The Case of PCOS:
Evaluating the difference between ovarian and adrenal hormones

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Objectives

- Understand the typical presentation
- Review how to diagnose true PCOS
- Discuss insulin's role
- Review the androgens
- Understand what other labs you might run
- Case review
- Understand different treatments

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PCOS:
polycystic ovarian syndrome

It seems to fall on a spectrum
sometimes it involves insulin
sometimes it's really an adrenal problem

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How the usual story goes…

- Menarche began later in teen years if at all or began ‘on time’ and then was very irregular ever since.
  - put on the birth control pill as a result
- Cystic acne started to develop as did hair growth in places she didn’t want
  - The nipple area, top lip, chin area →put on Spironolactone and/or Accutane
- Started gaining weight around the middle despite trying a “good diet” and regular exercise
- By the twenties and thirties hair started thinning/falling out

Why is she seeing you?

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She wants to get pregnant so she stopped the pill and never got her period back

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What is the typical presentation?

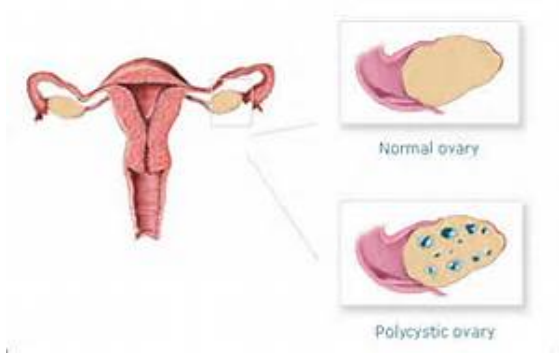
Androgen Excess

1. Hirsutism
2. Male pattern hair loss
3. Acne/cystic acne
4. Anger/irritation/mood swings

Ovulatory issues

1. Anovulation
2. Irregular cycles/oligomenorrhea
3. Fertility challenges

Polycystic Ovary Morphology (PCOM)



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Diagnostic: 2 out of 3

1. Androgen excess (labs and symptoms)
2. Ovulatory dysfunction
3. Polycystic Ovarian Morphology

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Is obesity part of the diagnosis?

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Is obesity part of the diagnosis?

Not always →30%-75% are obese
Insulin is the big culprit!

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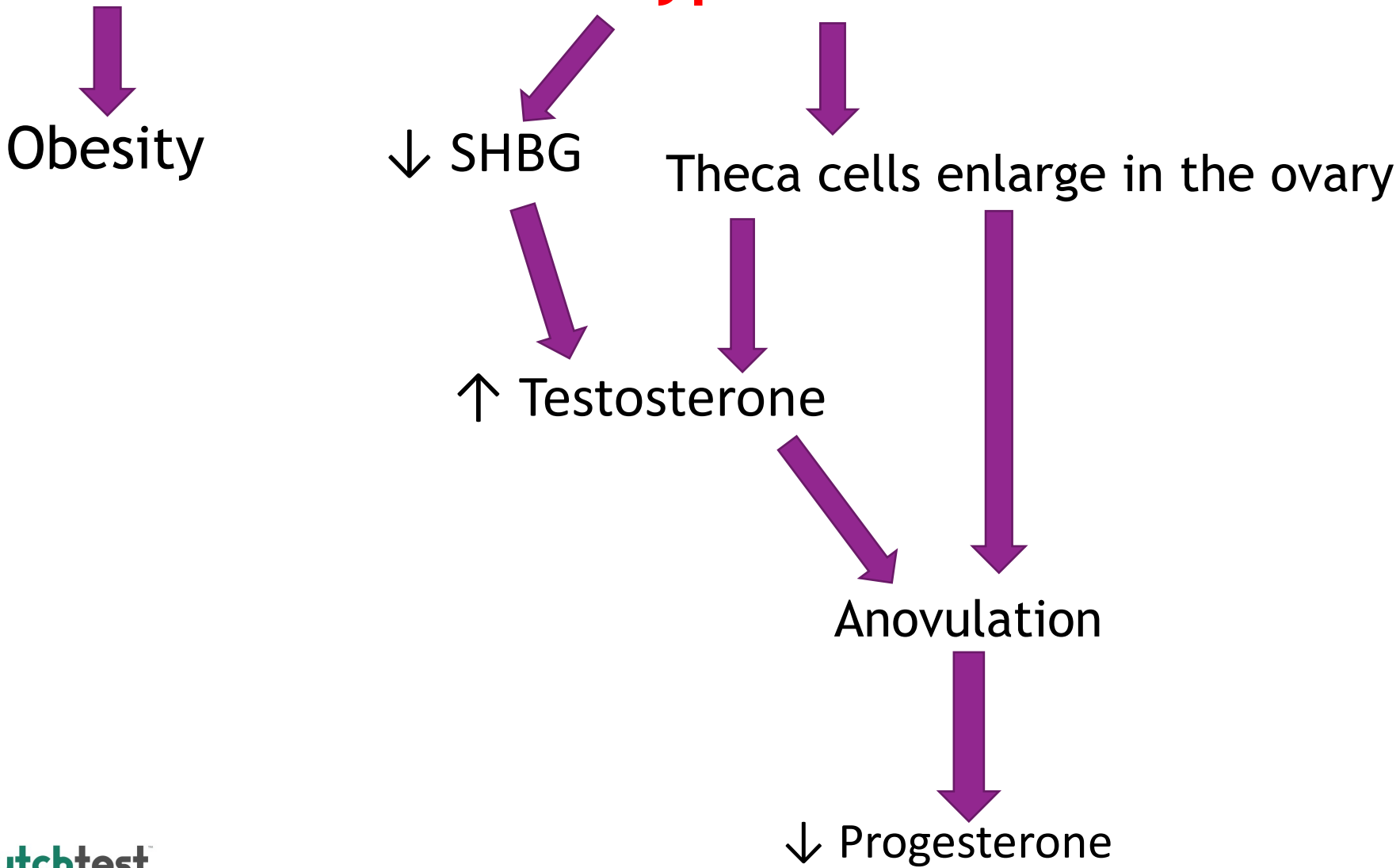
Insulin Resistance → Hyper-Insulinemia



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Remember: It's not just an ovarian problem

The Ovaries produce roughly:

→25% of the Testosterone

→50% of the Androstenedione

→ 20% of the DHEA (not DHEA-S)

The Adrenals produce roughly:

→25% of the Testosterone

→50% of the Androstenedione

→80% of the DHEA

→100% of the DHEA-S

The other 50% of Testosterone is made in adipose tissue via androstenedione conversion

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"While insulin resistance and elevated insulin often drive the ovarian production of testosterone, it is the hypothalamus-pituitary-adrenal (HPA) axis that stimulates the production of DHEA/DHEA-S and androstenedione. These hormones can be converted to testosterone by peripheral tissues in the body. This process can occur independently from the ovaries and any involvement with insulin.

This means that a woman with PCOS symptoms could have normally functioning ovaries with no cysts and no insulin resistance, yet still fit the symptomatic profile of the syndrome."

-Laura Schoenfeld, MPH, RD - www.chriskresser.com

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What you're telling me is… maybe it's the adrenal glands?

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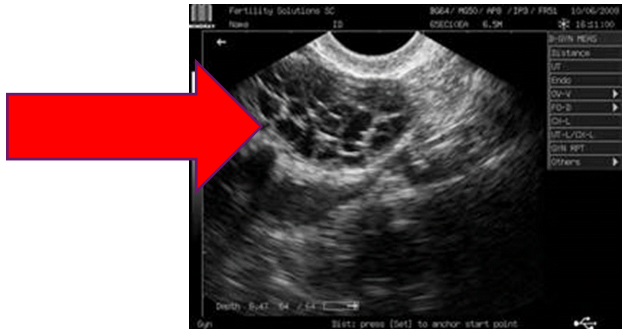
What should you consider testing?

- Fasting glucose/Fasting insulin (Hemoglobin A1c, 2hr glucose insulin tolerance test
- Thyroid panel with antibodies and rT3
- Prolactin
- FSH/LH
- Cardiovascular testing
- Leptin?

- 17, hydroxyprogesterone
- Anti-mullerian hormone
- *Consider a pelvic u/s



- Hormone testing

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Hormone testing: what is DUTCH?

- It's an acronym!

- Dried
- Urine
- Test for
- Comprehensive
- Hormones

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What do you get in a DUTCH test?

1. Androgen Metabolism
2. Estrogen Metabolism
3. Progesterone Metabolites
4. Metabolized Cortisol/Cortisone
5. Free Cortisol/Cortisone
6. The Diurnal Pattern (Can include the CAR)
7. DUTCH Extras: includes OATs, Melatonin and 8-OHdG

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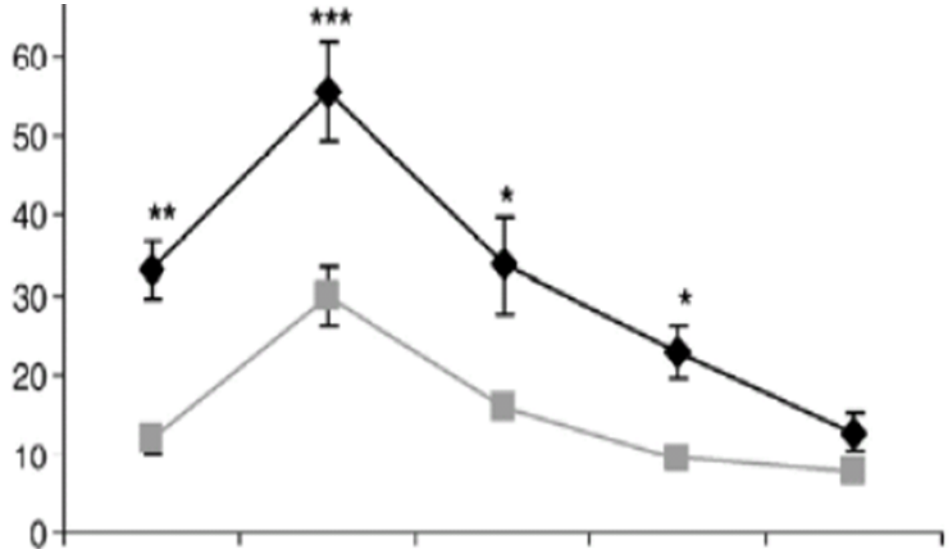
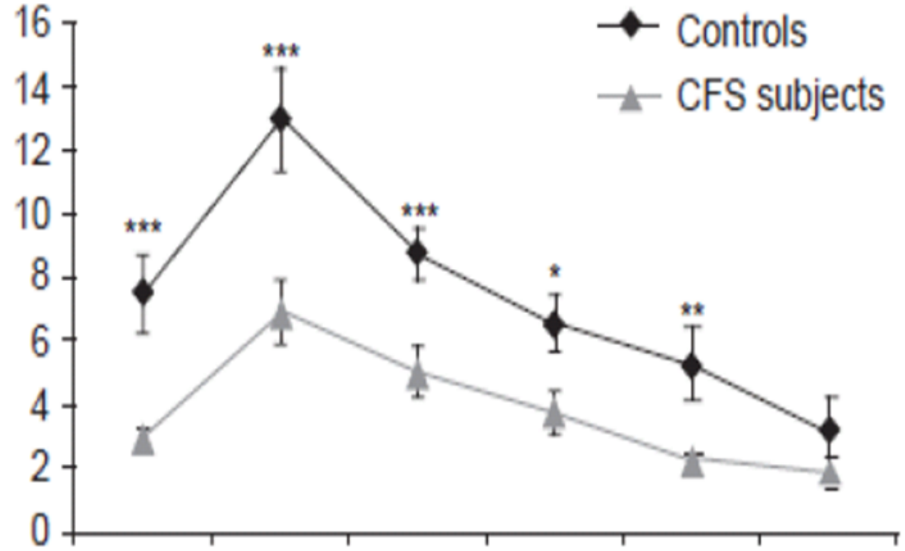
Those who are new to spot urine testing and use saliva:

Urinary Free Cortisol



Salivary Free Cortisol



Jerjes, (2005, 2006)

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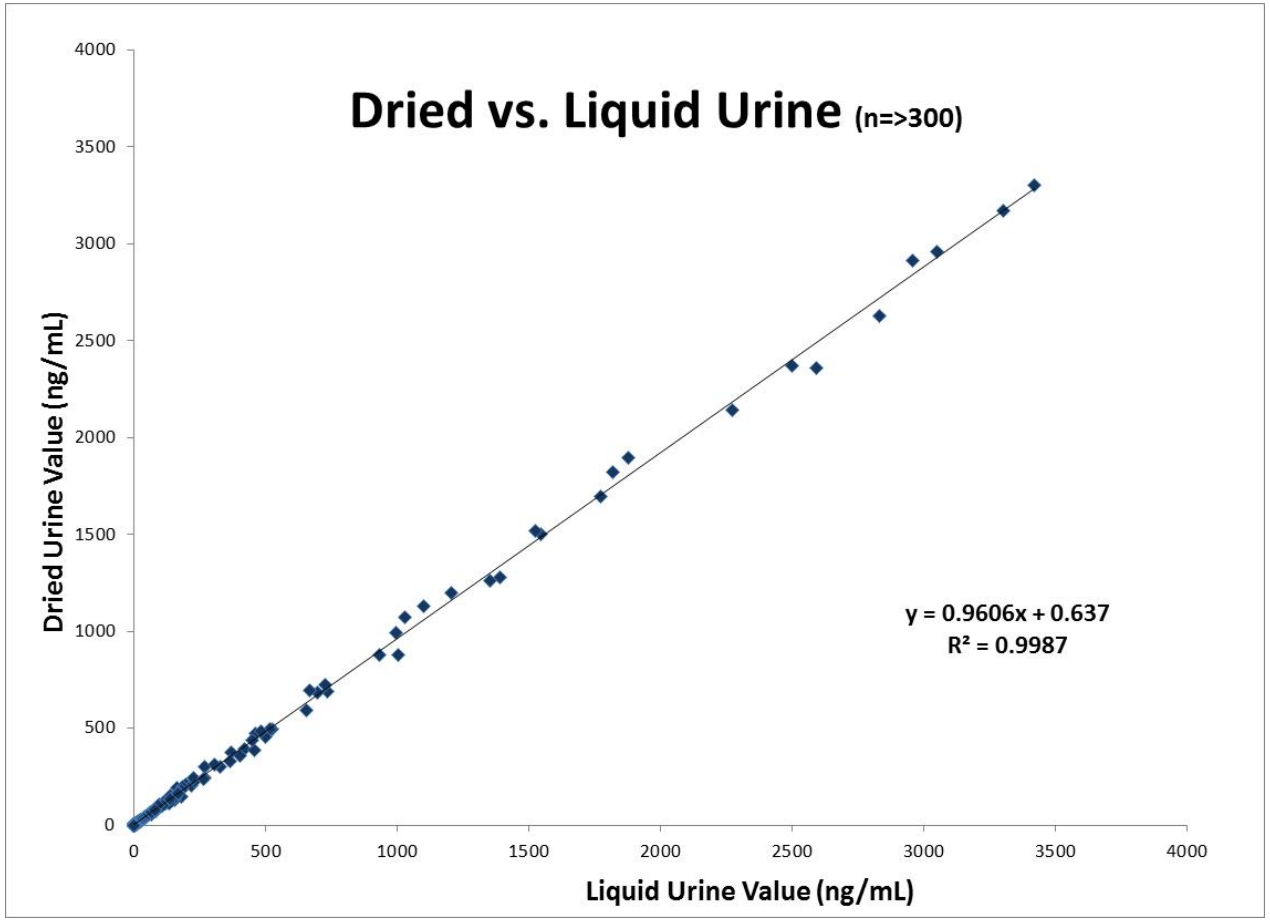
Dried versus Liquid Urine



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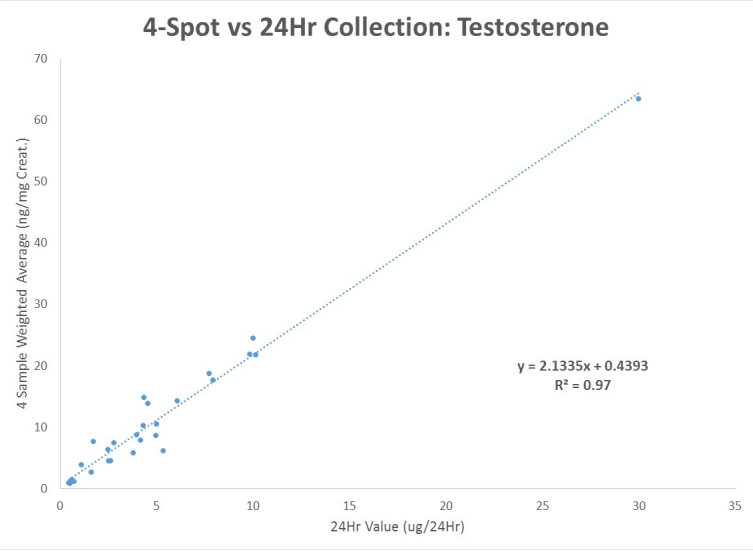
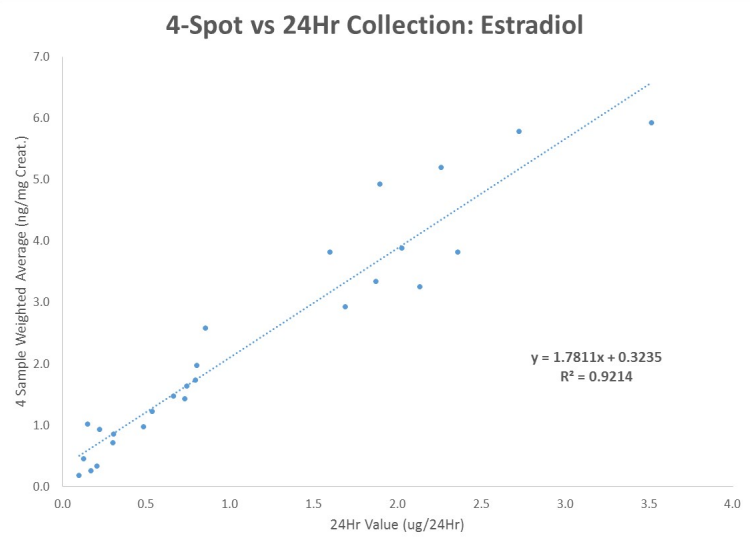
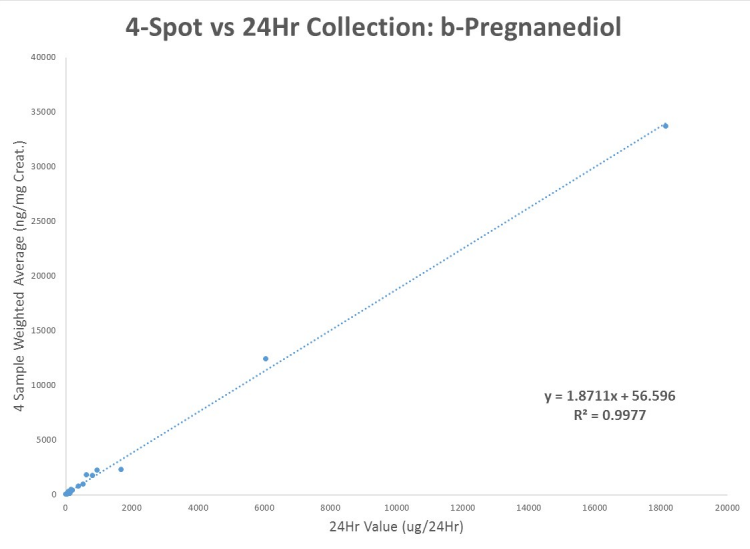
24-Hour Correlation







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Dried urine versus Serum

- Precision Analytical has shown statistical equivalence between dried urine results and serum results drawn on the same day – Publication pending (stay tuned!)

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DUTCH Complete Test Collection

The Flagship dried urine only test

4 urine samples done throughout the day and dried

1. First thing on waking
2. 2 hours later
3. Around dinner
4. Before bed
   - Optional 5th strip if wake and urinate in the middle of the night

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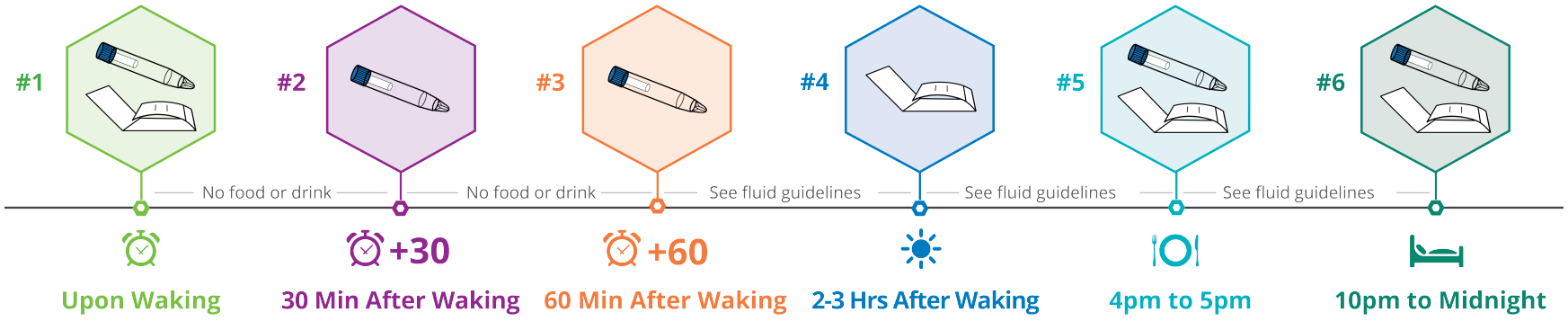
COMPLETE WITH CORTISOL AWAKENING RESPONSE

5 Saliva collections
- Waking, +30 min, +60 min, 5pm, Bedtime
- Easier collections using cotton swabs

4 Dried urine collections



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When should you test hormones?

- Still cycling regularly? Days 19, 20 or 21 of a typical 28 day cycle
- Long or short cycles but regular? Shift up or down accordingly
- Irregular cycles? Do ovulation predictor kits or track ovulation signs until positive then test 5-7 days after that
- No ovulation and irregular? Call the office for help.

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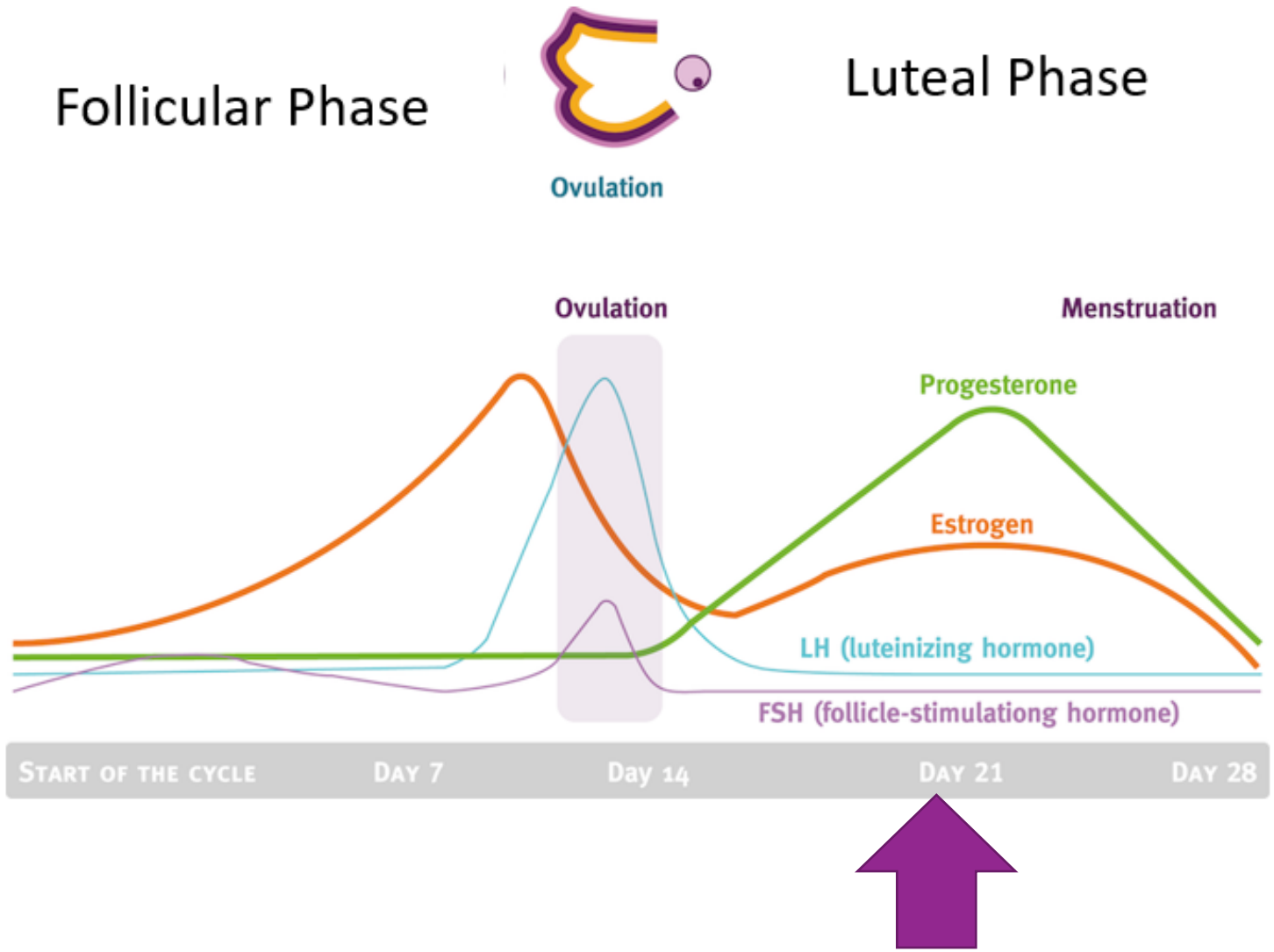
Why testing in the luteal phase is important



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Case Study: 33yo female presents with

- Recent (!) irregular cycles the last 6 months
- Noticing more acne and hair growth on her face
- Her primary doctor diagnosed PCOS = suggested the pill

- High stress (married mother of 2, in a PhD program)
- Gut infection – recently diagnosed with SIBO, has symptoms
- Normal weight, glucose/insulin wnl, Thyroid wnl, prolactin wnl

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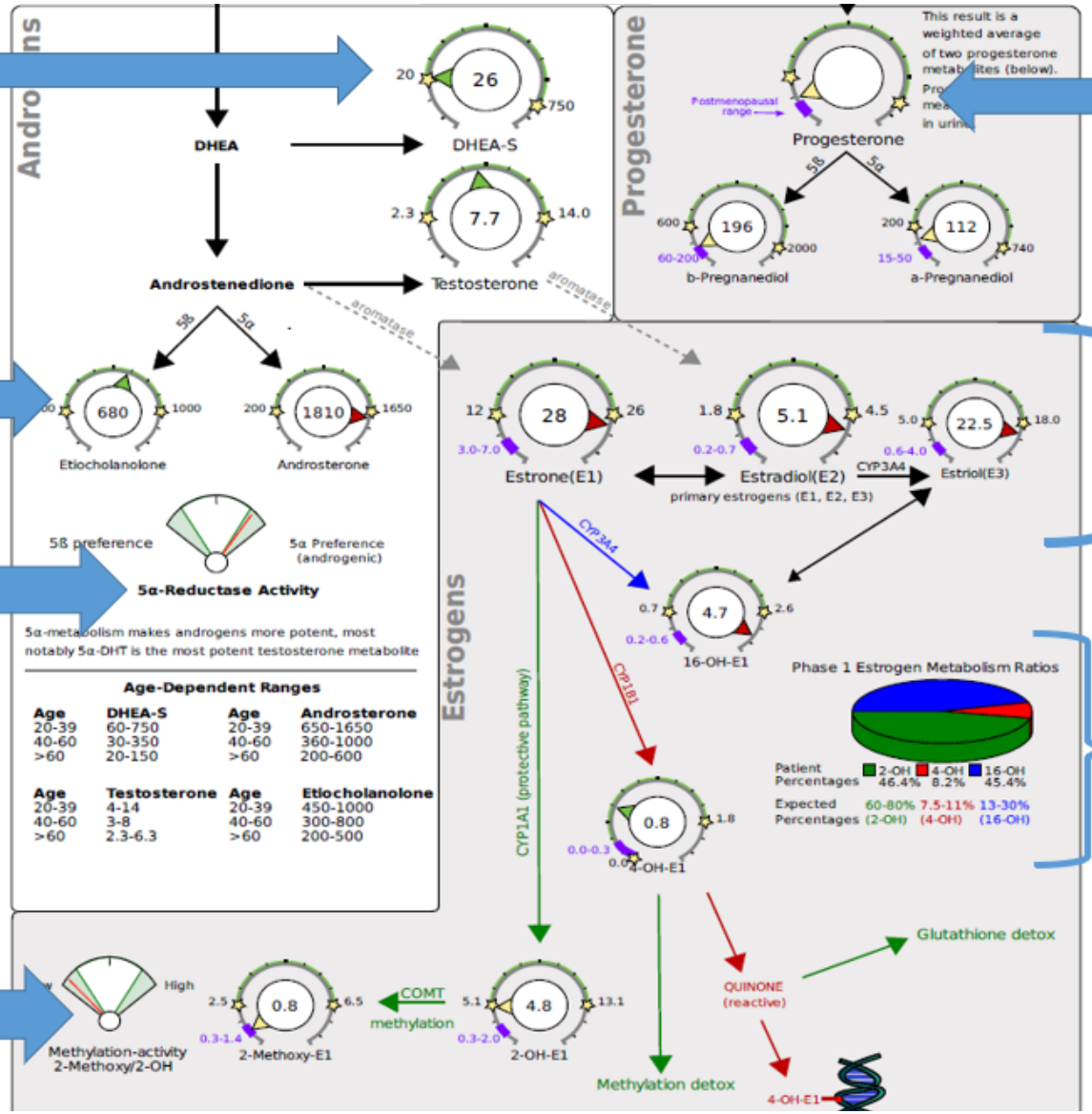
Lower DHEA-s
=inflammation

Elevated
DHEA
metabolites

5a Reductase
dominant

Sluggish phase
2 detox



Not ovulating = low
progesterone

Estrogen
dominant

Unhealthy Phase 1 detox –
favors the 4OH and 16OH

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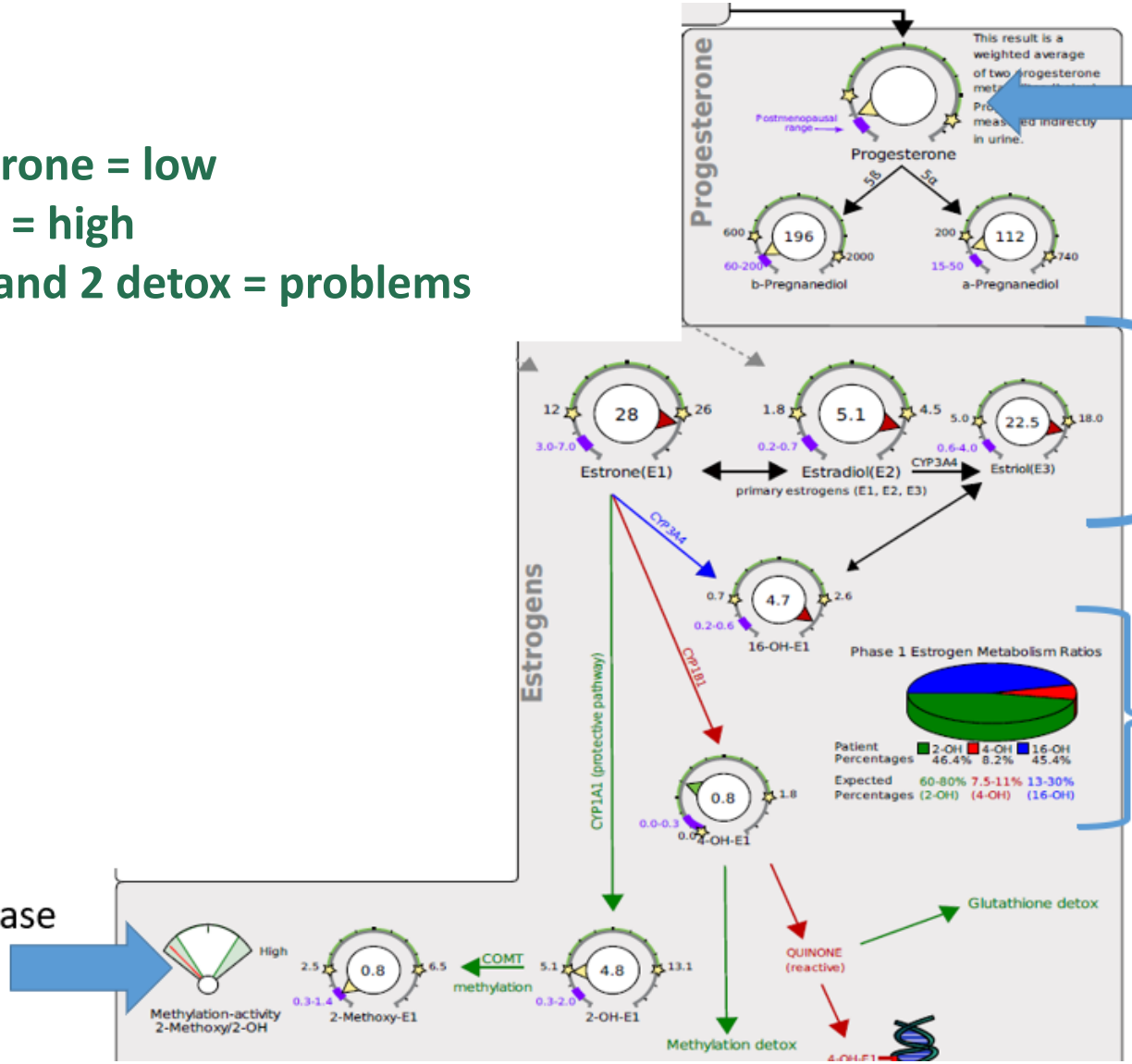
Summary:

- Progesterone = low
- Estrogen = high
- Phase 1 and 2 detox = problems



Not ovulating = low progesterone

Estrogen dominant

Unhealthy Phase 1 detox – favors the 4OH and 16OH

Sluggish phase 2 detox

(COMT?)

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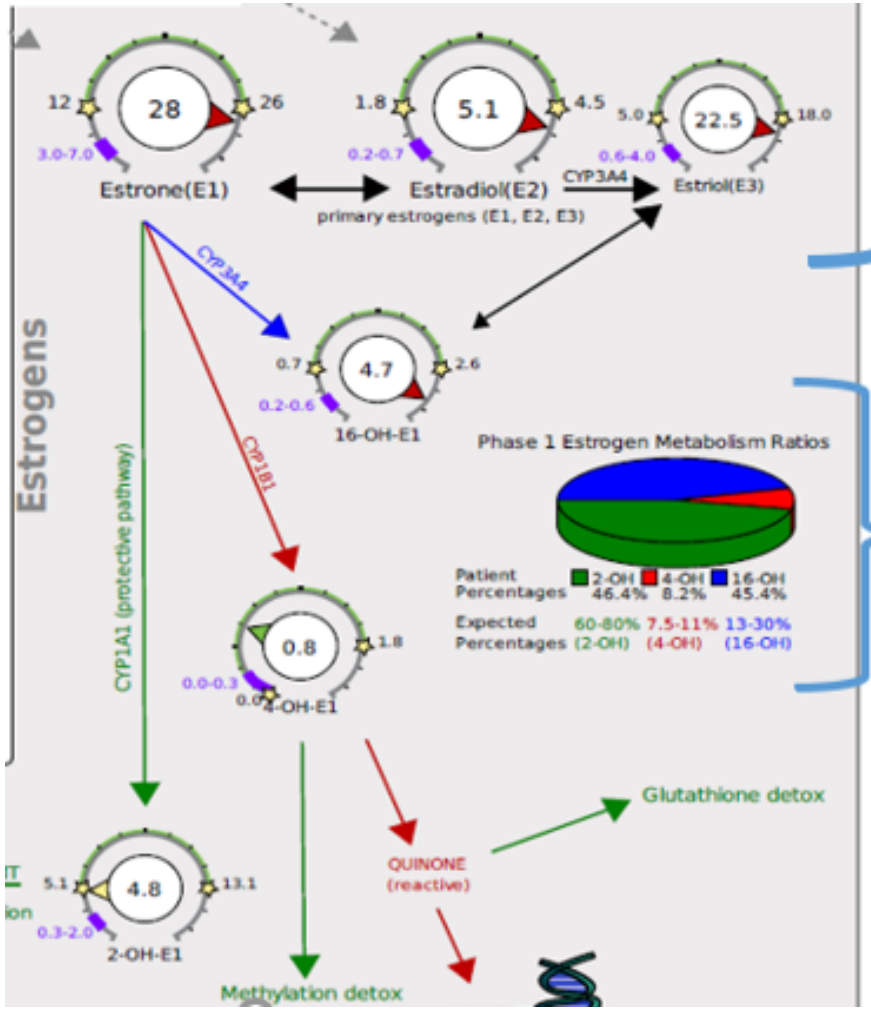
Quick review of estrogen detox phase 1:



Estrogen dominant

Unhealthy Phase 1 detox – favors the 4OH and 16OH

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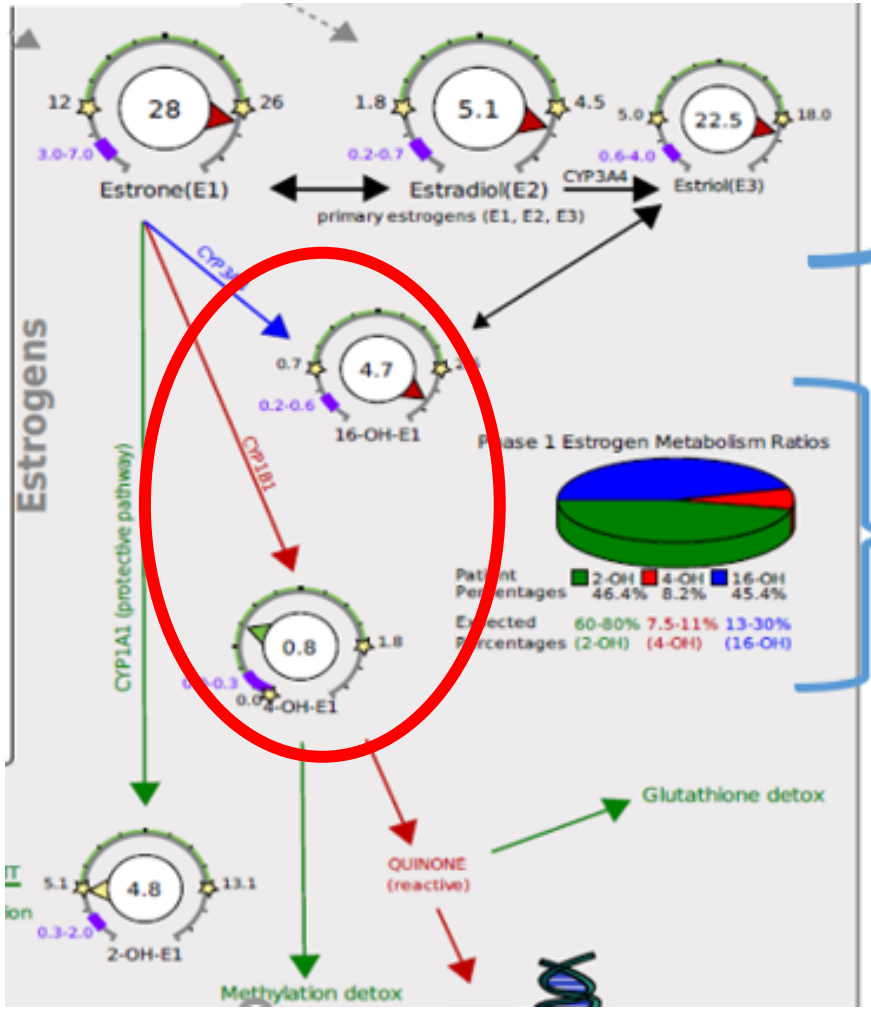
Quick review of estrogen detox phase 1:



Estrogen dominant

Unhealthy Phase 1 detox – favors the 4OH and 16OH compared to the 2OH

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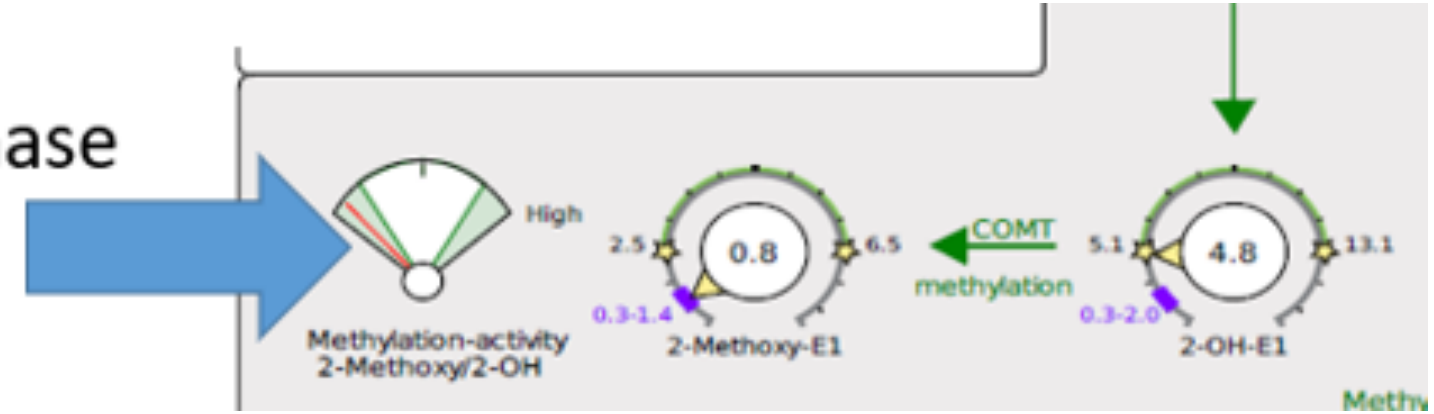
Quick review of estrogen detox phase 2:

Sluggish phase 2 detox (COMT?)



The ability to move from 2-OH to 2-Methoxy

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Androgens:

Do you go down the pathway that causes hair loss, acne, and facial hair growth in unwanted places?

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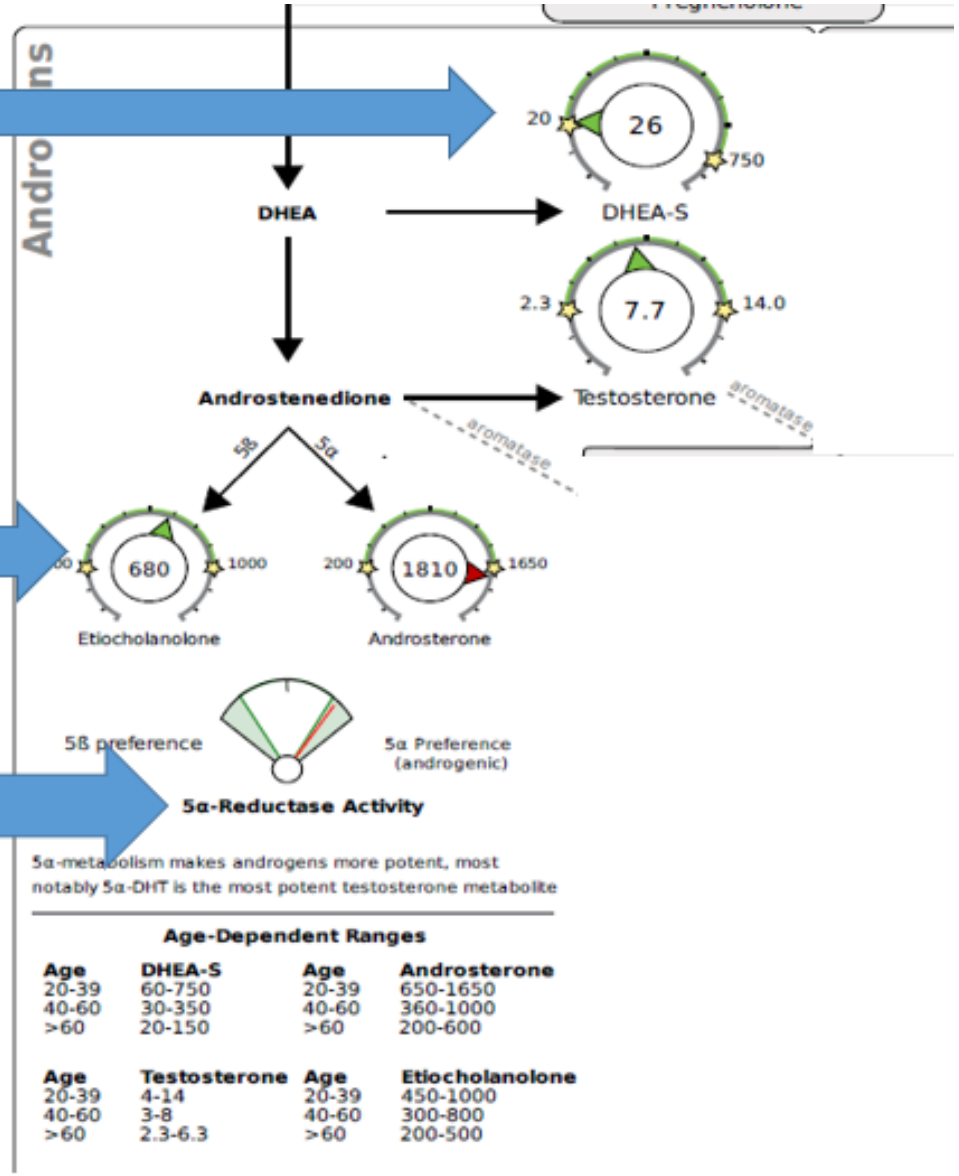
Lower DHEA-S
=inflammation

Elevated
DHEA
metabolites

5a Reductase
dominant



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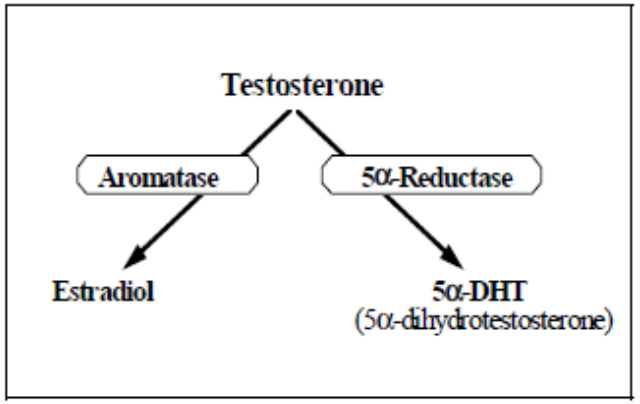
What is 5a-Reductase?

- Converts testosterone in to **more potent** DHT/alpha metabolites
- Symptoms: acne, hirsutism, hair loss on head, anger/irritation
- Increased via: genetics, inflammation, insulin, obesity



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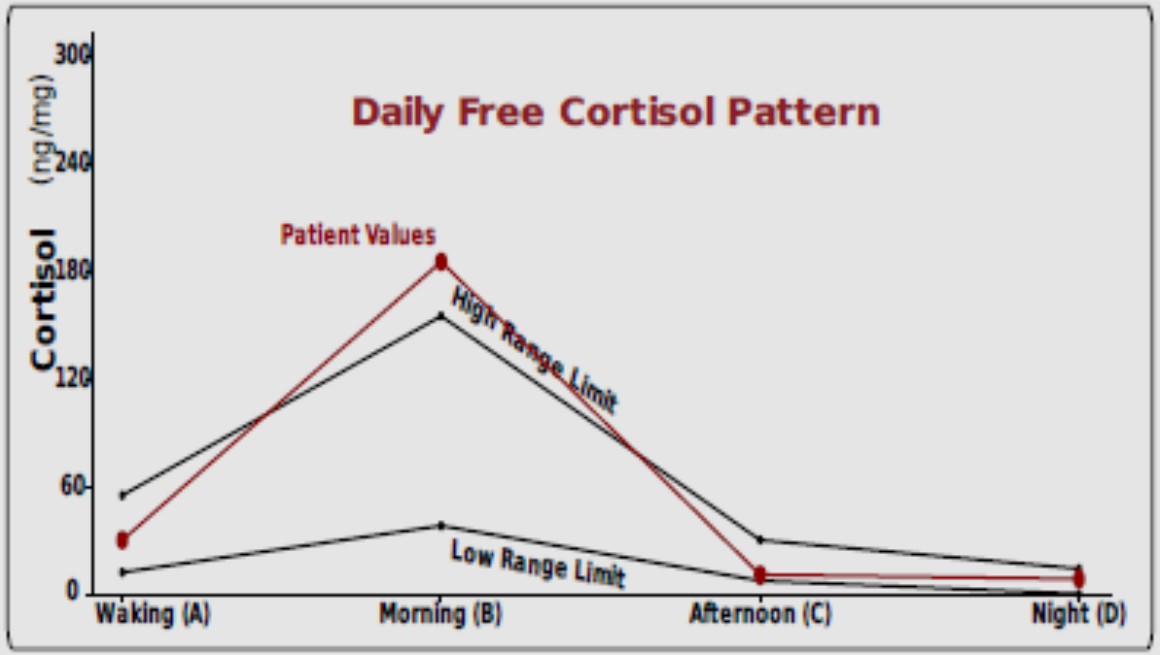
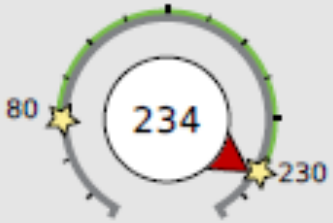
What did her adrenals look like?





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

cortisol metabolism

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

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

She's making a ton of cortisol – it's all red!

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What do her DUTCH Extras/Organic Acids look like?

DUTCH Extras					
Category	**Test**		**Result**	**Units**	**Normal Range**
Melatonin (*measured as 6-OH-Melatonin-Sulfate) - (Urine)					
	Melatonin* (Waking)	Within range	46.7	ng/mg	10 - 85
Oxidative Stress / DNA Damage, measured as 8-Hydroxy-2-deoxyguanosine (8-OHdG) - (Urine)					
	8-OHdG (Waking)	Within range	1.2	ng/mg	0 - 5.2
Nutritional Organic Acids					
Vitamin B12 Marker (may be deficient if high) - (Urine)					
	Methylmalonate (MMA)	Within range	0.9	ug/mg	0 - 2.8
Vitamin B6 Marker (may be deficient if high) - (Urine)					
	Xanthurenate	High end of range	1.3	ug/mg	0 - 1.6
Glutathione Marker (may be deficient if low or high) - (Urine)					
	Pyroglutamate	Below range	26.7	ug/mg	37 - 70
Neurotransmitter Metabolites					
Dopamine Metabolite - (Urine)					
	Homovanillate (HVA)	Low end of range	4.8	ug/mg	4.5 - 13
Norepinephrine/Epinephrine Metabolite - (Urine)					
	Vanilmandelate (VMA)	Below range	0.4	ug/mg	2.7 - 6.4
Serotonin Metabolite - (Urine)					
	5-Hydroxyindoleacetate (5HIAA)	Below range	2.5	ug/mg	3 - 7.5

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Let's focus in…

Neurotransmitter Metabolites				
Dopamine Metabolite - (Urine)				
Homovanillate (HVA)	Low end of range	4.8	ug/mg	4.5 - 13
Norepinephrine/Epinephrine Metabolite - (Urine)				
Vanilmandelate (VMA)	Below range	0.4	ug/mg	2.7 - 6.4
Serotonin Metabolite - (Urine)				
5-Hydroxyindoleacetate (5HIAA)	Below range	2.5	ug/mg	3 - 7.5

Low HVA and VMA: Maybe COMT?
Low 5HIAA? Maybe high estrogen/cortisol/gut

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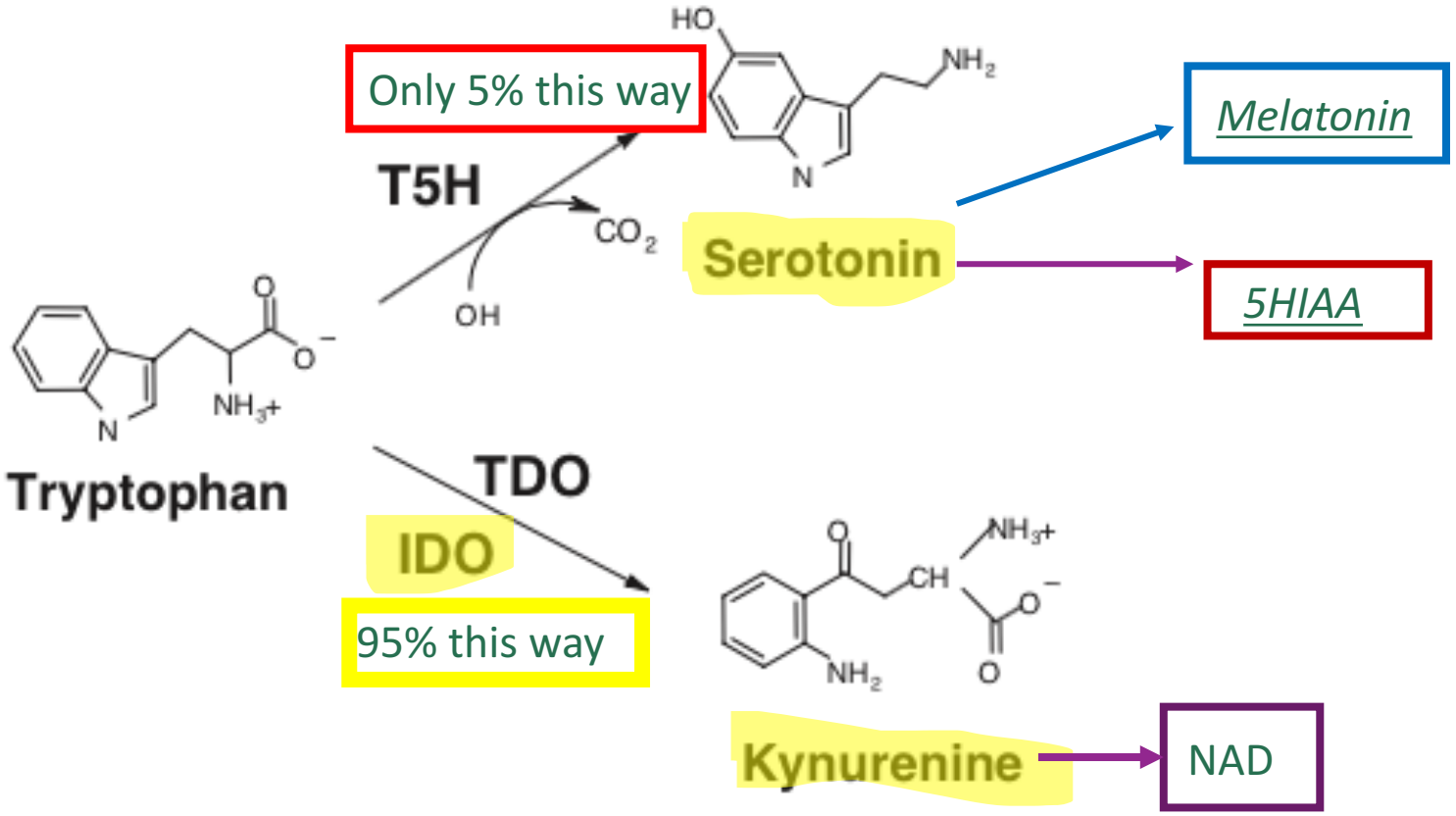
Tryptophan can choose 2 pathways



***Excess estrogen, cortisol, inflammation* and LPS push →**

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What do you do?
Where do you start?
Is it really PCOS?

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Health Goals:

- Address the cause!
- Focus on diet and lifestyle
- Improve cortisol levels!
- Address blood sugar and insulin
- Restore ovulation, improve estrogen balance
- Reduce androgenic symptoms

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First, address the cause

In the case study, high stress and gut inflammation is likely upregulating the HPA axis resulting in high cortisol (weight gain, irregular cycles), and elevated androgens (acne and hirsutism)

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Second: address diet/insulin/lifestyle factors

- Berberine – 500mg TID with meals
- Inositol – 1000-2000mg/day (some use inositol as cheaper than D-pinitol)
- D-pinitol – 1000-2000mg/day
- Chromium – 500-1000mcg/day
- Fish oil – average dose is 1000-3000mg/day
- Cinnamon – consider using as a spice routinely
- N-acetyl-Cysteine – 500mg-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, drinking several cups/day helps too
- Gymnema – 250-500mg/day
- Medication: Metformin (Glucophage)
- Weight training and resistance training

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Third: address the stress/cortisol

- Address the cause, meditation, acupuncture, journaling, counseling, finding joy/happiness, proper sleep hygiene
- Adaptogens
- Calming support examples:
  - Phosphatidyl Serine – 100-400mg
  - Ocimum sanctum (Holy Basil) – 500-1500mg/day in divided doses
  - Magnolia bark – 250-500mg at night
  - Scutellaria lateriflora (Skullcap) – 200-500mg/day often at night
  - l-theanine – 200-1000mg/day divided doses

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Fourth: Improve ovulation/progesterone

- Vitex agnus-castus (Chaste Tree berry) – 250mg-500mg daily
- Vitamin B6 (P5P) – 25-100mg P5P
- Maca (be aware this could also raise androgens and estrogen) – 1000-2000mg/day
- Cordyceps – 500-1000mg/day
- Evening primrose oil – 500mg-1000mg/day
- Homeopathics
- Seed cycling
- Improve melatonin release from the pineal gland
- Bio-identical Progesterone
  - Topical, oral, sublingual, vaginal
  - Often done in the luteal phase only if the luteal phase is known
- Acupuncture

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Lastly: reduce androgen/5a symptoms

- Address the insulin and/or cortisol causes
- Spearmint tea is anti-androgenic
- 5a-Reductase “blockers”:
  - Serenoa repens (Saw palmetto) – 250-1000mg/day
  - Zinc – depends on needs and if deficient, 10-100mg/day (watch copper)
  - Urtica dioica (Stinging Nettles root) – 500-1000mg/day
  - Pygeum africanum (bark) – 500mg/day
  - Reishi mushroom- 500-1500mg/day
  - EGCG from green tea – 250-500mg/day
  - Spironolactone - medication

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What did I do for her?

- Sleep hygiene
- Morning routine/ask for help/stress reduction
- Regular eating patterns/be prepared
- Address her SIBO/gut symptoms first for a month
  - Then added:
  - Adrenal adaptogen
  - Chaste tree berry every morning
  - B-Complex with P5P

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5 month follow-up

- Husband and her mom were helping more with the kids
- Her digestion was significantly improved
- She worked hard to NOT skip meals
- She worked hard to NOT be on her computer at night (school)
- She had more energy, was in a better mood!
- Her last 2 cycles were perfectly normal
- Her skin had improved – breakout sometimes with PMS
- The hair growth was still there but not worse
- Repeating DUTCH Test and will go from there (ie. Estrogen detox)

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Having the most comprehensive,
easy to collect adrenal and hormone test
(now with DUTCH extras)
available allows you to make
a greater impact on your patients
at a deeper level.

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