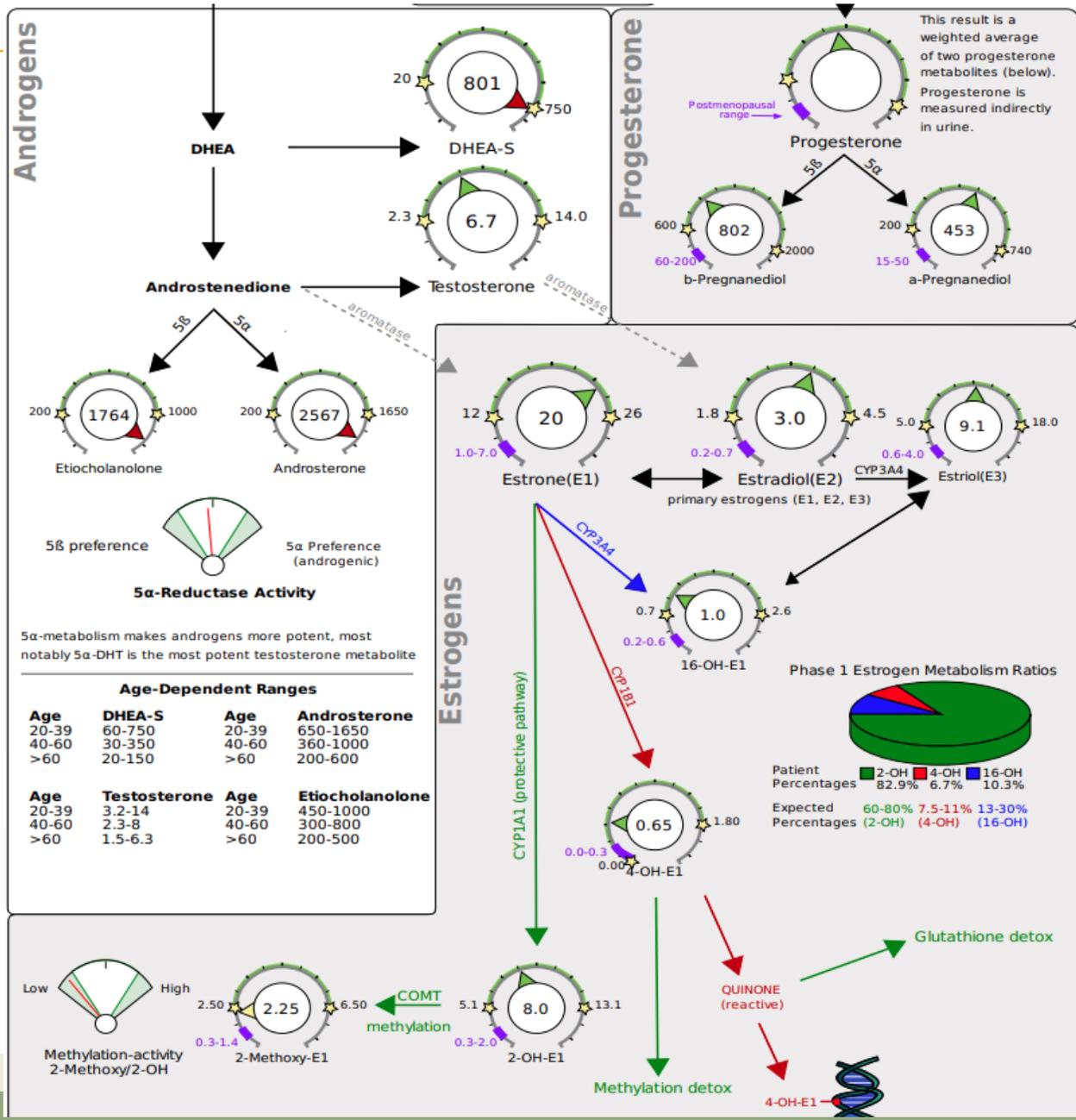
→ cortisol metabolism →

2750 3272 6500

Metabolized Cortisol (THF+THE) (Total Cortisol Production)

DUTCH Test Example #1

- DHEA markers are elevated:
 - DHEA-S
 - Etiocholanolone
 - Androsterone
- Testosterone within range
- She ovulated!



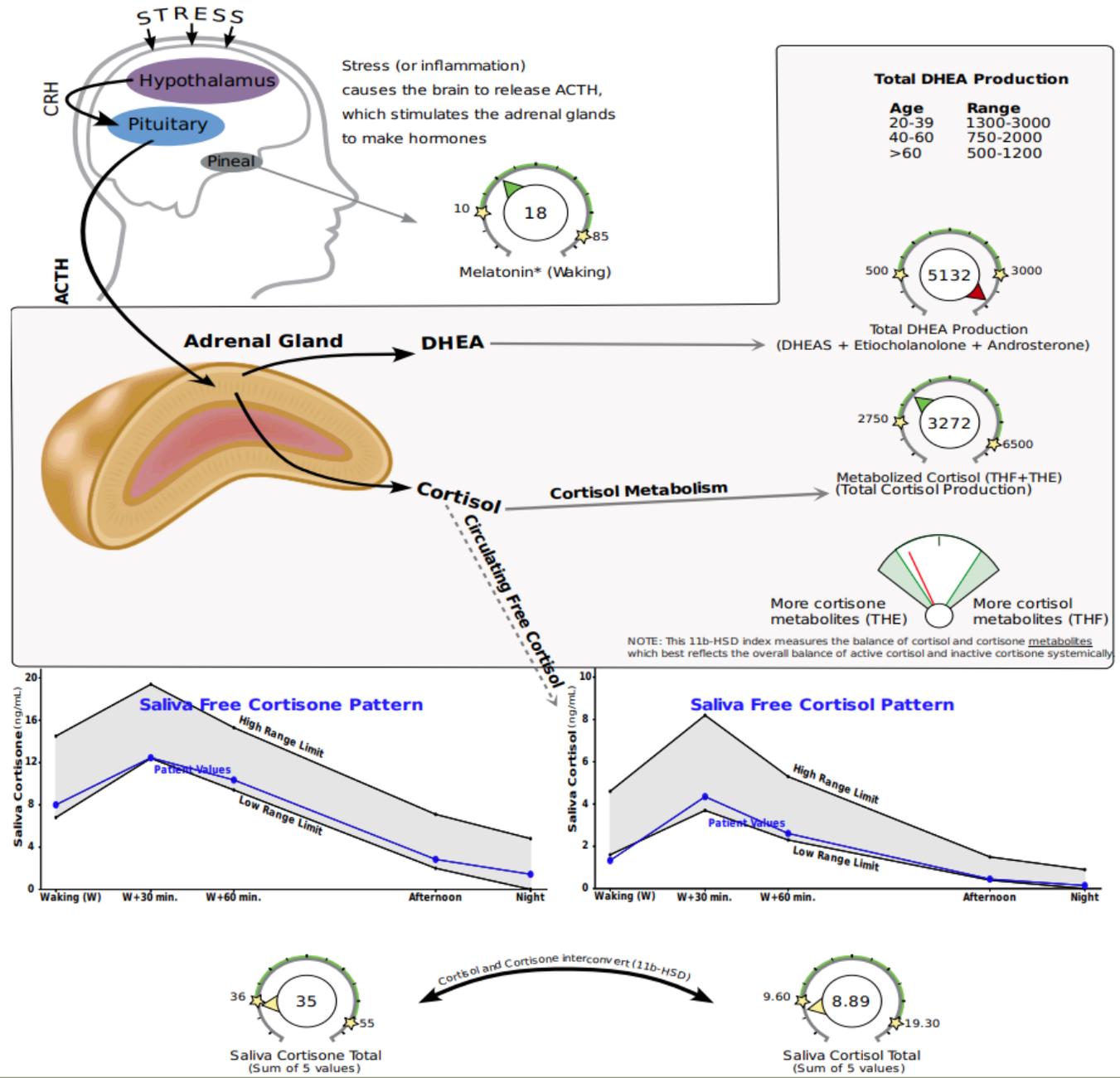
DUTCH Test Example #1

- One of her downstream testosterone metabolites (5a-androstanediol) is slightly above range.

Androgens and Metabolites (Urine)				
DHEA-S	Above range	801.2	ng/mg	20 - 750
Androsterone	Above range	2567.0	ng/mg	200 - 1650
Etiocholanolone	Above range	1764.0	ng/mg	200 - 1000
Testosterone	Within range	6.7	ng/mg	2.3 - 14
5a-DHT	Within range	3.9	ng/mg	0 - 6.6
5a-Androstanediol	Above range	39.3	ng/mg	6 - 30
5b-Androstanediol	Within range	58.2	ng/mg	20 - 75
Epi-Testosterone	Within range	9.2	ng/mg	2.3 - 14

DUTCH Test Example #1

- Cortisol is normal-low
- Having low cortisol does not rule out adrenal PCOS. Remember that in adrenal PCOS, the zona reticularis is *hyperresponsive* to ACTH.
- In this case, it's also paramount to rule out NCAH and hyperprolactinemia.
- An adrenal tumor is also possible, but unlikely (rare).



DUTCH Test Example #2

- 32-year-old female with suspected PCOS and struggling with hair loss, increased body/facial hair, and moderate anxiety. BMI 31 with known dysglycemia. Irregular cycles.

Hormone Testing Summary

Key (how to read the results):

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

<p>Estradiol(E2)</p> <p>Value: 2.8</p> <p>Range: 1.8 - 4.5</p> <p>Postmenopausal range: 0.2-0.7</p>	<p>Progesterone (Serum Equivalent, ng/mL)</p> <p>Value: 9.2</p> <p>Range: 6.0 - 20.0</p> <p>Postmenopausal range: 0.3-2.0</p> <p><small>Progesterone Serum Equivalent is a calculated value based on urine pregnanediol.</small></p>	<p>Testosterone</p> <p>Value: 10.9</p> <p>Range: 2.3 - 14.0</p>
--	---	--

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

Daily Free Cortisol Pattern

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

Total DHEA Production

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

Value: 4052

Range: 500 - 3000

Total DHEA Production (DHEAS + Etiocholanolone + Androsterone)

65

Value: 111

Range: 200

24hr Free Cortisol (A+B+C+D)

Value: 3409

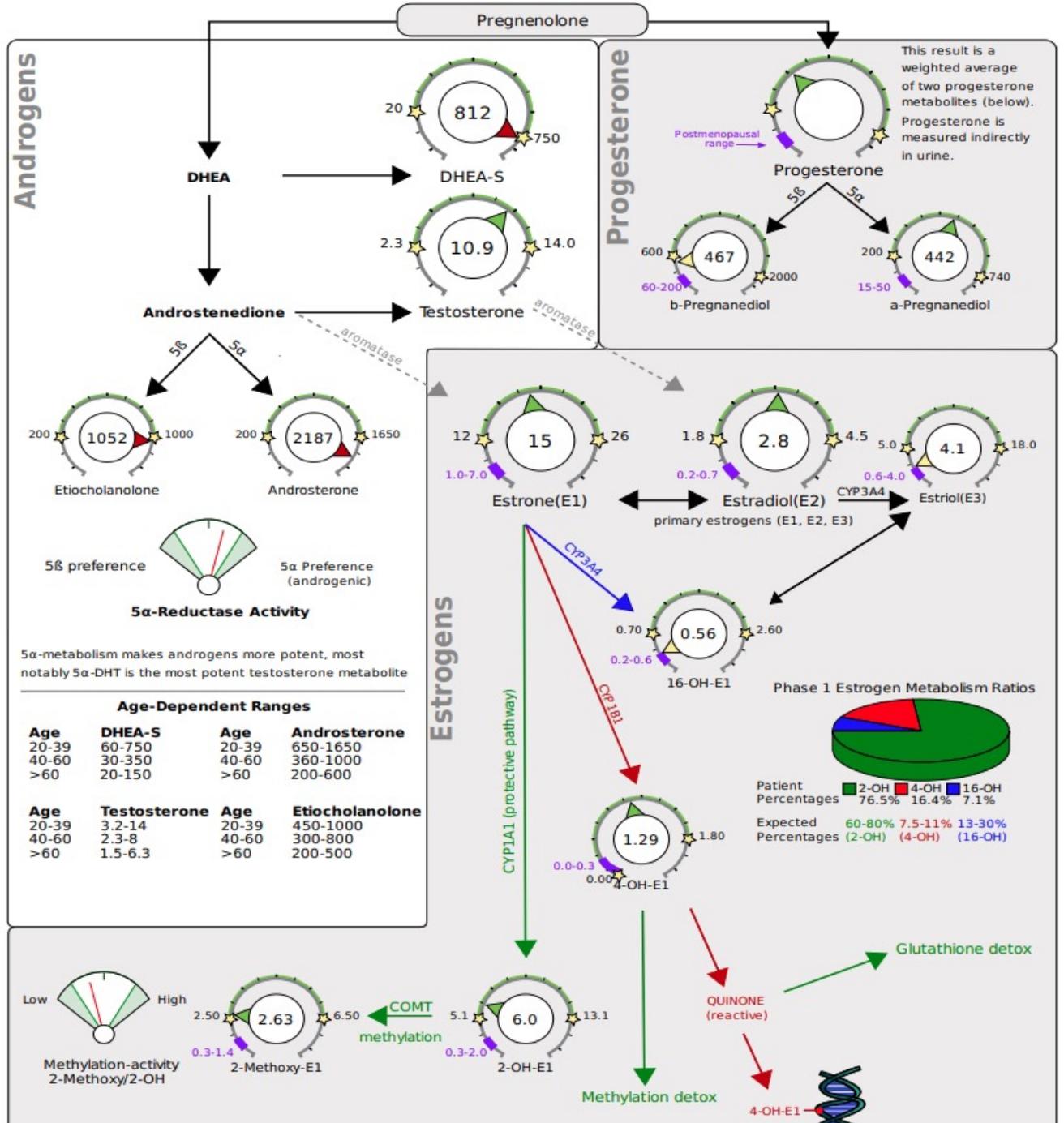
Range: 2750 - 6500

Metabolized Cortisol (THF+THE) (Total Cortisol Production)

cortisol metabolism

DUTCH Test Example #2

- DHEA markers are elevated:
 - DHEA-S
 - Etiocholanolone
 - Androsterone
- Testosterone within range, but getting toward the higher side
- She also ovulated!



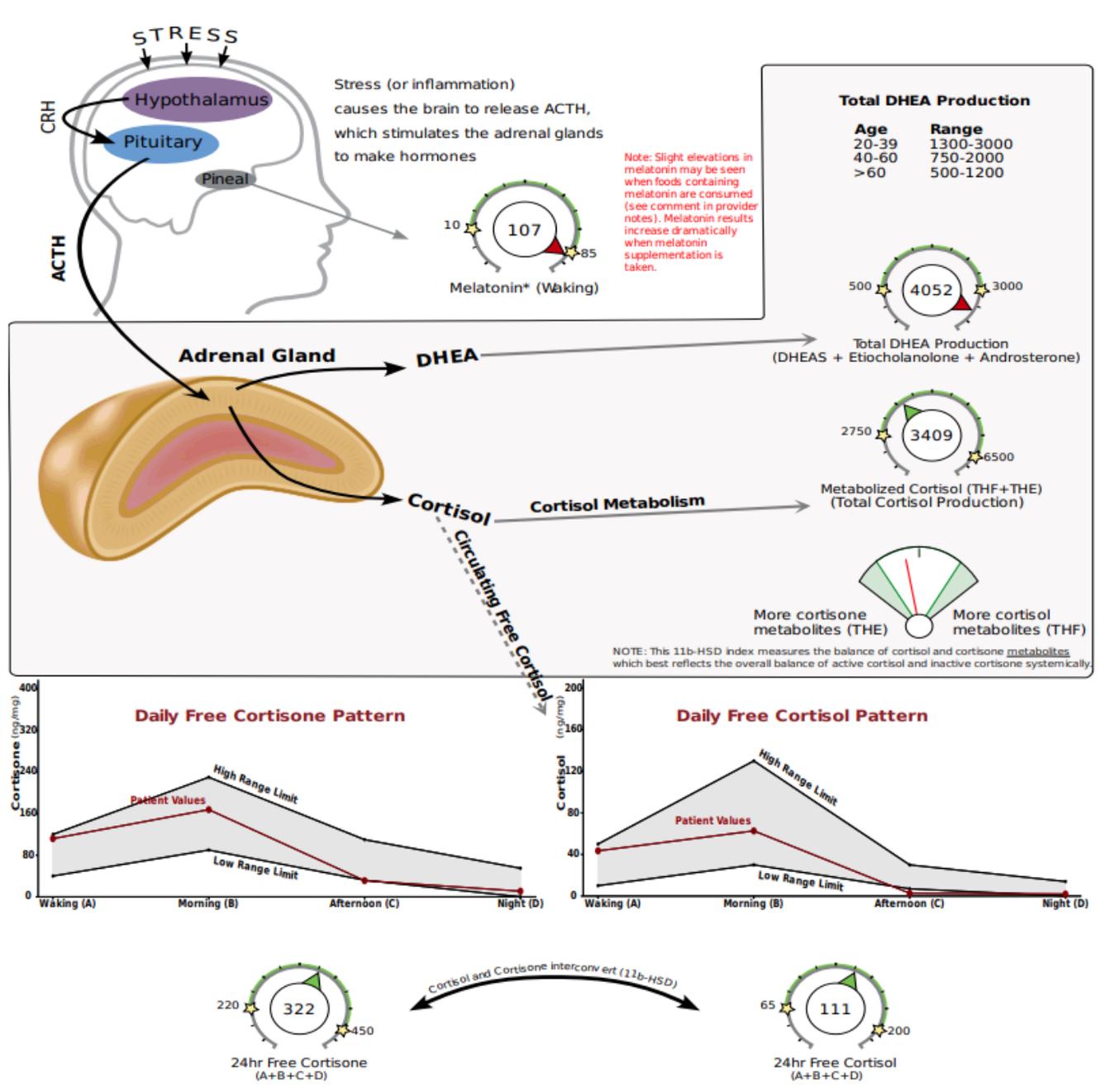
DUTCH Test Example #2

- Two of her downstream testosterone metabolites (5a-DHT and 5a-androstanediol) are above range. Likely also ovarian involvement, which makes sense with her high BMI and blood sugar issues.

Androgens and Metabolites (Urine)				
DHEA-S	Above range	812.0	ng/mg	20 - 750
Androsterone	Above range	2187.0	ng/mg	200 - 1650
Etiocholanolone	Above range	1052.0	ng/mg	200 - 1000
Testosterone	Within range	10.9	ng/mg	2.3 - 14
5a-DHT	Above range	6.72	ng/mg	0 - 6.6
5a-Androstanediol	Above range	72.5	ng/mg	6 - 30
5b-Androstanediol	Within range	63.4	ng/mg	20 - 75
Epi-Testosterone	Low end of range	3.0	ng/mg	2.3 - 14

DUTCH Test Example #2

- Cortisol is normal-low like previous case.
- Again, having low cortisol does not rule out adrenal PCOS.
- Again, it's also paramount to exclude NCAH and hyperprolactinemia.
- An adrenal tumor is also possible, but unlikely (rare).



DUTCH Test Example #3

- 20-year-old female diagnosed with PCOS and struggling with symptoms of moderate androgen excess and anxiety. BMI 25. Regular cycles.

Hormone Testing Summary

Key (how to read the results):

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

Estradiol(E2) 1.80 - 4.50 Patient result: 8.47 Postmenopausal range: 0.2-0.7	Progesterone (Serum Equivalent, ng/mL) 6.0 - 20.0 Patient result: 3.7 Postmenopausal range: 0.3-2.0	Testosterone 2.3 - 14.0 Patient result: 10.4
--	--	---

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

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

Daily Free Cortisol Pattern

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

Total DHEA Production

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

Patient result: 3613

Total DHEA Production (DHEAS + Etiocholanolone + Androsterone)

65

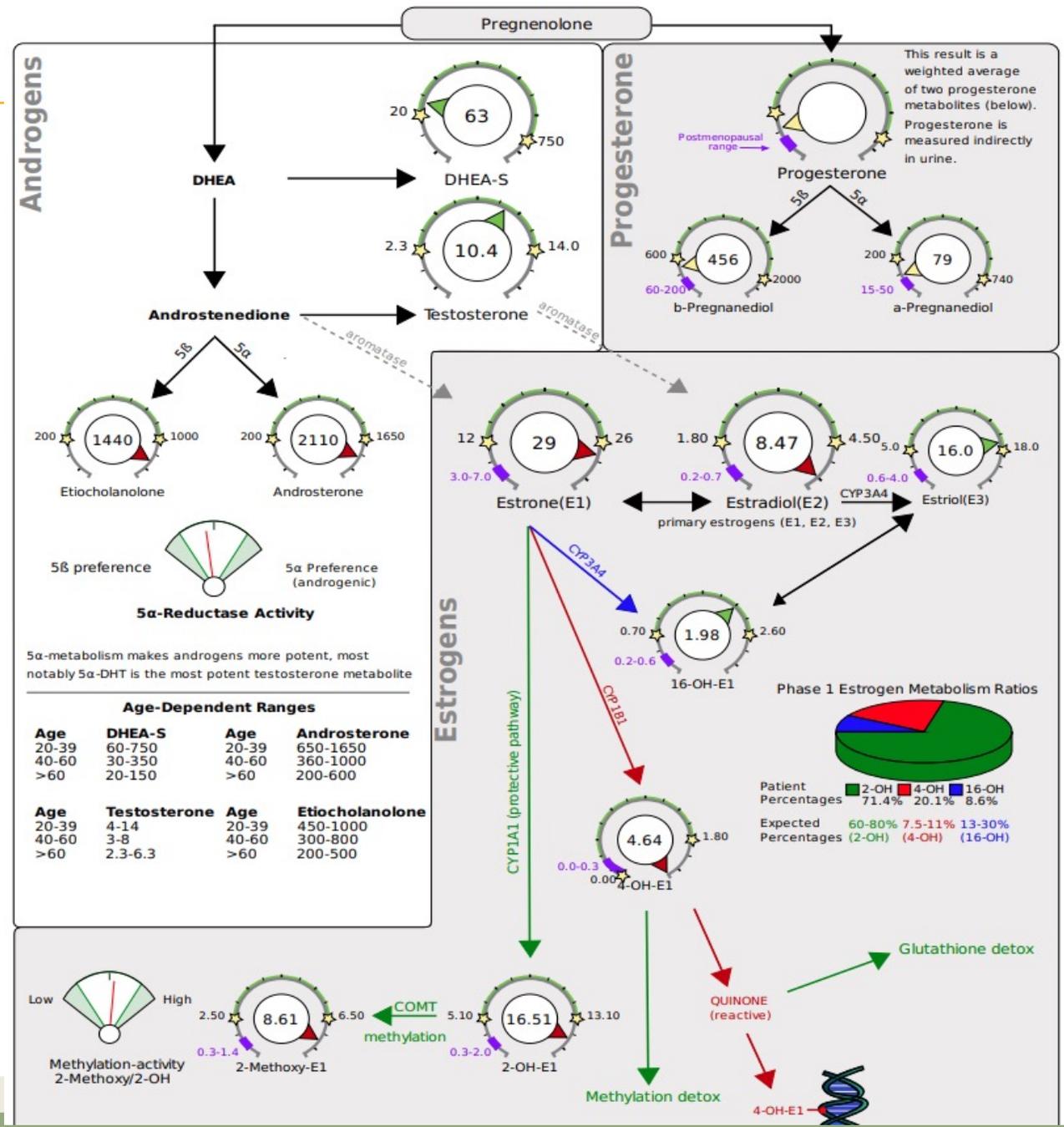
24hr Free Cortisol (A+B+C+D)

cortisol metabolism

Metabolized Cortisol (THF+THE)
(Total Cortisol Production)

DUTCH Test Example #3

- Two DHEA markers are elevated:
 - Etiocholanolone
 - Androsterone
- **All DHEA markers do not have to be elevated in adrenal PCOS.**
- Testosterone within range, but getting toward the higher side
- Did she ovulate?



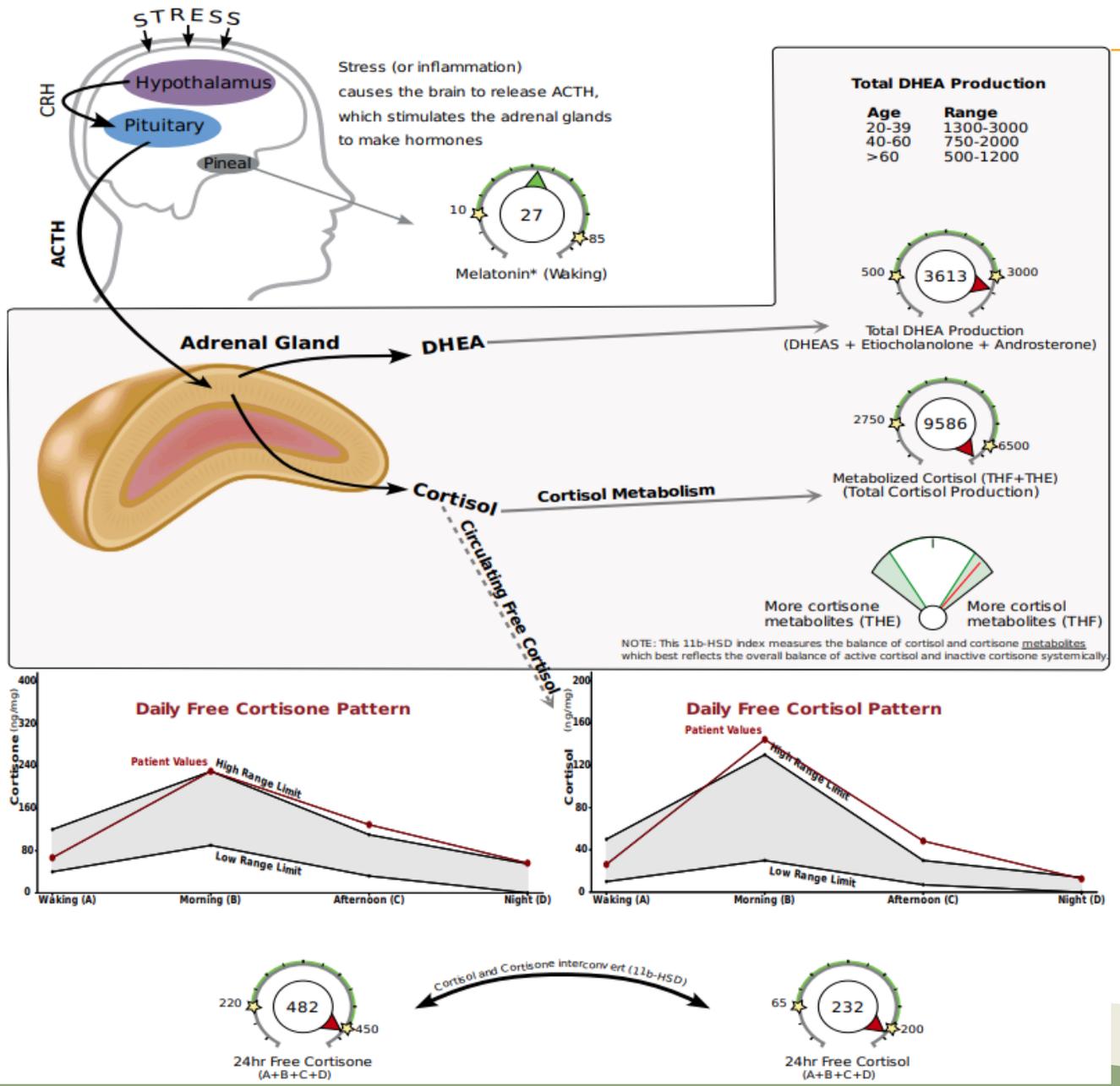
DUTCH Test Example #3

- One of her downstream testosterone metabolites (5a-androstanediol) is slightly above range. Possible ovarian involvement. Even if I don't suspect ovarian involvement, I'm still going to investigate dysglycemia, etc.

Androgens and Metabolites (Urine)				
DHEA-S	Low end of range	63.0	ng/mg	20 - 750
Androsterone	Above range	2110.0	ng/mg	200 - 1650
Etiocholanolone	Above range	1440.0	ng/mg	200 - 1000
Testosterone	Within range	10.4	ng/mg	2.3 - 14
5a-DHT	Within range	1.8	ng/mg	0 - 6.6
5a-Androstanediol	Above range	39.9	ng/mg	12 - 30
5b-Androstanediol	Within range	46.9	ng/mg	20 - 75
Epi-Testosterone	Within range	10.3	ng/mg	2.3 - 14

DUTCH Test Example #3

- Cortisol is elevated.
 - Could also contribute to hair loss...
- Overactive HPA axis that could be contributing to higher DHEA levels!
- Lowering cortisol may help to lower adrenal DHEA production.



DUTCH Test Example #4

- 15-year-old female with suspected PCOS and struggling with acne and mood swings. BMI 35. Irregular cycles.

Hormone Testing Summary

Key (how to read the results):

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

Estradiol(E2)

Progesterone
(Serum Equivalent, ng/mL)

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

Testosterone

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

Daily Free Cortisol Pattern

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

Total DHEA Production

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

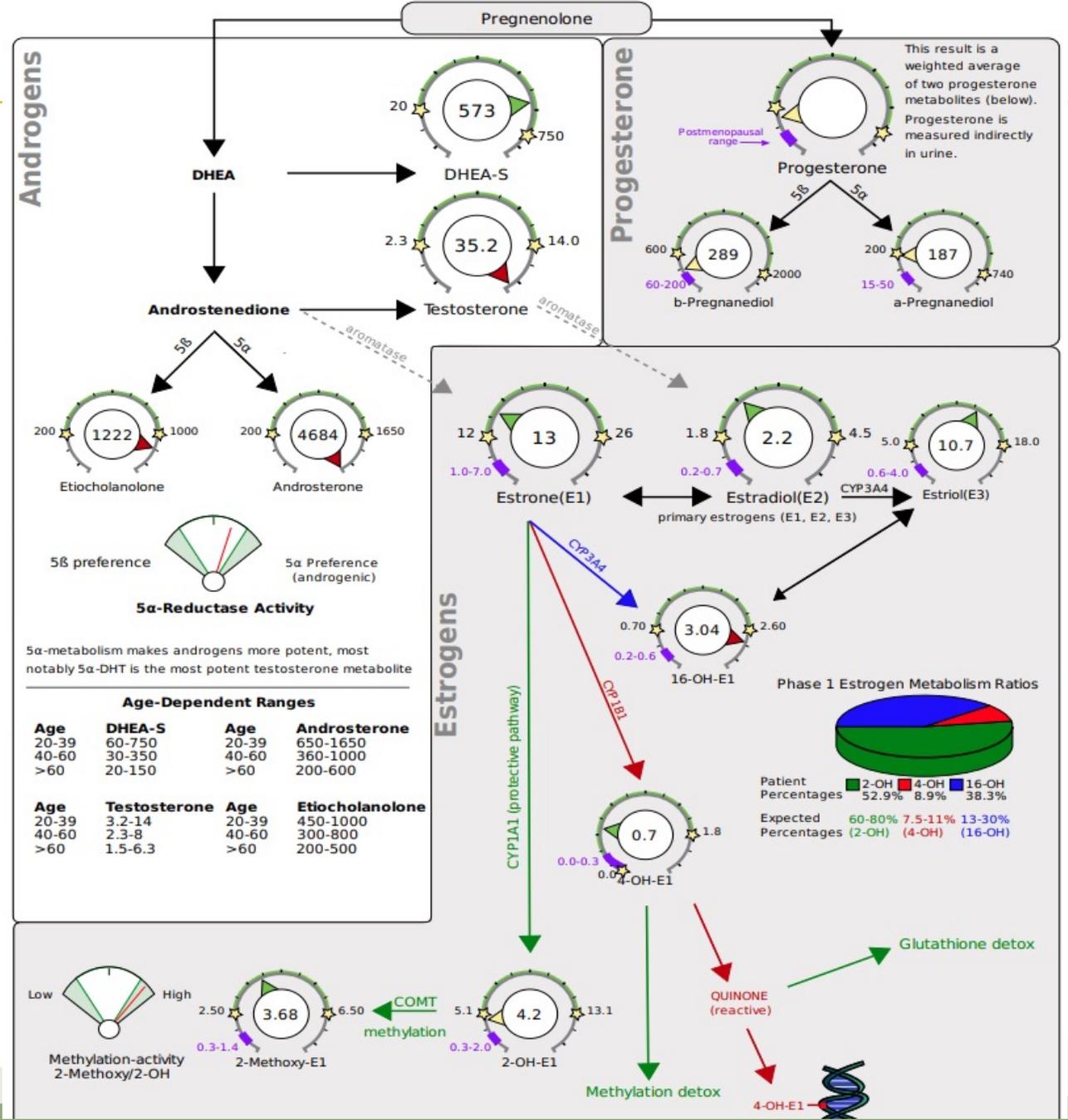
24hr Free Cortisol
(A+B+C+D)

cortisol
metabolism

Metabolized Cortisol (THF+THE)
(Total Cortisol Production)

DUTCH Test Example #4

- Two DHEA markers are elevated:
 - Etiocholanolone
 - Androsterone
- Testosterone elevated!
- Did she ovulate?



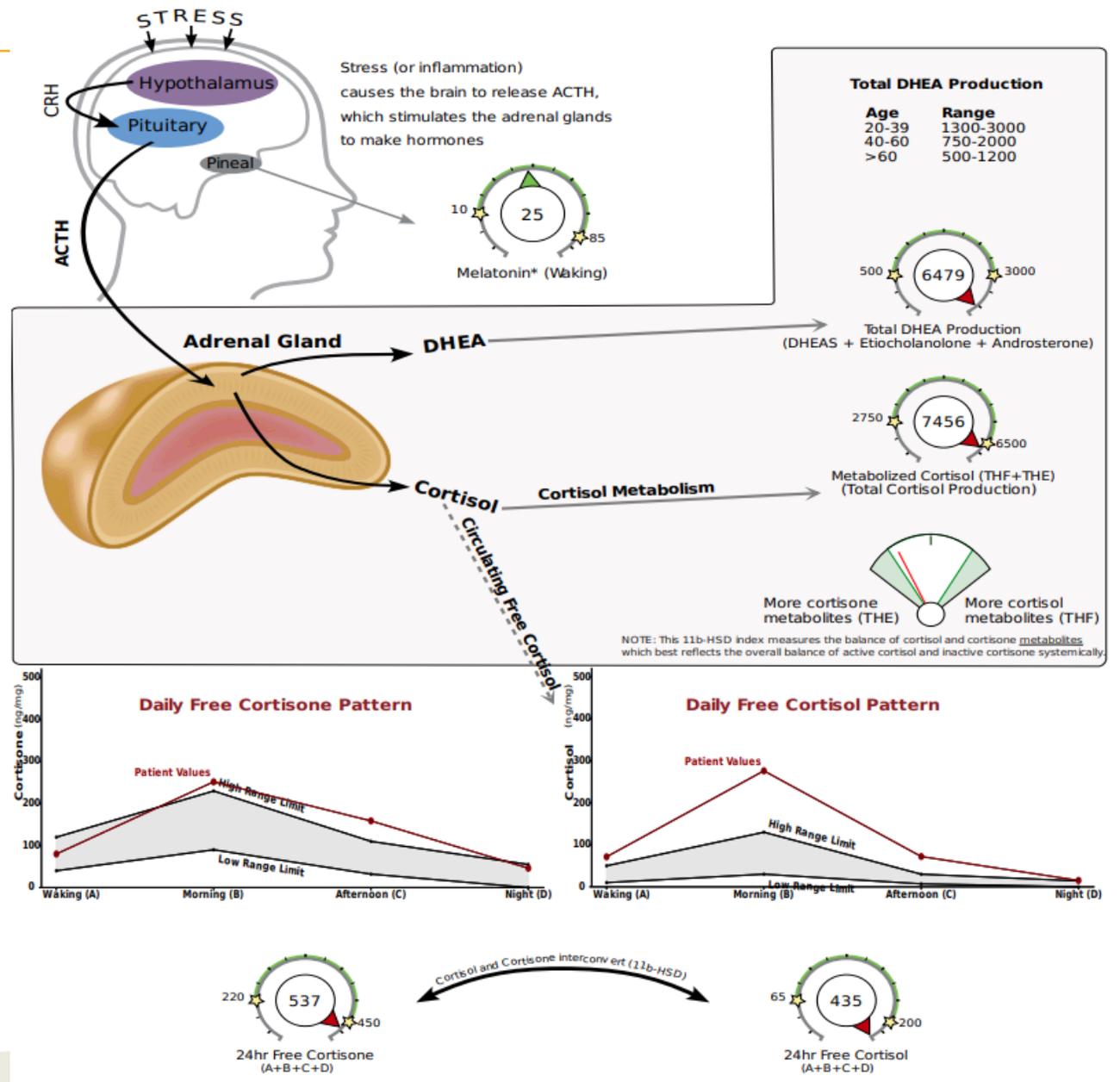
DUTCH Test Example #4

- All her downstream testosterone metabolites are elevated. Likely ovarian involvement.

Androgens and Metabolites (Urine)				
DHEA-S	Within range	573.2	ng/mg	20 - 750
Androsterone	Above range	4684.0	ng/mg	200 - 1650
Etiocholanolone	Above range	1222.0	ng/mg	200 - 1000
Testosterone	Above range	35.2	ng/mg	2.3 - 14
5a-DHT	Above range	10.44	ng/mg	0 - 6.6
5a-Androstenediol	Above range	111.7	ng/mg	6 - 30
5b-Androstenediol	High end of range	69.8	ng/mg	20 - 75
Epi-Testosterone	Above range	16.6	ng/mg	2.3 - 14

DUTCH Test Example #4

- Cortisol is elevated.
- Overactive HPA axis that could be contributing to higher DHEA levels!
- Lowering cortisol may help to lower adrenal DHEA production.



Potential Treatment Considerations

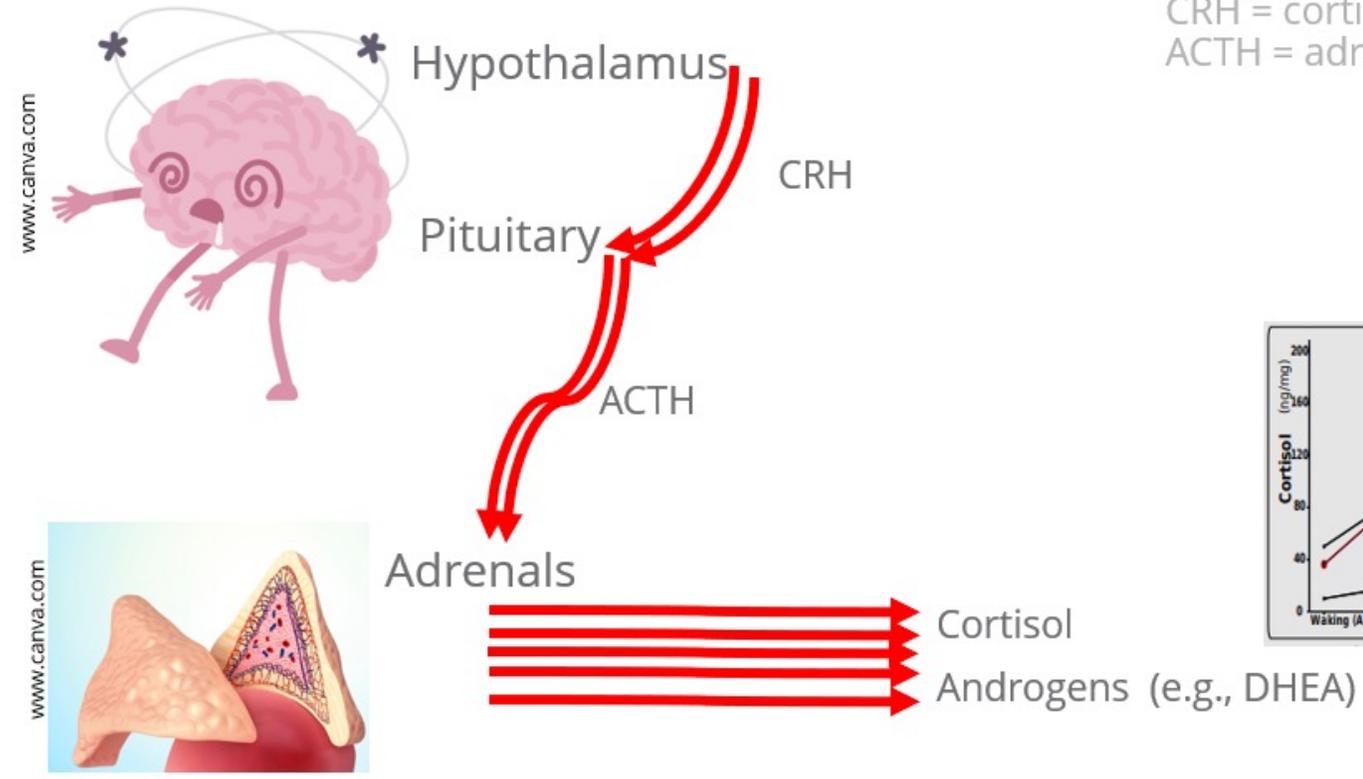
Potential treatment considerations

- Lower cortisol, if elevated
- Reduce stress and anxiety
- Avoid intense exercise
- Avoid a sedentary lifestyle
- Regulate blood sugars
- Herbal anti-androgens and 5a-blockers
- Support the circadian rhythm.
- Support sleep

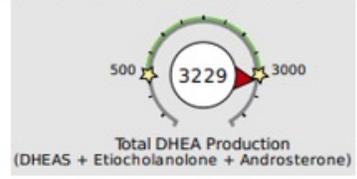
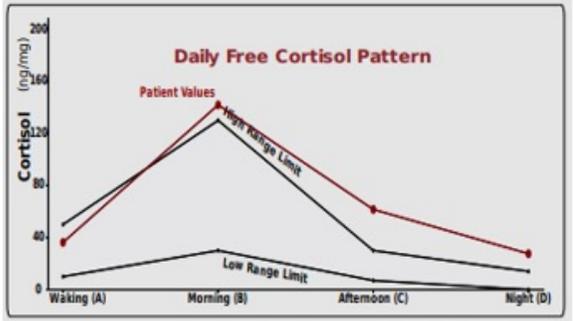


Elevated Cortisol

- If there is high cortisol, figure out what's contributing to it and try your best to lower it!



CRH = corticotropin-releasing hormone
ACTH = adrenocorticotropic hormone



What elevates cortisol?

- Psychological stress
- Anxiety
- Intense exercise
- Pain
- Inflammation
- Infection
- Blood sugar dips
- Caffeine, licorice, stimulants
- Hyperthyroidism or too much thyroid medication (tends to increase cortisol production)
- Obesity (also tends to increase cortisol production)
- Cushing's syndrome/disease



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Stress/anxiety reduction

- Deep breathing:
 - 4x4 breathing
 - 4,7,8 breathing
 - Alternate nostril breathing
- Meditation:
 - Insight Timer app
 - 10% Happier app
 - Mind Space app
 - Calm app
 - Healthy Minds app (donation-based)
- Affirmations:
 - ThinkUp app
 - Books by Louise Hay
- Grounding exercises
- Journaling, yoga, prayer



Stress/anxiety reduction

- Exercise/movement
- Eye Movement Desensitization and Reprocessing (EMDR)
- Anxiety Release App (based on EMDR)
- Emotional Freedom Technique (EFT) - tapping
- Heartmath™
- Reducing caffeine
- Improve sleep
- Heal the gut!!!
- Social connection – call friends/family, get together!
- Therapy, counseling, cognitive behavior therapy
- Medication, if indicated



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Stress/anxiety reduction

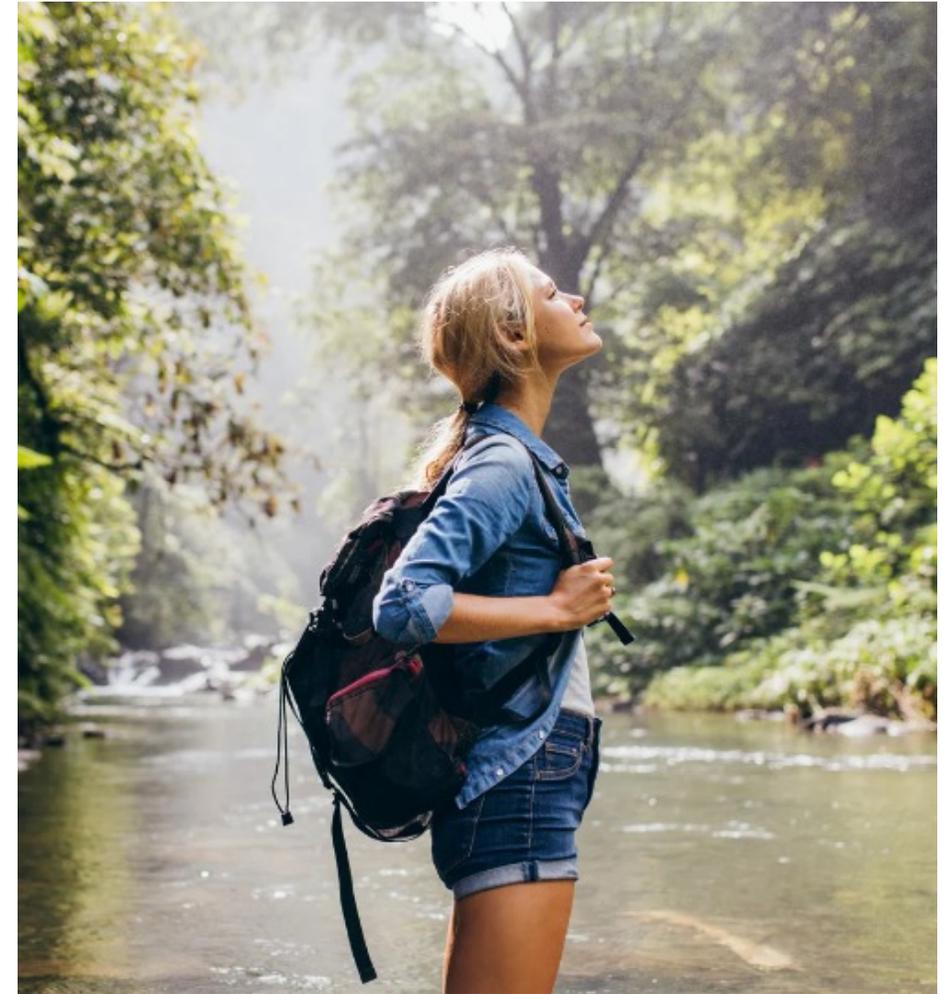
- Get into the great outdoors!

The health benefits of the great outdoors: A systematic review and meta-analysis of greenspace exposure and health outcomes

Caoimhe Twohig-Bennett*, Andy Jones

5. Conclusions

This review suggests that greenspace exposure is associated with wide ranging health benefits, with meta-analyses results showing statistically significant associations with reduced diastolic blood pressure, heart rate, salivary cortisol, incidence of type II diabetes and stroke, all-cause and cardiovascular mortality, as well as health-denoting associations with pregnancy outcomes, HRV, and HDL cholesterol, and self-



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Twohig-Bennett C, et al. The health benefits of the great outdoors: A systematic review and meta-analysis of greenspace exposure and health outcomes. Environ Res. 2018;166:628-637.

Stress/anxiety reduction



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Stress/anxiety reduction



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Stress/anxiety reduction



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Calming herbs, adaptogens and supplements

- Milky oats, Ziziphus (jujube), passionflower, chamomile, lemon balm, magnolia
- Valerian (stimulating in 10% of the population)
- California poppy (may also reduce pain)
- Holy basil adaptogenic herb (also helps to regulate blood sugars)
- Skullcap and Rhodiola adaptogenic herbs
- Ashwagandha (note that it is a nightshade)
- L-theanine, GABA, pregnenolone, Honokiol
- Phosphatidylserine



Holy basil

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Avoid intense exercise – Don't overdo it!

- Intense exercise increases cortisol.
- It can elevate androgens.
- It can lead to dysglycemia and insulin issues.
- It can negatively affect body systems, such as cardiovascular health and immune health.
- It can shut down sex hormone production and ovulation.
- It can lead to injuries.
- It can lead to nutrient deficiencies.



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Avoid sedentary lifestyle– Don't underdo it!

- Exercise helps improve insulin sensitivity.
 - It reduces stress and anxiety.
 - It helps with weight loss.
 - It improves sleep.
 - It improves mood.
-
- All things we want for our patients diagnosed with PCOS!
-
- Apps: Down dog, Tone It Up, IFIT, etc.



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Regulate blood sugars

- Berberine – 500mg TID with meals
- Inositol – 1000-2000mg/day (inositol cheaper than D-pinitol)
- D-pinitol – 1000-2000mg/day
- Chromium – 500-1000mcg/day
- Fish oil – 1000-3000mg/day
- Cinnamon – consider using as a spice routinely
- N-acetyl-cysteine – 500-1000mg/day
- Zinc – depends on needs and if deficient 10-100mg/day (be aware of copper)
- Alpha lipoic acid – 500-1000mg/day
- Green tea (EGCG) – 500-1000mg/day
- Gymnema – 250-500mg/day
- Medication: Metformin (Glucophage)
- Weight training and resistance training

Herbal anti-androgens

- Vitex (debatable)
- Spearmint tea
- Chamomile
- Licorice (caution if high blood pressure or high cortisol)
- White peony
- Green tea
- Black cohosh
- Red reishi
- Cordyceps



Cordyceps

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Natural 5 α -reductase blockers

- Saw palmetto – 250-1000mg/day
- Reishi mushroom – 500-1000mg/day
- Stinging nettle root – 250-500mg/day
- Pygeum africanum – 250mg/day
- Polyunsaturated fats (PUFAs)
- Epigallocatechin gallate (EGCG) – 250-500mg/day

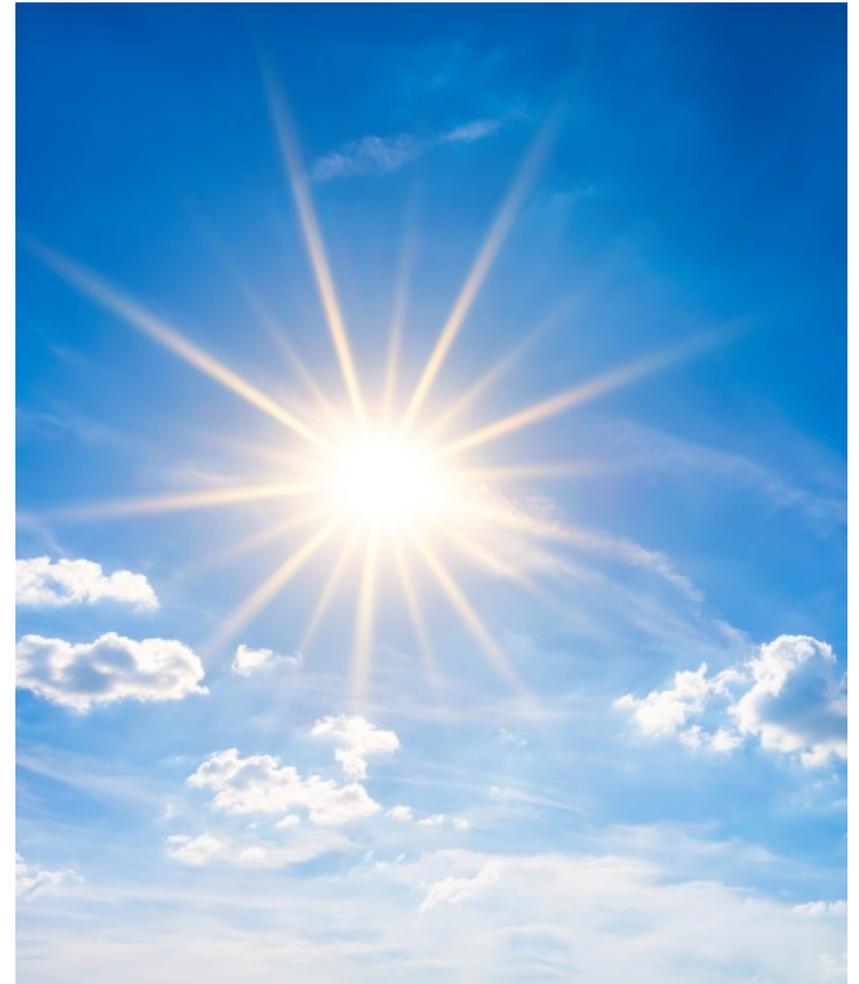


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Support the circadian rhythm and sleep

In the morning...

- 30 minutes minimum outdoors, preferably in the morning.
- No sunglasses, windows, or windshields – it will take 7 to 50+ times longer and you won't get enough to stimulate the cortisol pulse on time. Glasses/contacts don't interfere.
- A "happy light" will also work indoors (10,000 Lux; 20-30 minutes a day, 11-15 inches from the head; before 9 am).
- Enjoy caffeine (if desired and appropriate) before 12 pm.



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Support the circadian rhythm and sleep

During the day...

- Time-restricted eating:
 - Eating during daylight hours
 - Stop eating by 7 pm
 - Keep to a 12-hour eating window
- Eat earlier in the day rather than later - insulin sensitivity is best in the morning.



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Support the circadian rhythm and sleep

In the evening...

- Start winding down 1-2 hours before bedtime.
- Create bedtime rituals (favorite book, tea, face mask, bath, journal, meditate, pray).
- Clear your mind...keep a bedside journal to jot down notes.
- Consider lavender essential oil (diffuser, in bath, on a pillow).
- Avoid alcohol and sugar before bed.
- Avoid stimulatory exercise in the evening.



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Support the circadian rhythm and sleep

In the evening...

- Avoid blue/white light and screens 2 hours before bed.
- Dim household lights with the sunset.
- In the evening use lamps (low-angle light) instead of bright overhead lighting.
- Intrinsically photosensitive retinal ganglion cells (ipRGCs) are more easily activated by blue light than red lights so you can either use red wavelength lighting ≤ 10 lux (such as Philips Hue or similar smart bulbs) or wear blue blockers in the evening paired with dim lighting.
- Utilize F.lux app for computers and NightShift for iPhone which reduces blue light.



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Support the circadian rhythm and sleep

At night...

- Blue light signals "day" to our brains - block it at night!
- Create a sleep sanctuary (eye mask, blackout curtains, ear plugs, cotton sheets, weighted blanket).
- Keep bedroom cool (60-67 degrees F).
- Get a nightlight for the bathroom so that you do not need to turn the light on at night when you wake up and need to go!
- Keep to a regular schedule: Go to bed at the same time and wake up at the same time.
- Some say that sleep in the hours before midnight are twice as potent as hours after midnight.



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Support the circadian rhythm and sleep

At night...

- Consider choosing botanicals and sleep-building supplements before “sleeping pills.”
- Consider melatonin supplementation.
- Consider how pets, children, noises, your partner's snoring, street lights, etc. may be affecting your sleep.
- Consider a sleep study to evaluate for sleep apnea or other sleep disorders.
- Look into the possibility of medications you are taking affecting your sleep.
- Enjoy a few grams of protein before bed (if you suspect you are waking up due to low blood sugar).



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Thank You!

For questions, contact:

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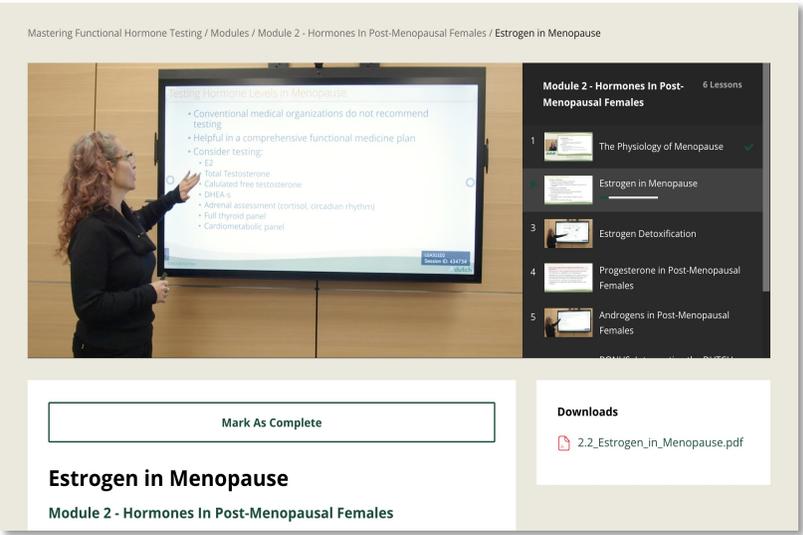


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