

# Assessment & Approach to the Estrogen Dominant Patient

**Achieving Balance**

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# Today's Agenda

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- The Basics – Estrogen Dominance in Cycling Females
  - Symptoms and implications
- Review the Menstrual Cycle
  - Dig in to Progesterone and Estrogen
  - How key estrogen metabolites are persistently estrogenic
- How and when do we test?
  - Serum + Urine + Metabolites
    - Total vs Bioavailable
    - Production → Tissue Uptake → Active Transitional States → Inert End Products
- Use Urine + Serum to:
  1. Calculate PG/E2 Ratio to help determine need for progesterone
  2. Identify estrogenic detox products connected to symptoms
  3. Identify the source of estrogens and treat the foundation
- Outline high-yield therapeutics



Estrogen

Progesterone

# Estrogen/Progesterone Balance

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gut-function neuroprotection  
endocannabinoids  
skin-integrity  
cardioprotection bones immune-system  
vaginal-health cognition  
histamine-balance hair libido  
vitality

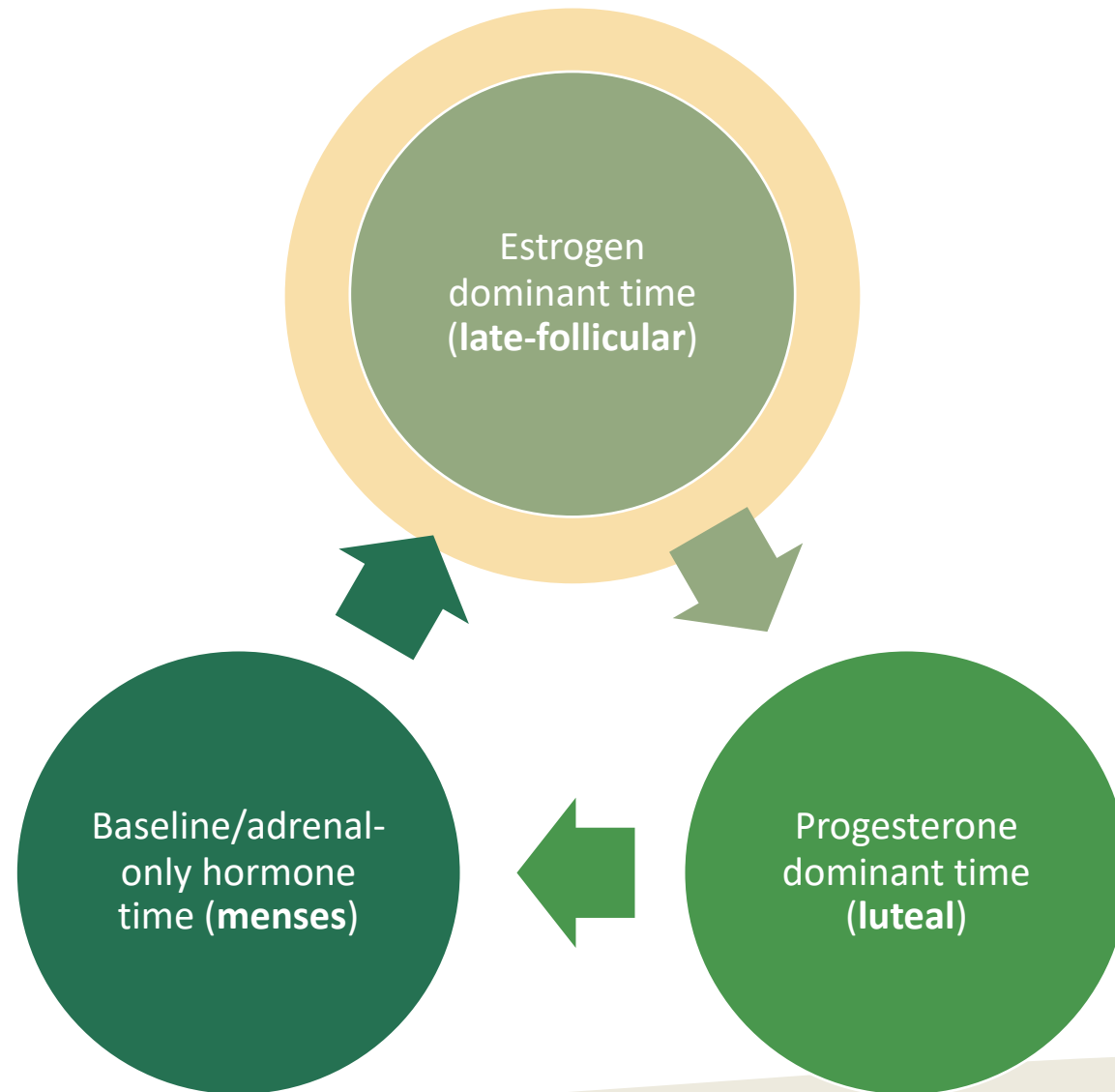
# Estrogen Dominant Clinical Signs

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- Acne (luteal)
- Allergic presentations/Histamine
- Autoimmune diseases
- Bleeding irregularities with cycles (can be absent, light, or heavy)
- Bloating
- Catamenial seizures
- Cyclic breast tenderness
- Fatty liver
- Fibroid development
- Headaches and Migraines
- Hot flashes (paradoxical)
- Inflammation
- Irregular or absent cycles (and fertility issues)
- Joint pain
- Mood lability (estrogen fluctuations)
- Recurrent pregnancy loss
- Skin discoloration including melasma
- Sleep problems
- Thyroid issues/Iodine deficiency
- Weight management problems

# Some Estrogen Dominance is Normal and Healthy

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# Consider the Menstrual Cycle

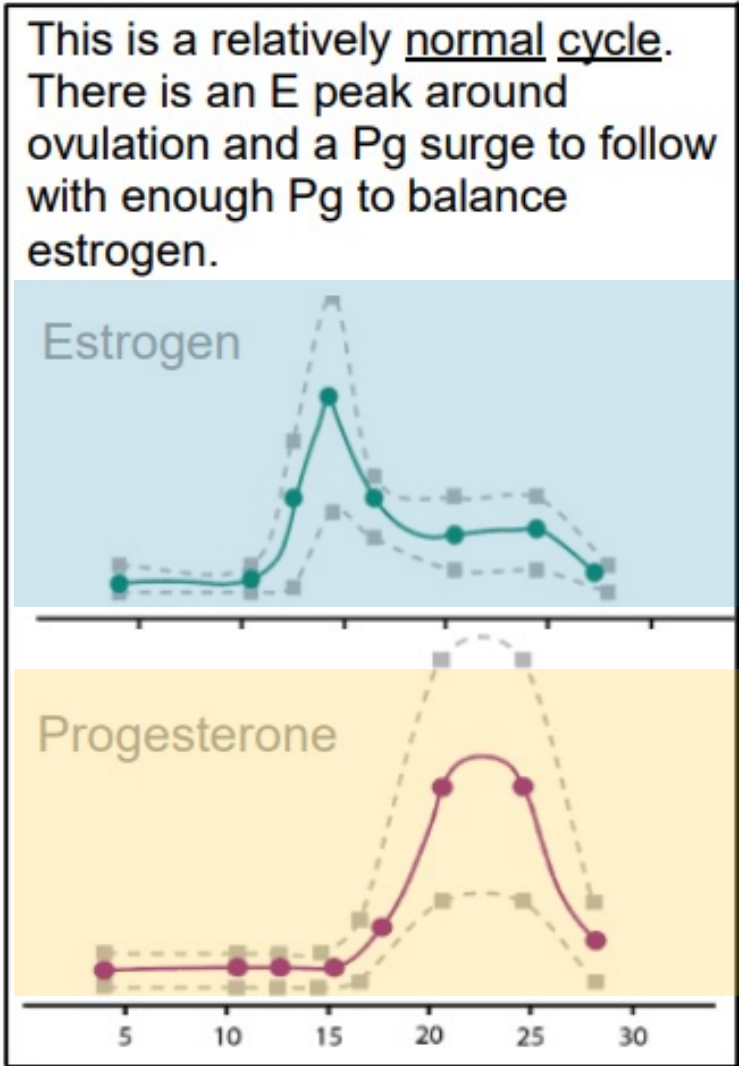
Estrogen and Progesterone **VARY** a LOT!  
But in a predictable way....



# Normal Menstrual Cycle (As depicted on a DUTCH Cycle Map)

- X axis = cycle day
- Y axis = hormone level result
- Ranges = gray dashed lines

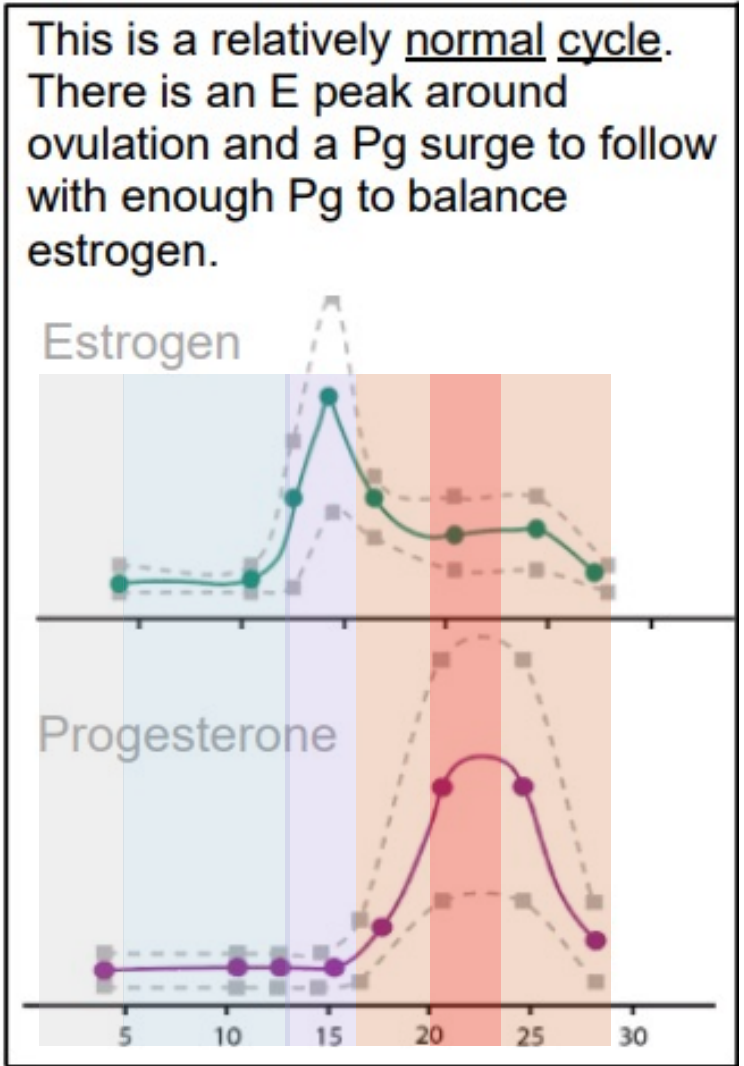
Menses	Hormone Withdrawal
Follicular Phase	Follicle Development
Periovulatory Phase	E2 +LH Surge
Luteal Phase	PG Surge
Mid-Luteal Single Spot	PG Peak Day



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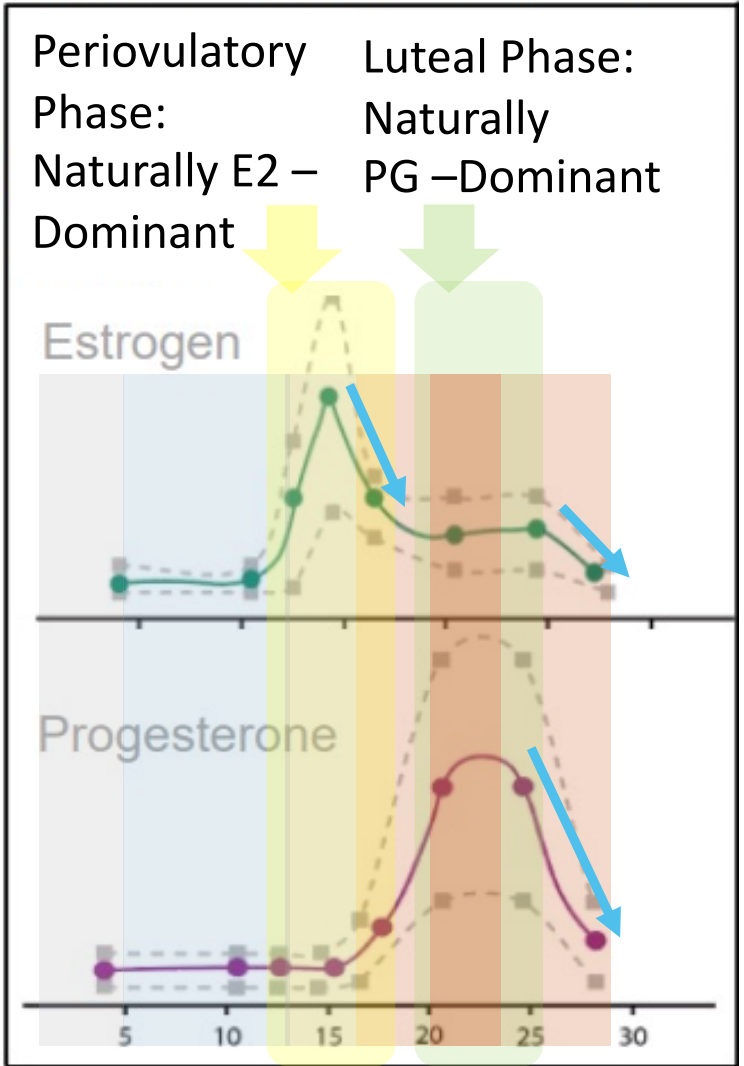
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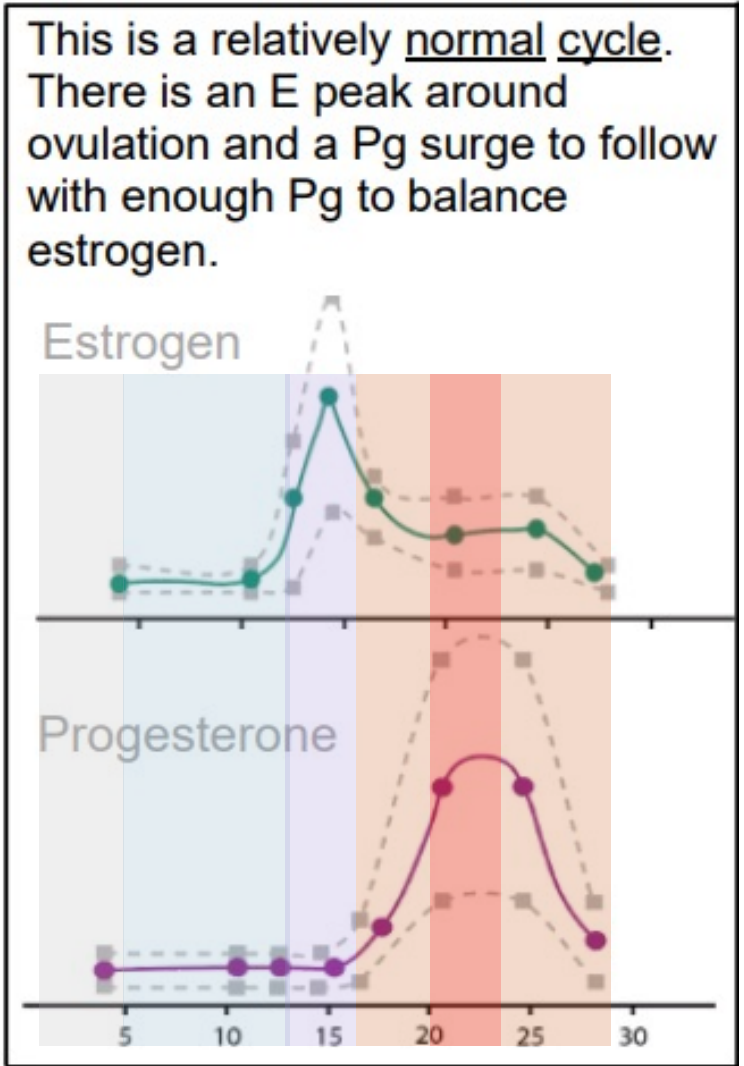
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Periovulatory Phase	E2 +LH Surge
Luteal Phase	PG Surge
Mid-Luteal Single Spot	PG Peak Day



# Normal Menstrual Cycle Nutritional and Hormonal Requirements

<b>Menses</b>	<b>Hormone Withdrawal</b>
Low FSH, LH, Estrogens and Progesterone Antioxidants + Nutrition: $\beta$ -carotene, C, $\alpha$ E, Sel, lutein, lycopene, P5P	
<b>Follicular Phase</b>	<b>Follicle Development</b>
Follicle development Oocyte GFs + FSH + LH communication - Myoinositol Normal T4 $\rightarrow$ T3, Testosterone, DHEA, E2, cortisol, Vitamin D, Melatonin Nutrition/Antiox: A,C, $\gamma$ E, rALA, Lutein, Lycopene, Zn, I <sub>2</sub> /GSH/NAC/Sel, $\Omega$ 3 Control follicular homocysteine: MTHF, HydroxoB12 Mitochondrial activity: CoQ10, Acetyl-l-carnitine, PQQ	
<b>Periovulatory Phase</b>	<b>E2 +LH Surge</b>
Normal LH + Androgens + Cortisol Nutrition: Myoinositol, Iron, I <sub>2</sub> , Zn, Vitamin D	
<b>Luteal Phase</b>	<b>PG Surge E2 Plateau</b>
Hormones: Progesterone, Vitamin D Inc Nutritional Needs: GLA oils, $\gamma$ E, Zn, Mg, P5P Higher protein intake requirement	



Progesterone is always  $>$  than Estrogen

# Notice the Units

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- Progesterone

- Serum ng/mL

- Typical Normal Luteal Range
      - 6 - 22 **ng**/mL (approx.)
    - Mid-Follicular Range
      - 0.3 – 0.5 **ng**/mL (approx.)

- Urinary  $\beta$ -Pregnanediol

- Normal Luteal Range
      - 600-2000 ng/mgCr (DUTCH)
    - Follicular Range
      - 100-300 ng/mgCr (DUTCH)

- Estradiol

- Serum pg/mL

- Typical Normal Luteal Range
      - 50 - 300 **pg**/mL (approx.)
    - Mid-Follicular Range
      - 20 - 60 **pg**/mL (approx.)

- Urinary Estradiol

- Normal Luteal Range
      - 1.8 - 4.5 ng/mgCr (DUTCH)
    - Follicular Range
      - 0.2 – 0.7 ng/mgCr (DUTCH)

# DUTCH 4-Spot Method Correlates with Serum

Our published research establishes how DUTCH urine testing methods yield results that correlate with:

- Serum tests
  - Estradiol
  - Progesterone (with  $\beta$ -pregnanediol)

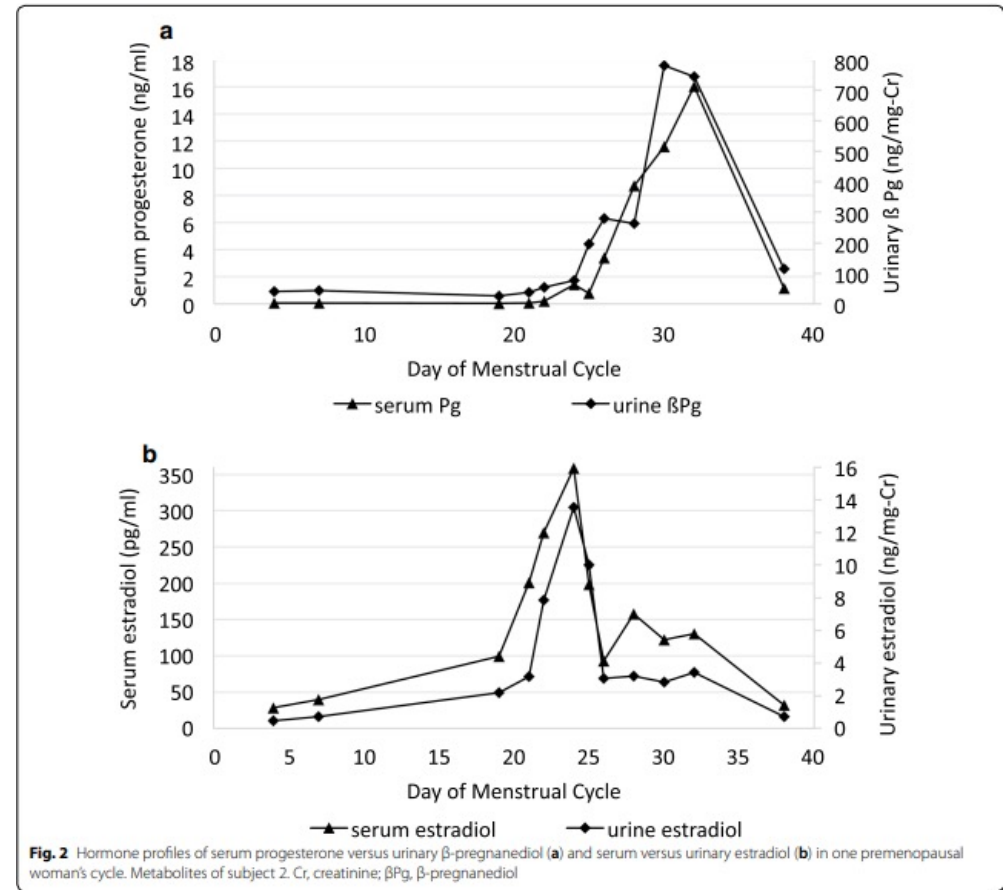
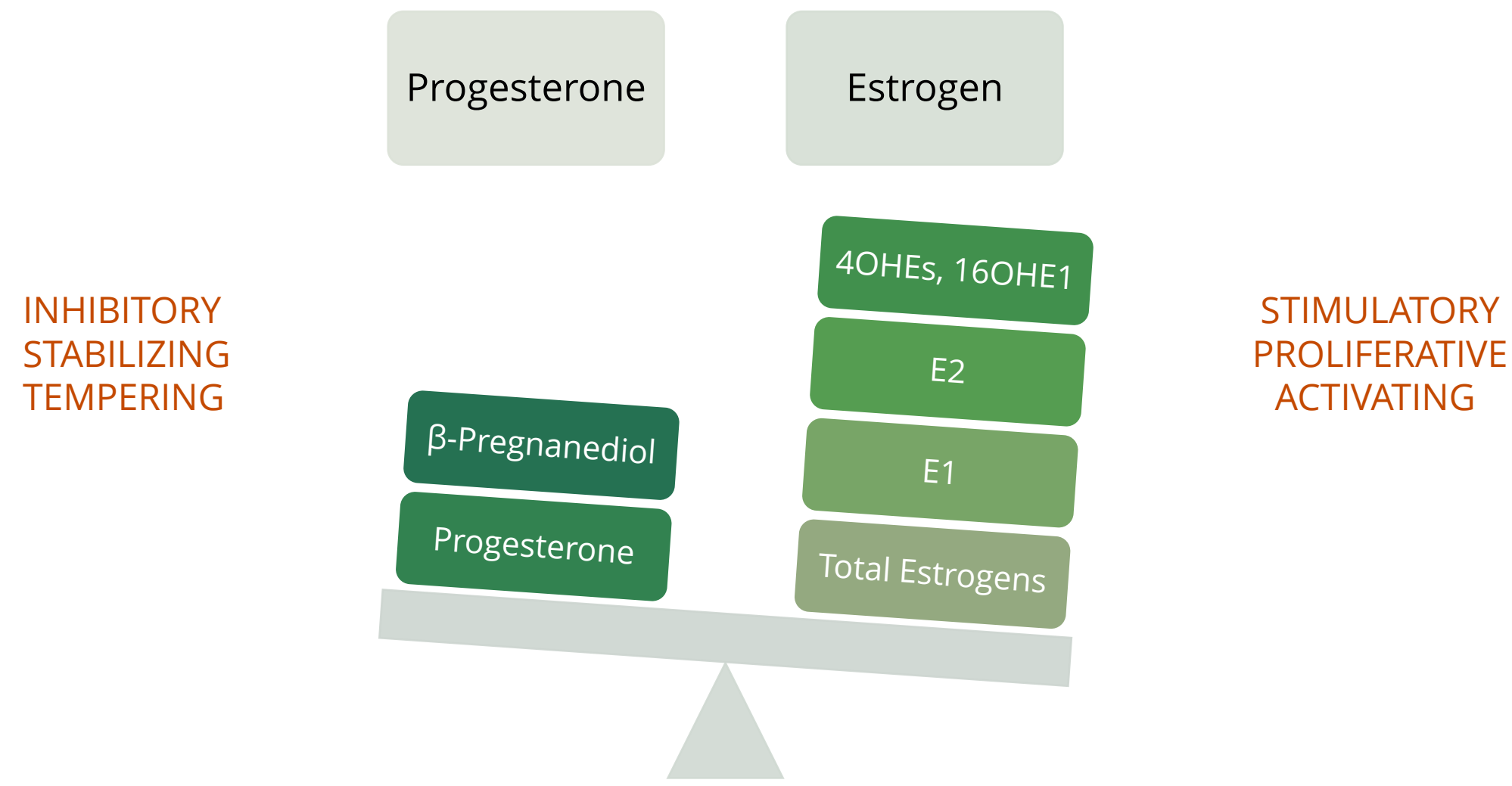


Fig 2.  
Liquid urine 24-hr estradiol vs 4-spot DUTCH  
2019 Newman

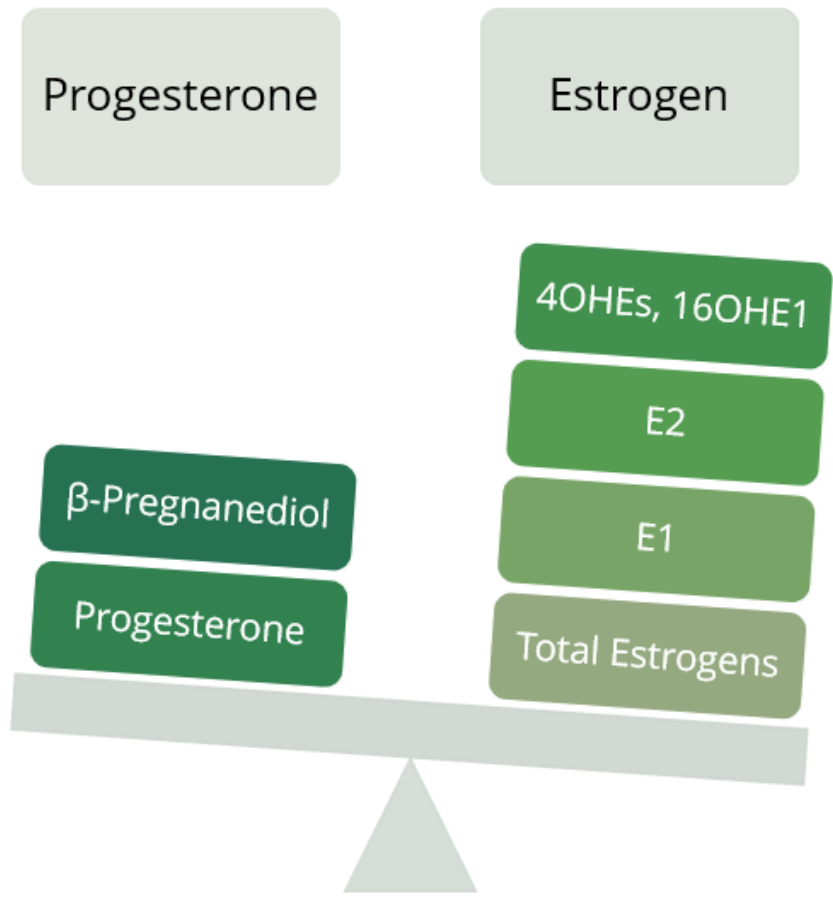
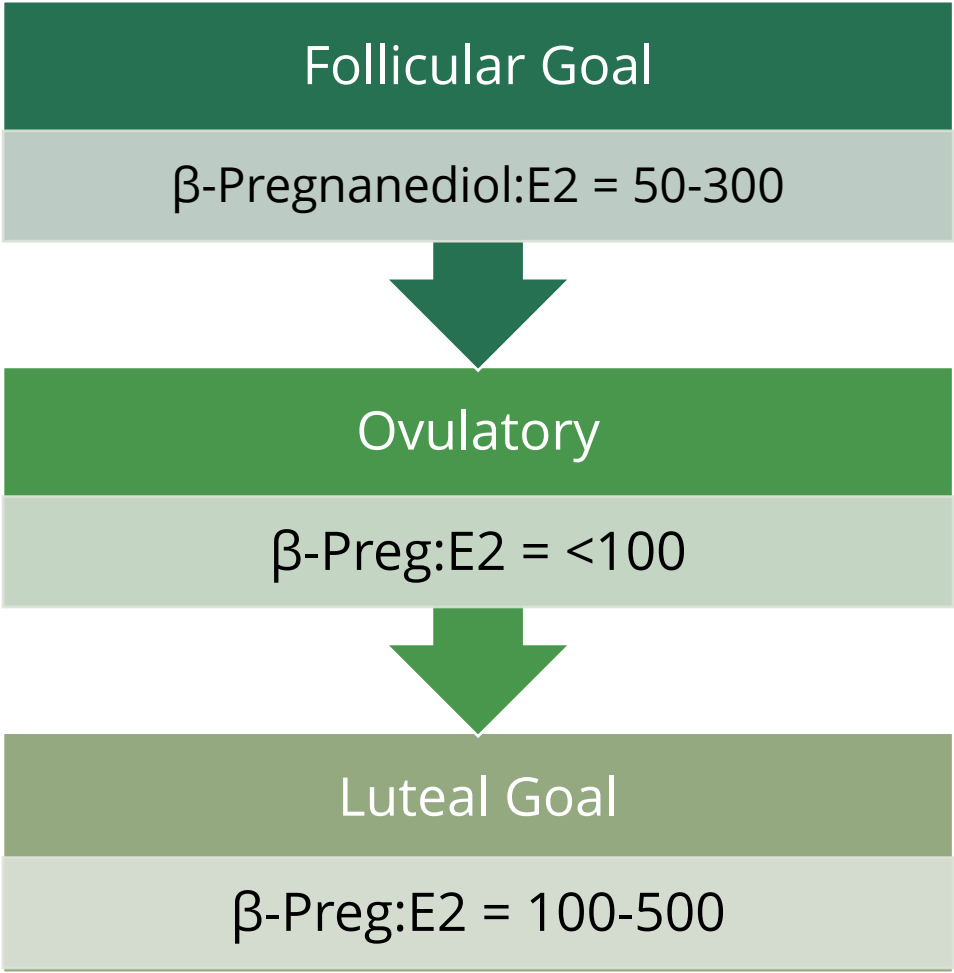
Newman M, et al. Evaluating urinary estrogen and progesterone metabolites using dried filter paper samples and gas chromatography with tandem mass spectrometry (GC-MS/MS). BMC Chem. 2019;13(1):20.

# Estrogen Dominance Defined





# Optimal Urinary PG/E2 Ratios



# Optimal Luteal PG/E2 Ratio in Serum

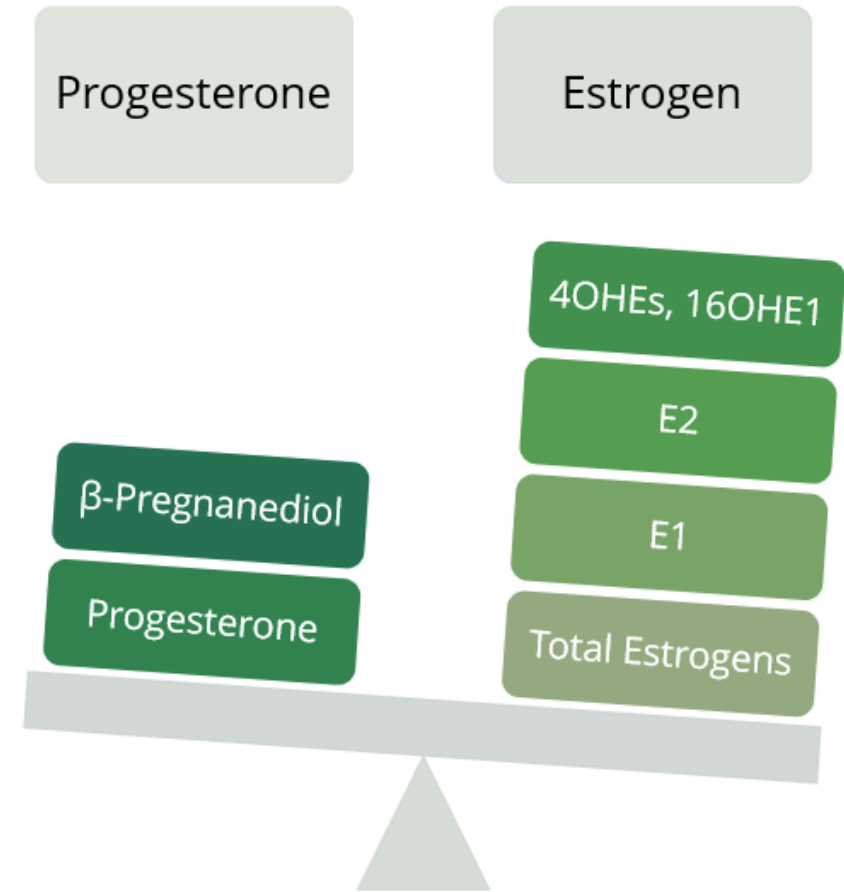
## Luteal PG/E2 Goal in Serum

Progesterone : Total E2 = 100-500

Make sure you convert to the same units or multiply by 1000!

Example:

- PG = 8.0 ng/mL
- E2 = 180 pg/mL = 0.180 ng/mL
- $8.0/0.180 = 44.4$  **L**

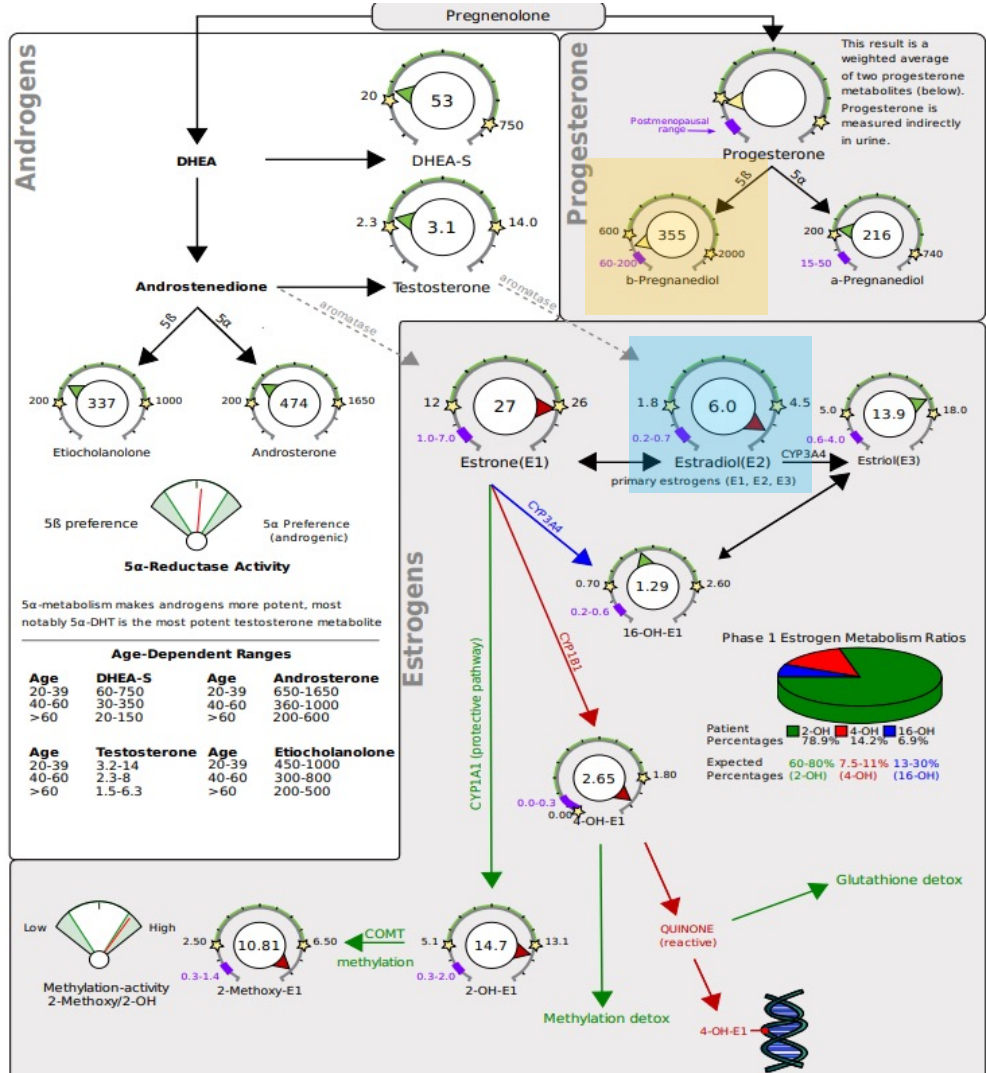


# Low Luteal PG/E2 Ratio = Estrogen Dominance

• Low Luteal PG:E2 ratio = Estrogen Dominance

- B-PG = 355
- E2 = 6.0
- $355/6 = 59.2 L$

Luteal Goal  
 $\beta$ -Preg:E2 = 100-500



# Low Luteal PG/E2 Ratio = Estrogen Dominance

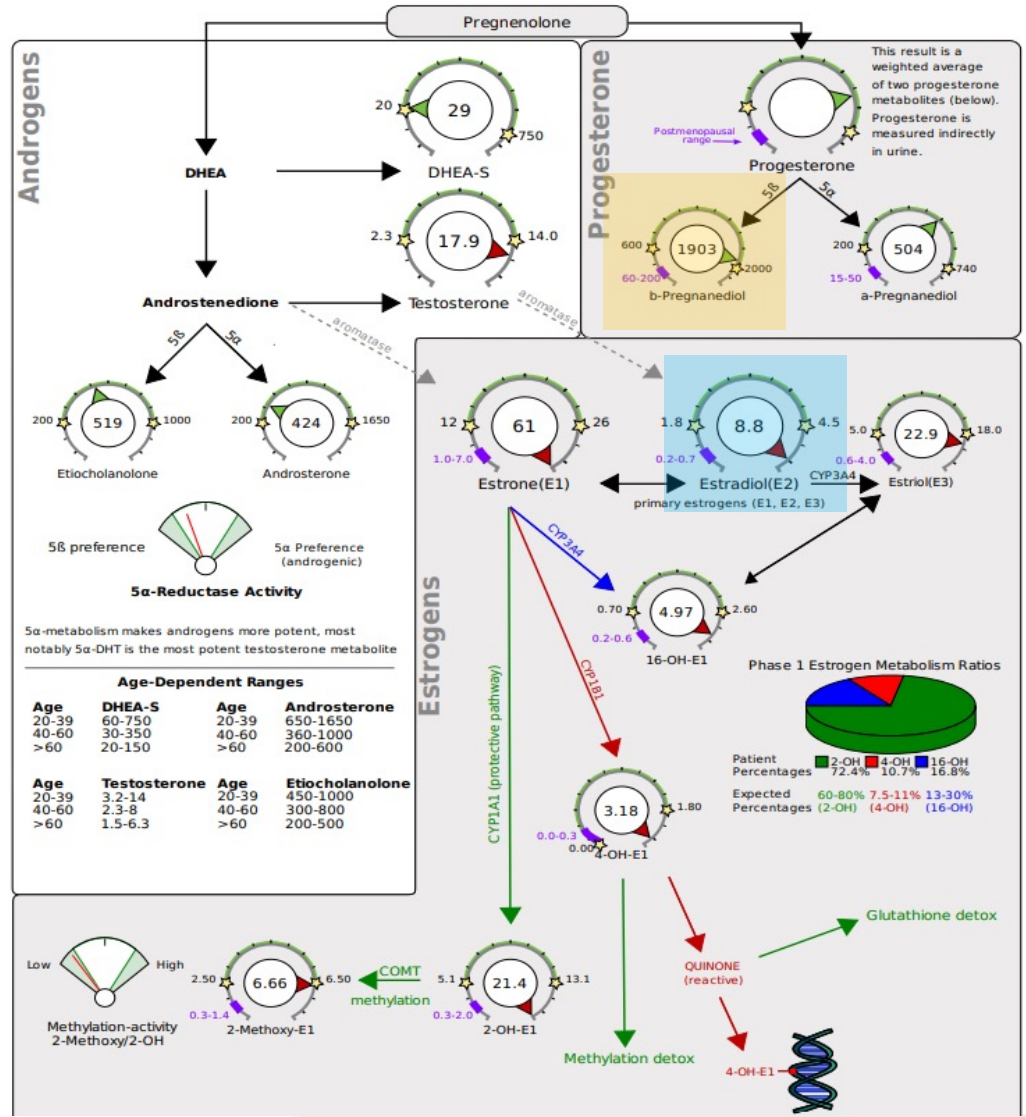
• Low Luteal PG:E2 ratio = Estrogen Dominance

• B-PG = 1903

• E2 = 8.8

•  $1903/8.8 = 216.3$  N

Luteal Goal  
 $\beta$ -Preg:E2 = 100-500



# Low Luteal PG/E2 Ratio = Estrogen Dominance

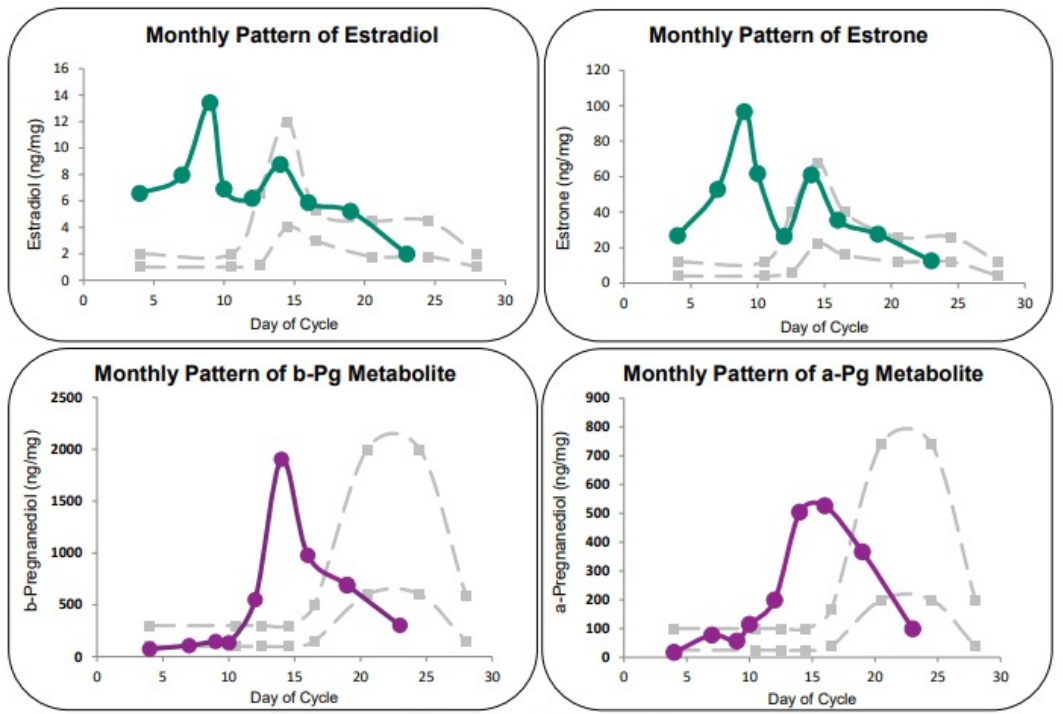
- **Low Luteal PG:E2 ratio = Estrogen Dominance**
- But the PG:E2 ratio can be assessed during follicular and ovulatory phases as well via Cycle Mapping
- Is this person estrogen dominant?

**Follicular Goal**

$\beta$ -Pregnanediol:E2 = 50-300

**Ovulatory**

$\beta$ -Preg:E2 = <100



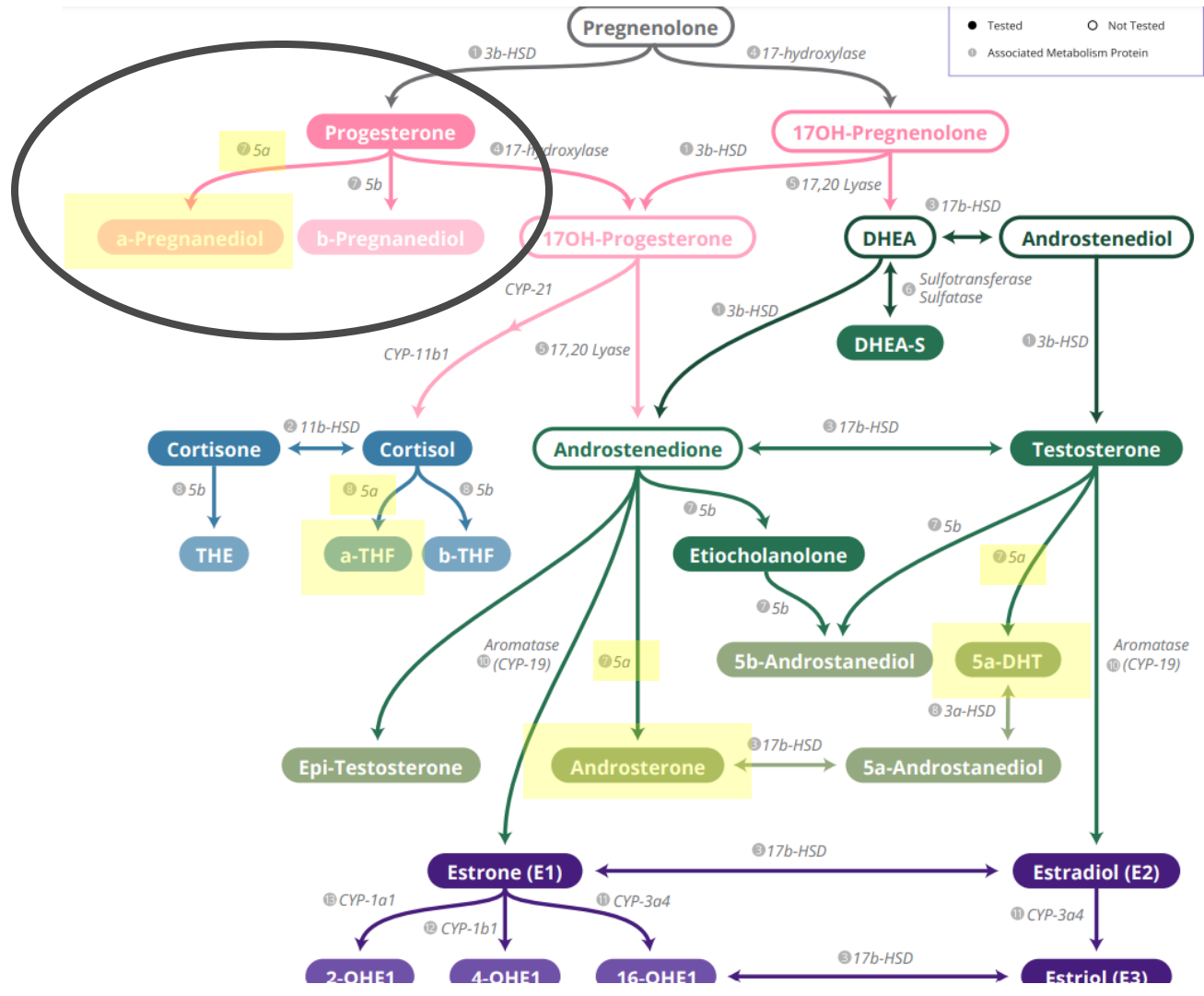
All values given in ng/mg creatinine

Measurement	1	2	3	4	5	6	7	8	9
Day(s) of Cycle	4	7	9	10	12	14	16	19	23
Estradiol (E2)	6.56	7.95	13.42	6.90	6.19	8.76	5.86	5.21	1.98
Estrone (E1)	26.8	52.8	96.6	61.8	26.4	61.0	35.4	27.6	12.6
a-Pregnanediol	17	77	56	114	198	504	526	366	99
b-Pregnanediol	74	107	147	134	549	<b>1903</b>	978	688	302
b-Pregnanediol/E2 Ratio	11	13	11	19	89	217	167	132	152
Creatinine		0.17	0.41	0.36	0.71	0.88	1.20	0.17	0.49

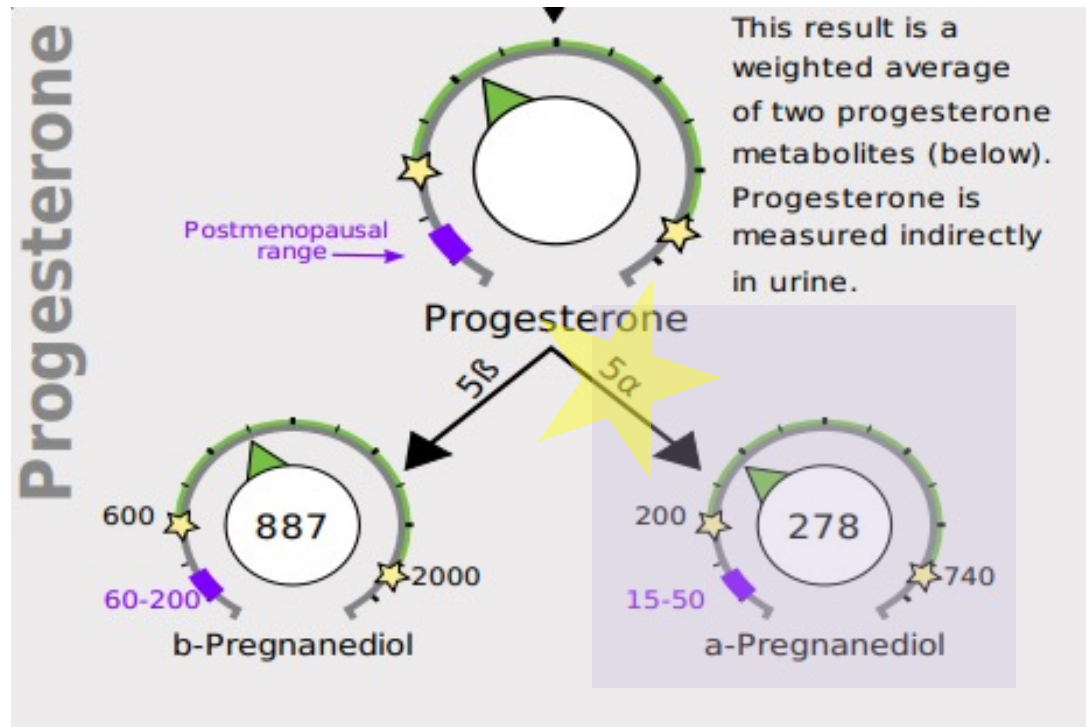
The days listed above were used for measurements. Two samples are used and listed for long cycles or patients without a normal cycle.

Follicular Ovulatory Luteal

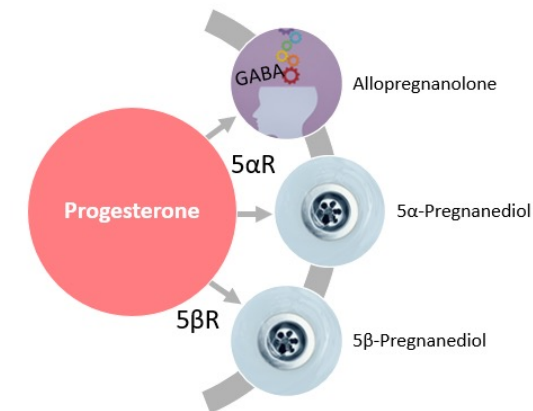
# Why look at $\alpha$ -Pregnanediol?



# Why look at $\alpha$ -Pregnanediol?



- Progesterone converts to its active neurosteroid (GABAergic) metabolites via: **5 $\alpha$ -Reductase pathway**
- $\alpha$ -Pregnanediol represents progesterone's 5 $\alpha$ -Reductase activity
- The "feel" of progesterone dictated by:
  - $\beta$ -PG/E2 balance
  - 5 $\alpha$ R metabolite formation (ex: Allopregnanolone) and its appropriate action on GABA receptor



# A Cautionary Note about Progesterone and Negative Mood

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- Paradoxical GABA Effect
- Normal, physiologic luteal progesterone levels makes some people feel bad
- Inverse U dose-relationship in some patients with progesterone
  - Physiologic luteal levels = EXACERBATION
  - Follicular levels = FINE
  - Supraphysiologic levels = FINE
- Treatment options:
  - Suppress ovulation (GnRH agonists, combo OCPs)
  - Overrun GABA with supraphysiologic allopregnanolone (Andreen used 400 or 800mg USP progesterone suppositories)
  - Inhibit 5 $\alpha$ -Reductase activity
    - Ganoderma (Reishi), Green tea (EGCG), Saw Palmetto, Nettle Root, Pygeum africanum

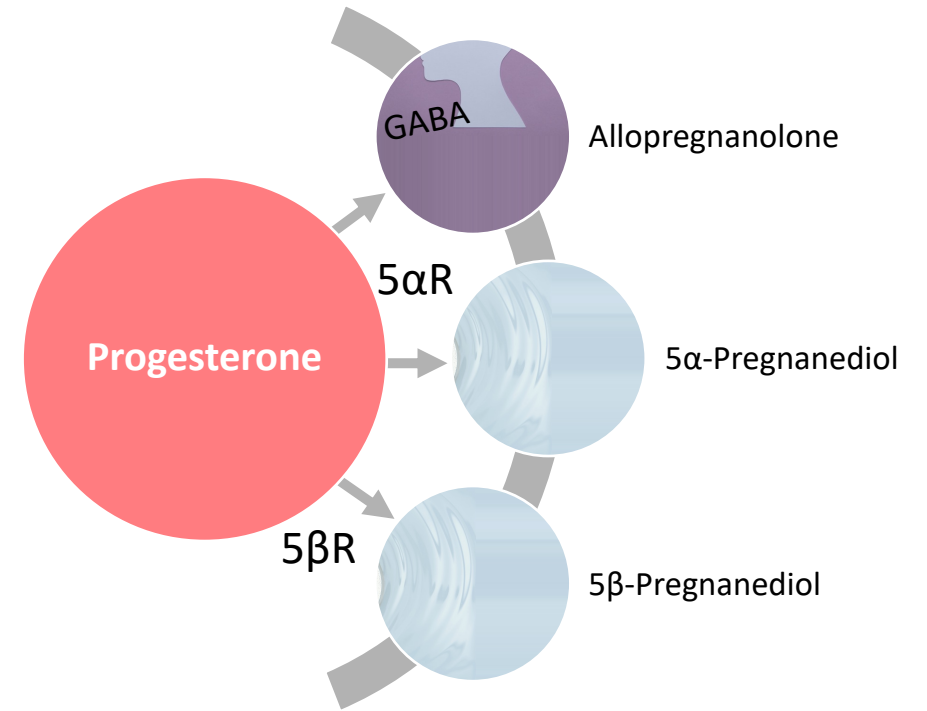
Andreen L, et al. Relationship between allopregnanolone and negative mood in postmenopausal women taking sequential hormone replacement therapy with vaginal progesterone. *Psychoneuroendocrinology*. 2005;30(2):212-224.

Sundstrom-Poromaa I, et al. Progesterone - Friend or Foe? *Front Neuroendocrinol*. 2020;59.



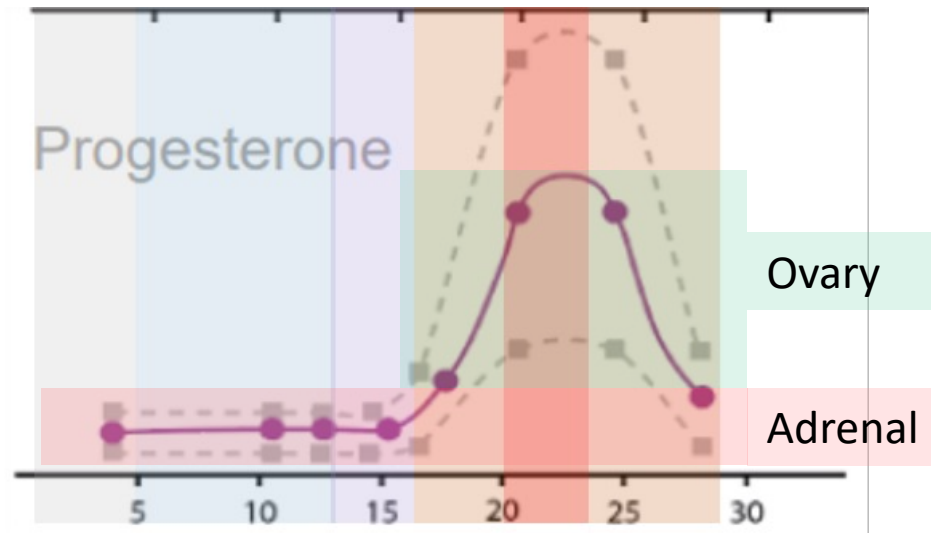
# Quick and Dirty Review on Progesterone

- Production: Adrenals, Ovaries
- Tissue interaction: Progesterone receptors (PR) all over the body, GABA receptors in the CNS
- Active Metabolites: Progesterone, Allopregnanolone (by 5 $\alpha$ -Reductase)
- Overall action: Calming, inhibiting, estrogen-tempering, estrogen-suppressing
- Excretion Products:  $\alpha$ -Pregnanediol (by 5 $\alpha$ -Reductase) and  $\beta$ -Pregnanediol (by 5 $\beta$ -Reductase)
- Total Progesterone in circulation: Binds to Cortisol Binding Globulin (CBG)



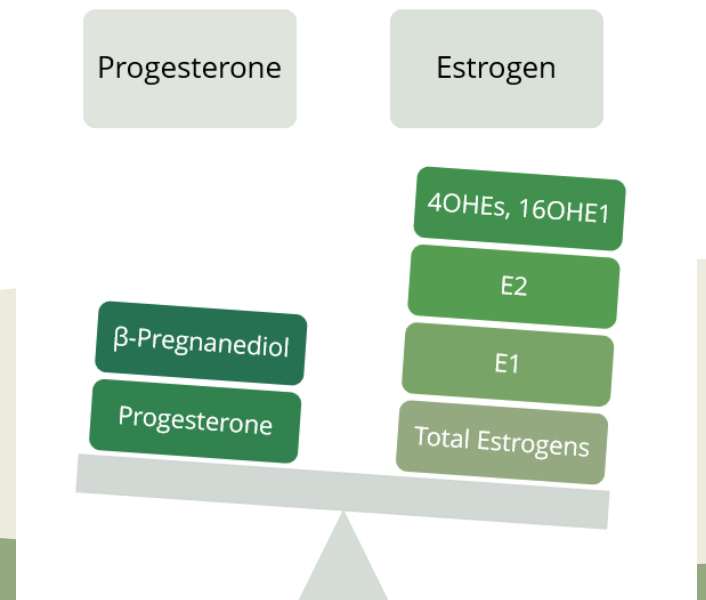
# Quick and Dirty Review on Progesterone

- Progesterone baseline levels come from adrenal output all cycle long



- Deviations from baseline adrenal output = corpus luteum production
  - Blip at the end of follicle development to help signal LH
  - Rise and sustained high output during the luteal phase
    - Stabilize the endometrium, hone breast development

# Step 1: Raise Progesterone



# Treating Low Progesterone without Hormones



## Support Follicle Development/Egg Quality

- Androgen supports (reduce if high, increase during FP if low)
  - Reduce androgens: Myoinositol, Licorice Extract, White Peony, Spearmint tea
  - Increase androgens: DHEA, Maca, Tribulus, Shatavari, Sarsaparilla
- Mitochondrial-type nutrition
  - CoQ10, ALA, Carnitine, Vitamin D, Glutathione, NAC, Resveratrol, Melatonin
- Follicular phytoestrogen supports
  - Black cohosh, Maca, Ground flax, Dong Quai

## Support Ovulation/Luteal Sufficiency

- LH modulators: (*I always use these pan-cycle*)
  - Myoinositol - 2-4g daily
  - Vitex agnus-castus - 200-600mg daily
- Adaptogens: (increase stress resilience)
  - Ashwagandha, Schisandra, Ginseng, Holy basil, Rhodiola

# Treating Low Progesterone with HRT

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- Before treating low luteal progesterone with hormones, ensure the patient's samples were collected during the mid-luteal phase
  - ~ 1 week after ovulation occurred and/or ~ 1 week before the next menses
- Progesterone can be given during the luteal phase
  - Progesterone Receptors (PRs) on the corpus luteum that control further endogenous luteal progesterone production (feed-forward)
  - Precautions:
    - Given in high doses too early in follicular phase it can delay follicle development
    - If given right at ovulation and fertilization occurs, higher rate of tubal pregnancy
      - if TTC, wait 3 days after ovulation to start PG.

# Treating Low Progesterone with HRT

- OTC USP Progesterone Transdermal Creams and Topical Oils
  - Large dosing range 10-50mg most common
- Rx Oral Progesterone
  - Orally delivered is more anxiolytic and sleep inducing
  - Dose at bedtime, can cause rapid relaxation and drowsiness;
  - 100-400mg QHS commonly used
  - Prometrium IR Micronized Progesterone 100mg increments (FDA approved)
  - Compounded SR Micronized Progesterone in E4M matrix
- Rx Vaginal Progesterone/Suppositories
  - Suppository dosing typically 100 – 800mg



# Progesterone Rx Pearls

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- Delivery → Where it acts + How it feels
  - Orals
    - Verrrrry relaxing, sleep-inducing, use before bedtime
    - Doesn't seem to last long – 12 hrs so may need BID dosing if needed (and tolerated)
  - Sublinguals
    - Act like orals if/when swallowed (see above)
  - Topicals
    - Above the waist applications may be more relaxing similar to orals
    - Below the waist may be more local to pelvic complaints
  - Vaginal
    - Suppositories may have greater effect on cervix and endometrium and reach systemic circulation if applied in top 1/3 of vaginal vault
    - Labial applications seem to feel similar to 'below the waist' topical progesterone - think pelvic complaints

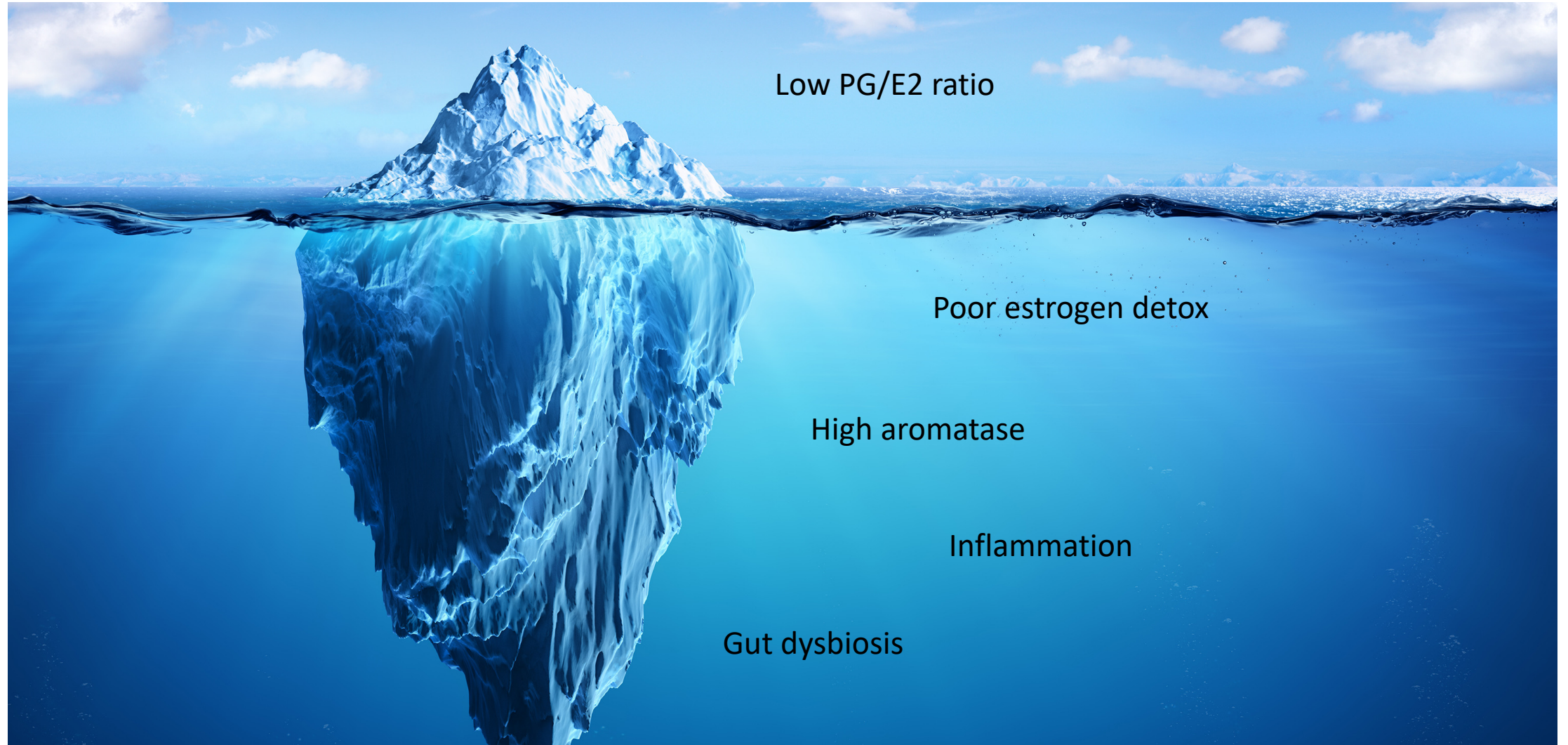
# Note on Using Pregnenolone to increase Progesterone

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- Pregnenolone therapies may modestly increase adrenal output of progesterone
  - Pregnenolone and progesterone both break down to same pregnanediols
- Immunoassays measuring progesterone will pick up pregnenolone metabolites especially if giving pregnenolone orally or sublingually
  - ONLY monitor progesterone when giving pregnenolone using LC-MS/MS methodologies no matter what body fluid



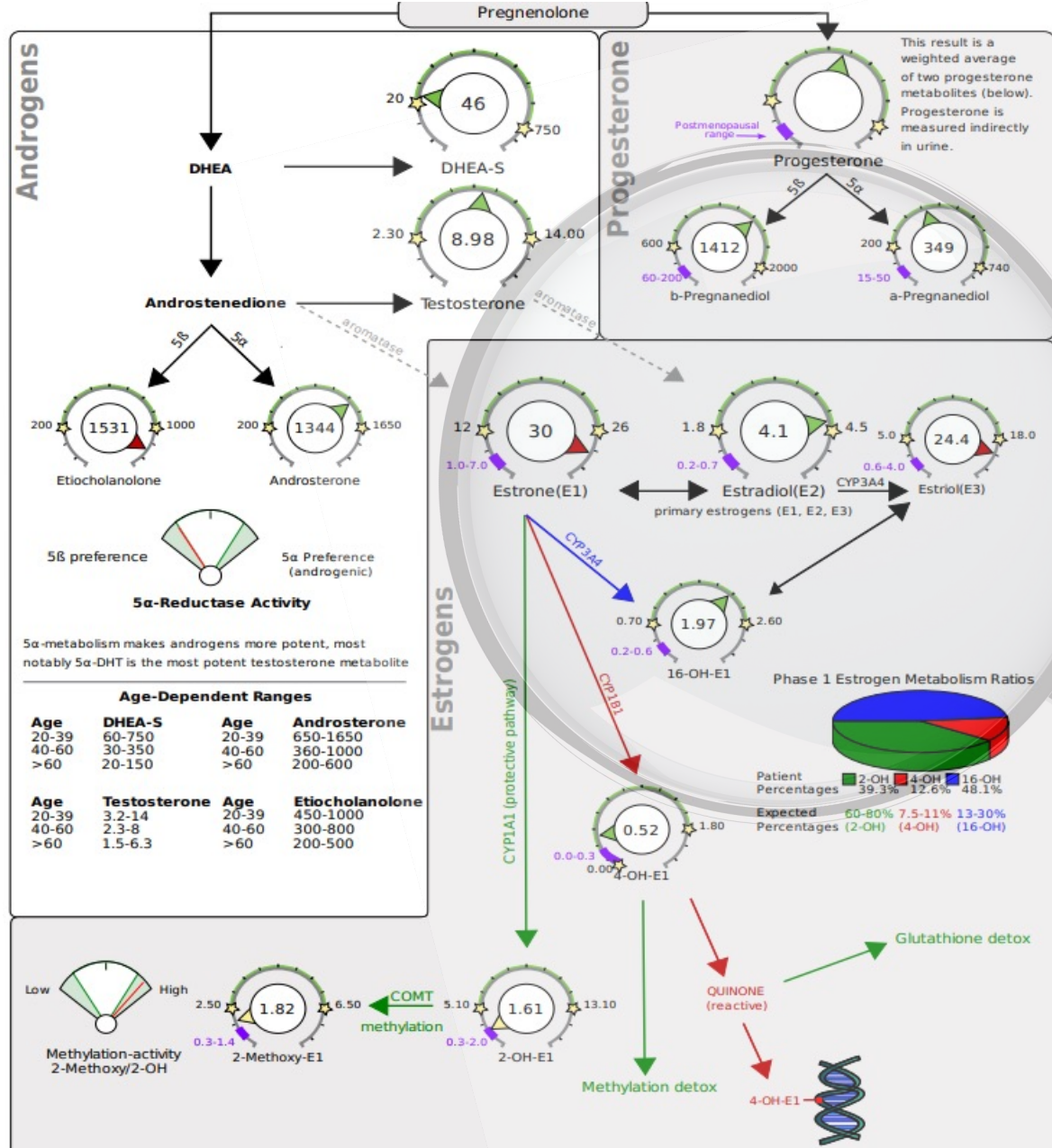
# PG/E2 Ratio - the tip of the iceberg



# Quick and Dirty on Estrogen

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- Production: Adrenals, Ovaries, Adipose Tissue, Gut (and others to smaller degrees)
- Tissue interaction: ER $\alpha$ , ER $\beta$ , GPER
- Active Estrogens and Estrogen Metabolites at receptors:
  - Estradiol (17 $\beta$ E<sub>2</sub>; strongest endogenous estrogen at all ERs),
  - Estrone (E<sub>1</sub>; higher for ER $\alpha$ ),
  - Estriol (E<sub>3</sub>; higher for ER $\beta$ ),
  - 2OHEs (weak affinity overall but 2OHE<sub>2</sub>>2OHE<sub>1</sub> and for ER $\beta$ , GPER),
  - 4OHEs (higher affinity than 2OHEs but 4OHE<sub>2</sub>>4OHE<sub>1</sub> and for ER $\alpha$ ),
  - 16OHE<sub>1</sub> (covalent binding to ER $\alpha$ , does not down-regulate E receptor like other estrogens do)
- In general, ER $\alpha$  receptors are the most stimulating/proliferative
- Overall action: Stimulating, proliferating, activating, “estrogenic”
- Total Estradiol in circulation: Binds to sex hormone binding globulin (SHBG)



High E2 production?  
or  
Low SHBG?

# Serum and Urine Hormones Are Complementary

- Serum

- Hormones (mostly non-bioavailable) are in transit TO tissues at the time of collection

- Production



Blood Stream



- Urine

- Hormones (only free/bioavail) have been taken up by tissues AND metabolized / 24 hr

- Blood stream



Tissue Uptake



Utilization  
Metabolism

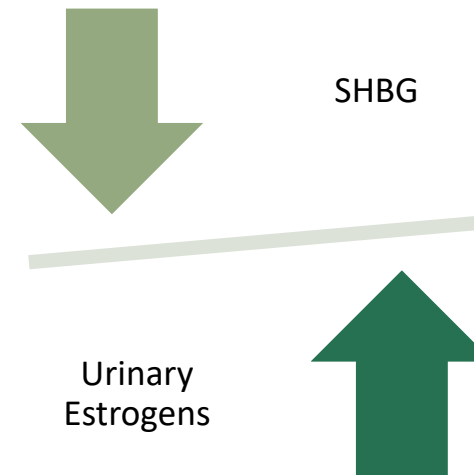
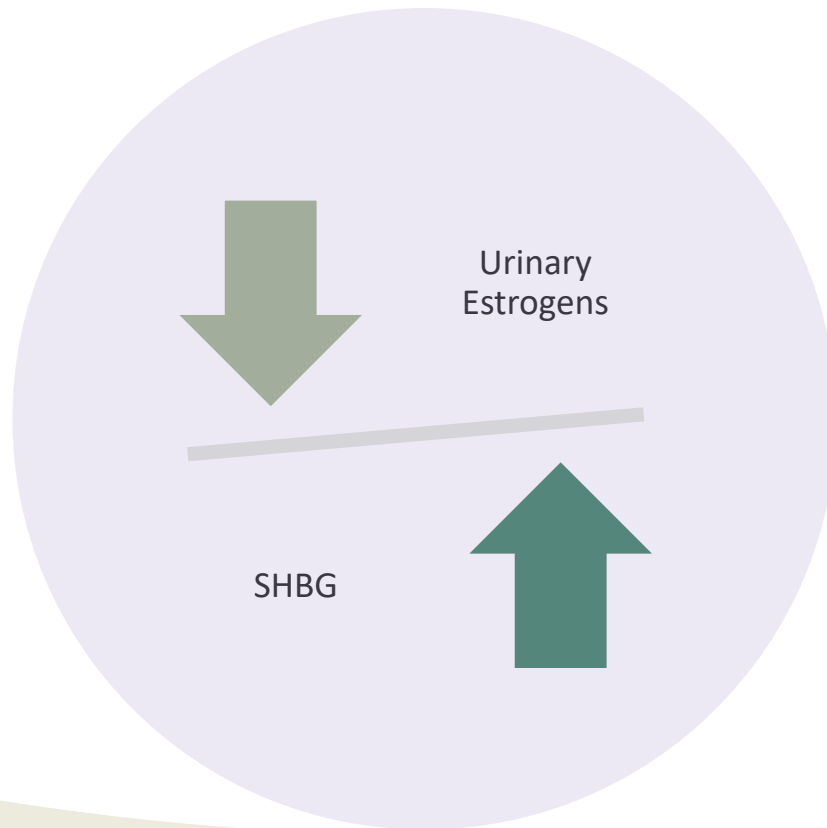


Urine



# SHBG = Sex Hormone Binding Globulin

- Binds to Estradiol and Testosterone in SERUM
- High SHBG decreases bioavailable fraction of E2 and T
  - less available for tissue uptake, lower estrogens in the urine



# Sex Hormone Binding Globulin (SHBG) – optimal 60-100 nmol/L

- High SHBG Associated with:

- Anorexia nervosa and other hypocaloric intake situations
- Estrogen deficiency complaints
- Fatigue
- Fertility problems
- Hyperthyroid
- Hypoandrogen complaints (low libido, fatigue, decreased muscle mass)
- Medications (hx combo OCPs, oral estradiol, some anticonvulsants, spironolactone)
- Metals toxicity (lead, cadmium)
- Urinary Estrogens **lower** than Serum Estrogens

- Low SHBG Associated with:

- **Estrogen-dominant complaints**
- Fatty liver
- Fertility problems
- Hyperandrogen complaints (acne, hair loss, hirsutism, etc)
- Hypercortisolism
- Hypothyroid
- Inflammation
- Insulin Resistance
- Metabolic Syndrome
- Obesity
- Progestin-Use
- Urinary Estrogens **higher** than Serum Estrogens

# A Serum Panel Companion to Mid-Luteal DUTCH Testing

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- Blood sugar
  - Fasting insulin
  - Fasting glucose
  - HgbA1c
- Liver Function/Lipids
  - Lipid Panel
  - Liver enzymes  
AST/ALT/AlkP/GGT
- Thyroid Function
  - TSH
  - Total T4, fT4, fT3
  - Antibodies – Anti-TPO and -TG
- 25-OH Vitamin D
- Sex Hormones – Cycle Day 3
  - Total Estradiol
  - Progesterone
  - Total Testosterone
  - LH
  - FSH
  - SHBG
  - Prolactin
- Inflammatory
  - hs-CRP
  - Leptin
- DHEA-S
- Homocysteine

# Why do hormone metabolites matter?

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## Affinity for hormone receptors

- 16OHE1 for ER $\alpha$
- 4OHE2 for ER $\alpha$
- E3 for ER $\beta$
- DHT for AR

## Form complexes that damage DNA and increase cancer risk

- 4OHE1 and 4OHE2 form catechol-quinone complexes

## Affinity for neurotransmitter receptors

- $\alpha$ -pregnanediol for GABA receptors

## Valuable info about DETOX

- I - hydroxylation
- II – methylation and sulfation
- Clearance rate of cortisol

## Anti-proliferative metabolite formation

- 2MeOE1



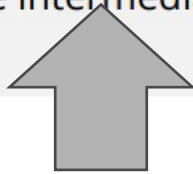
# Step 2: Treat the Transitional States of Estrogen

Target the Pathways

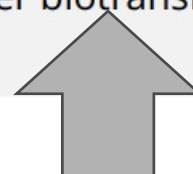
# Phase 1 Detoxification: Cytochrome Enzyme Systems

"2-OH" 2-hydroxyestrone & 2-hydroxyestradiol	"4-OH" 4-hydroxyestrone & 4-hydroxyestradiol	"16-OH" 16-hydroxyestrone
CYP1A1 & CYP1A2	CYP1B1	CYP3A4
Most stable and generally "preferred"	Potentially genotoxic	Proliferative Can be good for bones, but not so good with breast/fibroids/endo
Weakest binding potential to E receptor Anti-proliferative effects on cancer cell lines	If not properly metabolized, it can turn down a different pathway to become the free radical 3,4-quinone which can cause DNA damage	Binds most strongly to estrogen receptor, though still weakly

All of these metabolites are reactive oxidative intermediates- they require further biotransformation!



INFLAMMATION  
THYROID, TOXINS



OBESITY, ANDROS  
GUT, AUTOIMMUNE

# Treatment Considerations for Phase One

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## Treat Causes of Aberrant Phase One Metabolism

Inflammation

High simple CHO diet

Toxics/Xenoestrogens

Hypothyroid

Infections

Mold illness

Vitamin D def

Autoimmune

Sedentary Lifestyle

## Support CYP1A1 (and modulate CYP1B1/CYP3A4) - PROTECTIVE

Cut the simple CHOs

Ground flaxseeds

Brassica family veggies

Bioflavonoids/Anti-inflam

Soy Isoflavones

Green Tea/Extract

Humulus 8-PN

Resveratrol

Root veggies

↓ Alcohol

DIM/I3C/SFN

Rosemary

B2, B3, B6, B9, B12

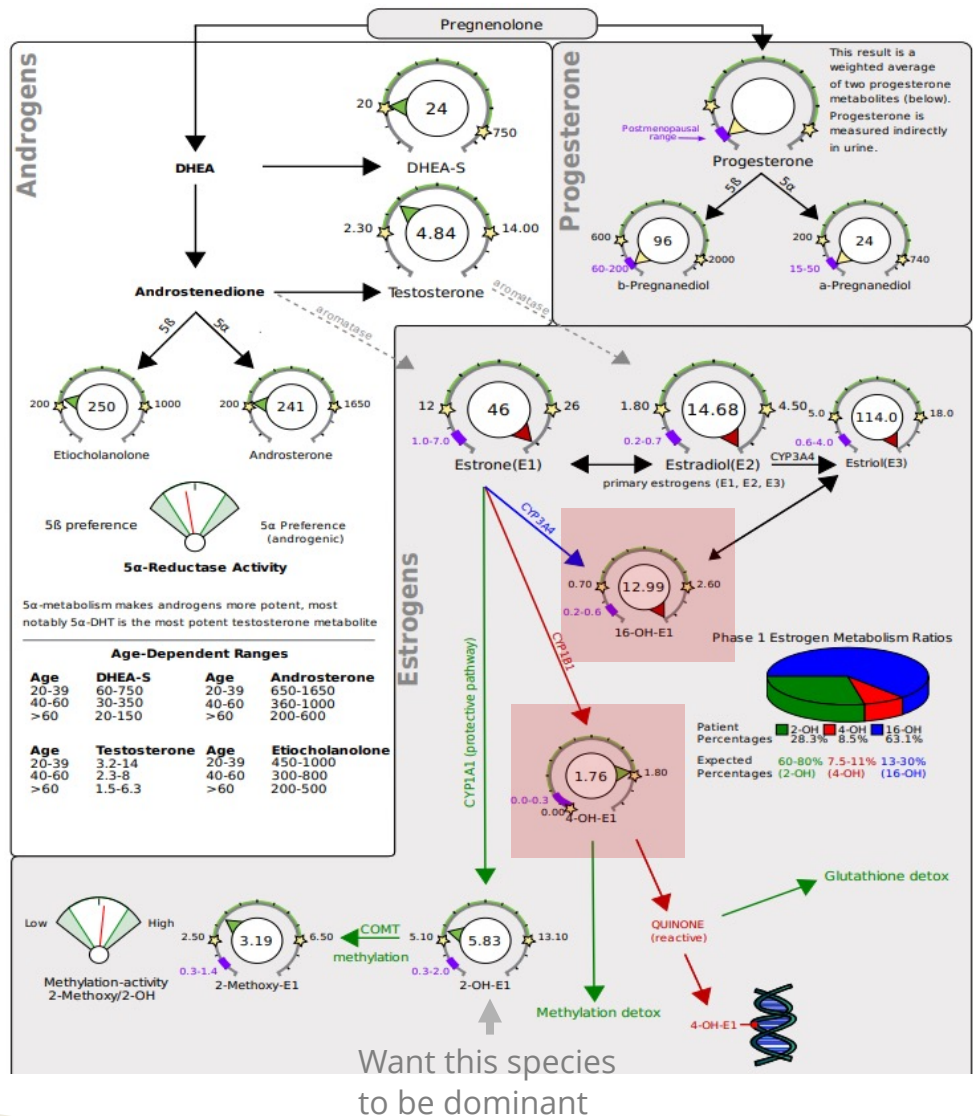
↑ Iodine Sufficiency

Omega-3s

Reishi/Shiitake

DIM = Diindolylmethane; I3C = Indole-3-Carbinol; SFN = Sulforaphane

# 44yoF – Heavy menses, regular cycles, bloating



## Assessment:

- PG/E2 = 6.4 L
- ↑ 16OHE1 and E3
- ↑ 4-OHE1 compared to 2-OHE1
- ↑ 4-OHE2 compared to 2-OHE2

Estrogens and Metabolites (Urine)					
Estrone(E1)	Above luteal range	45.81	ng/mg	12 - 26	1.0-7.0
Estradiol(E2)	Above luteal range	14.68	ng/mg	1.8 - 4.5	0.2-0.7
Estriol(E3)	Above luteal range	114.0	ng/mg	5 - 18	0.6-4.0
2-OH-E1	Low end of luteal range	5.83	ng/mg	5.1 - 13.1	0.3-2.0
4-OH-E1	High end of luteal range	1.76	ng/mg	0 - 1.8	0-0.3
16-OH-E1	Above luteal range	12.99	ng/mg	0.7 - 2.6	0.2-0.6
2-Methoxy-E1	Low end of luteal range	3.19	ng/mg	2.5 - 6.5	0.3-1.4
2-OH-E2	Within luteal range	0.38	ng/mg	0 - 1.2	0-0.3
4-OH-E2	Above luteal range	0.77	ng/mg	0 - 0.5	0-0.1
Total Estrogen	Above range	199.4	ng/mg	35 - 70	4.0-15

Androgens and Metabolites (Urine)				
DHEA-S	Low end of range	24.3	ng/mg	20 - 750
Androsterone	Low end of range	241.3	ng/mg	200 - 1650
Etiocholanolone	Low end of range	250.3	ng/mg	200 - 1000
Testosterone	Within range	4.84	ng/mg	2.3 - 14
5α-DHT	Low end of range	1.3	ng/mg	0 - 6.6
5α-Androstanediol	Within range	20.6	ng/mg	6 - 30
5β-Androstanediol	Low end of range	24.5	ng/mg	20 - 75
Epi-Testosterone	Within range	9.8	ng/mg	2.3 - 14
<b>Gut Marker (potential gut putrefaction or dysbiosis if high) - (Urine)</b>				
Indican	Above range	103.1	ug/mg	0 - 100

# 40HE Drivers and Busters

# Known CYP1B1 4-OHE Drivers

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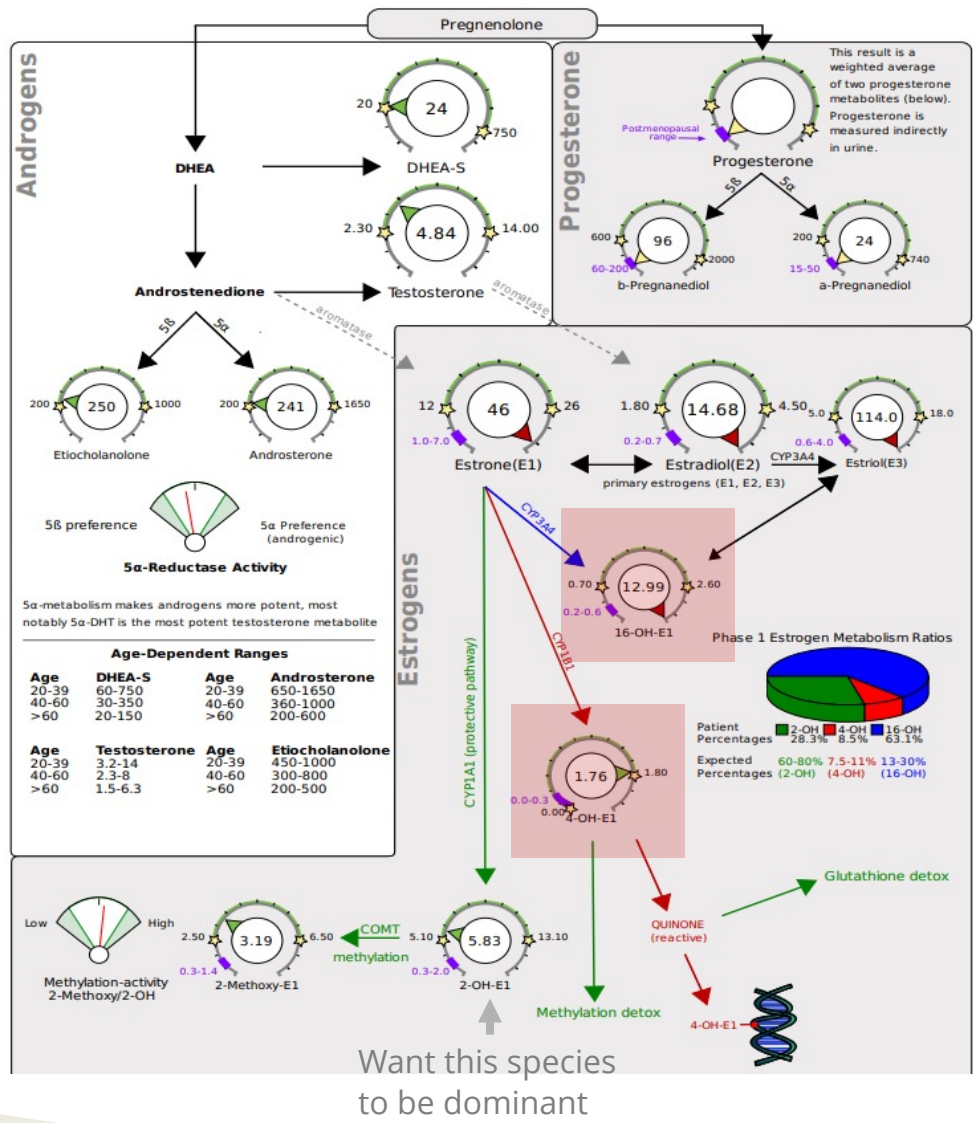
- Inflammation
- Genetics
- Hypothyroid
- Toxic Exposures
  - PAHs
- Mold Toxins
  - Zearalonone

# CYP1B1 4-OHE Busters

---

- Antioxidants
  - Foods:
    - Brassicas, Citrus fruit, Red pepper, Tarragon, Rosemary
  - Flavonoids/Polyphenols:
    - Quercetin, Citrus bioflavonoids, Rutin, Hesperidin, Apigenin, Resveratrol
- Optimize thyroid function
- Avoid toxic exposures
- Test for and treat mold toxicities (or refer)
- Support **Phase 2 Detox** to mitigate effects of high 4-OHEs (helpful for CYP1B1 snp carriers)
  - Support reduced glutathione
    - Liposomal glutathione, NAC, glycine, C, B6
  - Support quinone reductase (to cleave apart 4-OHcatechol-quinone complexes)
    - Sulforaphane (SFN), Soy isoflavones, Resveratrol
  - Support methylation
    - MTHF, Hydroxocobalamin, SAmE, Magnesium, B6, PhosCholine, TMG, MSM, SFN

# 44yoF – Heavy menses, regular cycles, bloating



## Assessment:

- PG/E2 = 6.4 L
- ↑ 16OHE1 and E3
- ↑ 4-OHE1 compared to 2-OHE1
- ↑ 4-OHE2 compared to 2-OHE2

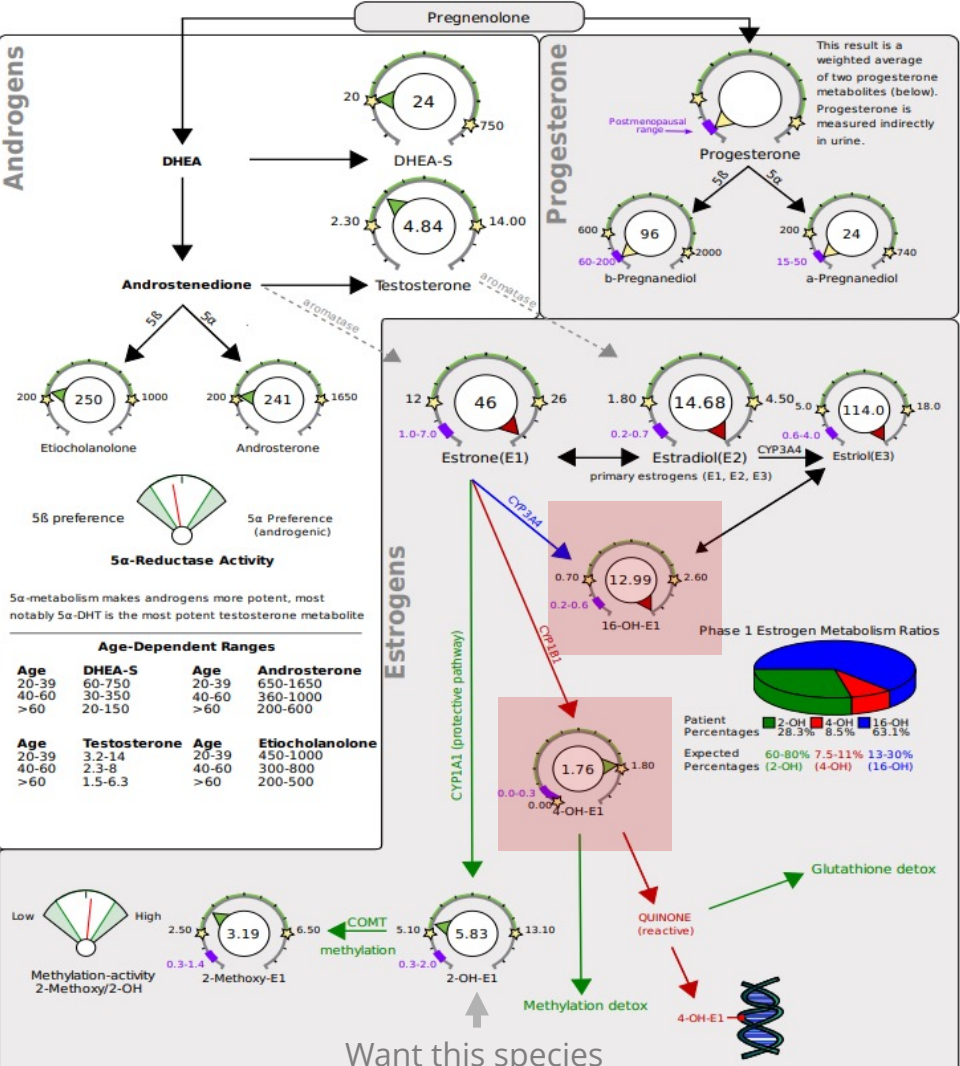
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5α-DHT	Low end of range	1.3	ng/mg	0 - 6.6	
5α-Androstenediol	Within range	20.6	ng/mg	6 - 30	
5β-Androstenediol	Low end of range	24.5	ng/mg	20 - 75	
Epi-Testosterone	Within range	9.8	ng/mg	2.3 - 14	

Gut Marker (potential gut putrefaction or dysbiosis if high) - (Urine)					
Indican	Above range	103.1	ug/mg	0 - 100	



# 44yoF – Heavy menses, regular cycles, bloating



Want this species to be dominant

- Down-regulate 4OHEs
  - Nutritional supplement containing: Citrus bioflavonoids, Hesperidin, Rutin, Quercetin, Vitamin C
    - Also are known to downregulate ERα in the endometrium to decrease bleeding
  - Compare 4OHEs with inflammatory and thyroid markers on your serum panel to get more specific
- Now for 16OHE1

# 16-OHE1 Drivers and Busters

# Known CYP3A4 Drivers

---

- Obesity
- Moderate Alcohol Consumption
- Pesticides exposures
- Smoking
- Caffeine
- Medications and supplements can affect it (long list including St. Johns Wort)
- High 16-OHE1 is associated with high prolactin levels, gut inflammation, autoimmune diseases (esp RA and SLE) and high DHEA

Note: 16-OHE1 is the CYP3A4 metabolite of estrone which **FEELS very estrogenic**. When it is dominant compared to 2OHE1 or elevated (*even if urinary E2 isn't high*), the chief complaint(s) will almost always fall into the estrogen dominant category.

# Drivers of LOW CYP3A4

---

- Low Vitamin D in circulation
  - Check 25-OH Vitamin D
- High systemic inflammation
  - Check hs-CRP
- Chronic infections/exposures
  - Viral, Lyme, Some mold toxin exposures
- Intake of Grapefruit juice (dietary)
- Medications (including some SSRIs)

# Known 16OHE1 Busters

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- Direct down-regulators:
  - DIM/I3C (Diindolylmethane/Indole-3-Carbinol)
    - Therapeutic Dosing 100-300 mg daily
    - Some will d/c during menses and resume day 7
  - Trans-Resveratrol
    - Net effect: decreased 16OHE1 and 4OHE1/4OHE2
    - May compete/inhibit estrogenic activity at tissues, often used with Quercetin
    - Common dosing: 100-500 mg daily
  - Rosemary Extract
    - Net effect: decreased 16OHE1, increased 2OHE1/2OHE2
    - Often found in combinations with DIM or I3C, also anti-inflammatory
    - Follow bottle for dosing (can affect blood pressure in some people)
- If High 16-OHE1 is correlated with high Prolactin levels:
  - Rule out or treat hypothyroid (TSH is co-released with Prolactin)
  - Check HVA in OATs section and treat lows (if low, could be inadequate dopaminergic inhibition of PRL)
  - Refer for pituitary imaging if very high and confirmed
- Support SULFATION – a sulfated estrogen cannot bind its receptor
  - Use anti-inflammatories (Curcumin, Green Tea, Scutellaria, Rosemary, etc)
  - Sulforaphane, Taurine, Methionine, NAC, Glutathione, Molybdenum, bile acid supports
- Feed CYP1A1 2-OHE pathway:
  - 150-min moderate to vigorous aerobic exercise per week
  - DIM/I3C (hard core)
  - Sulforaphane (gentle)
  - Ground flax
  - Root veggies: Spanish black radish, carrot, turnips, etc
  - Andrographis
  - Omega-3s

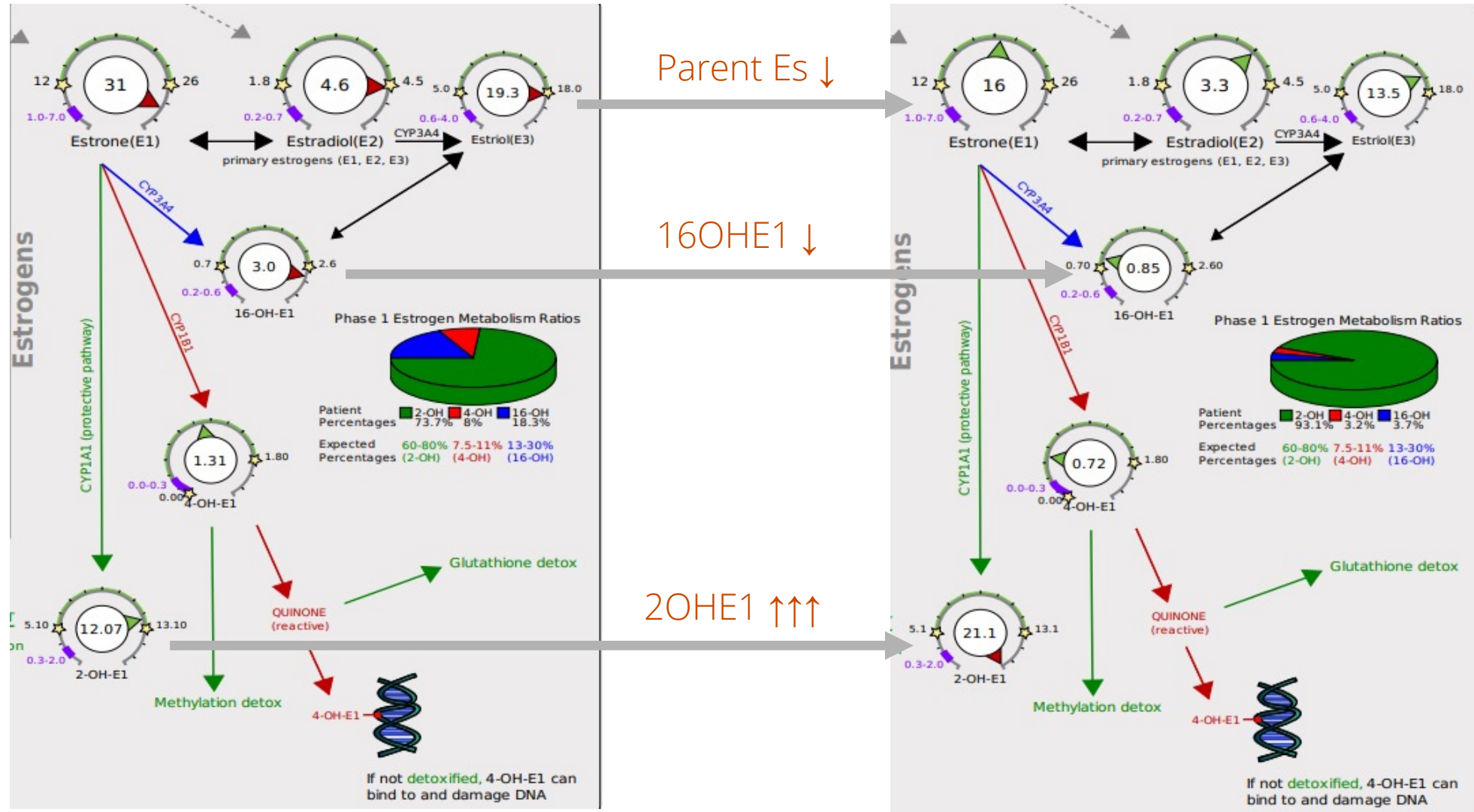
# 3,3'-Diindolylmethane = "DIM"

- Conversion product of Indole-3-Carbinol, constituent of *Brassica* family veggies
- Increases Estrogen Metabolism – Upregulates CYP1A1 → ↑ 2OHEs
  - Reroutes Phase One E metabolism away from “bad” pathways
  - Decreases urinary E1, E2, and 16OHE1 in so doing
- Decreases bioavailable E2 fraction
  - Increases SHBG
  - Decreases tissue access to estrogen but does not decrease estrogen production
- Anti-tumor activity (GI, Breast, Pancreas)
  - Tumor suppressor (multiple gene targets)
  - Influences on tumor DNA repair and apoptosis

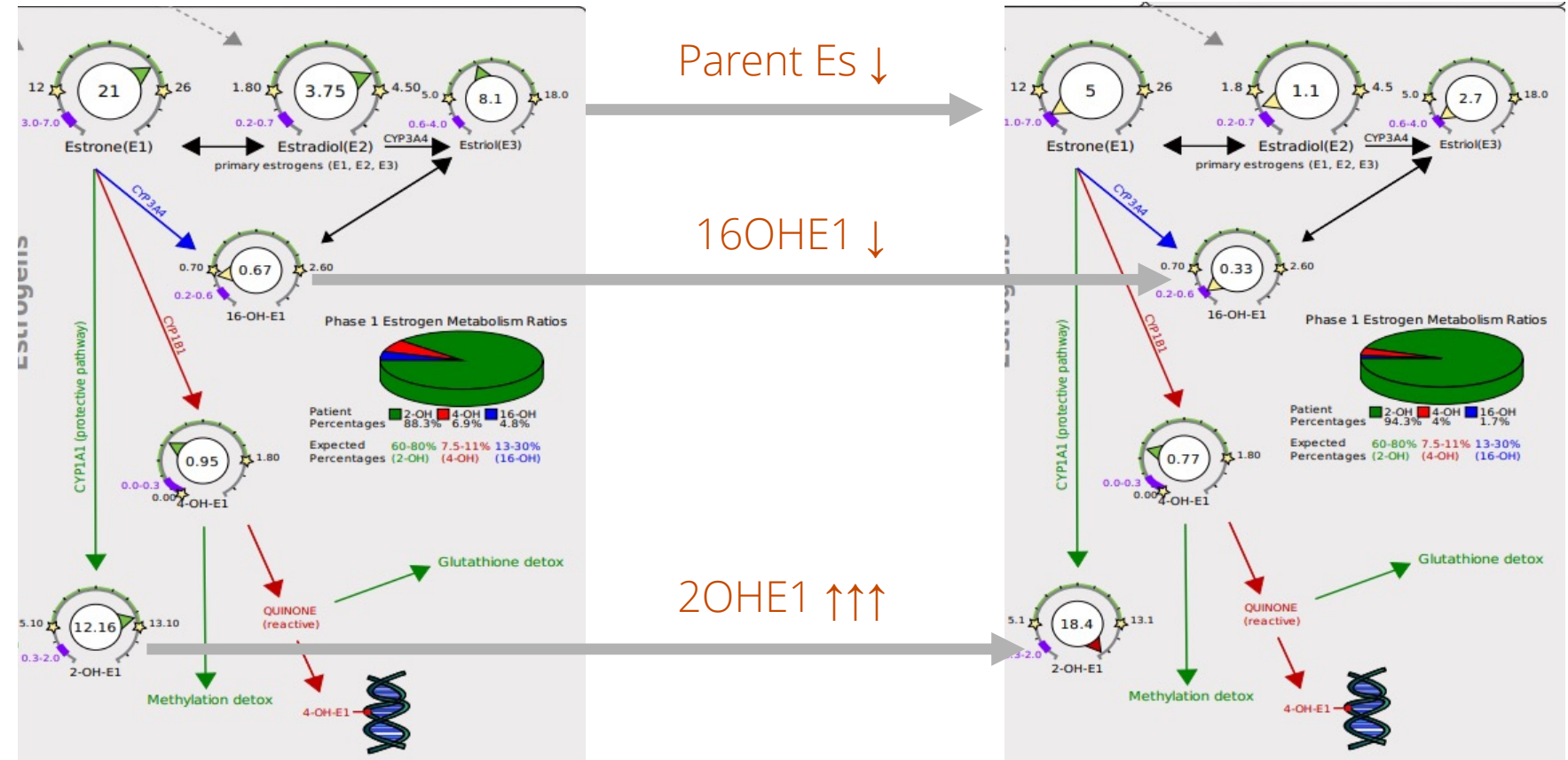


# 34yoF Before 200mg DIM

# After 6 months of DIM

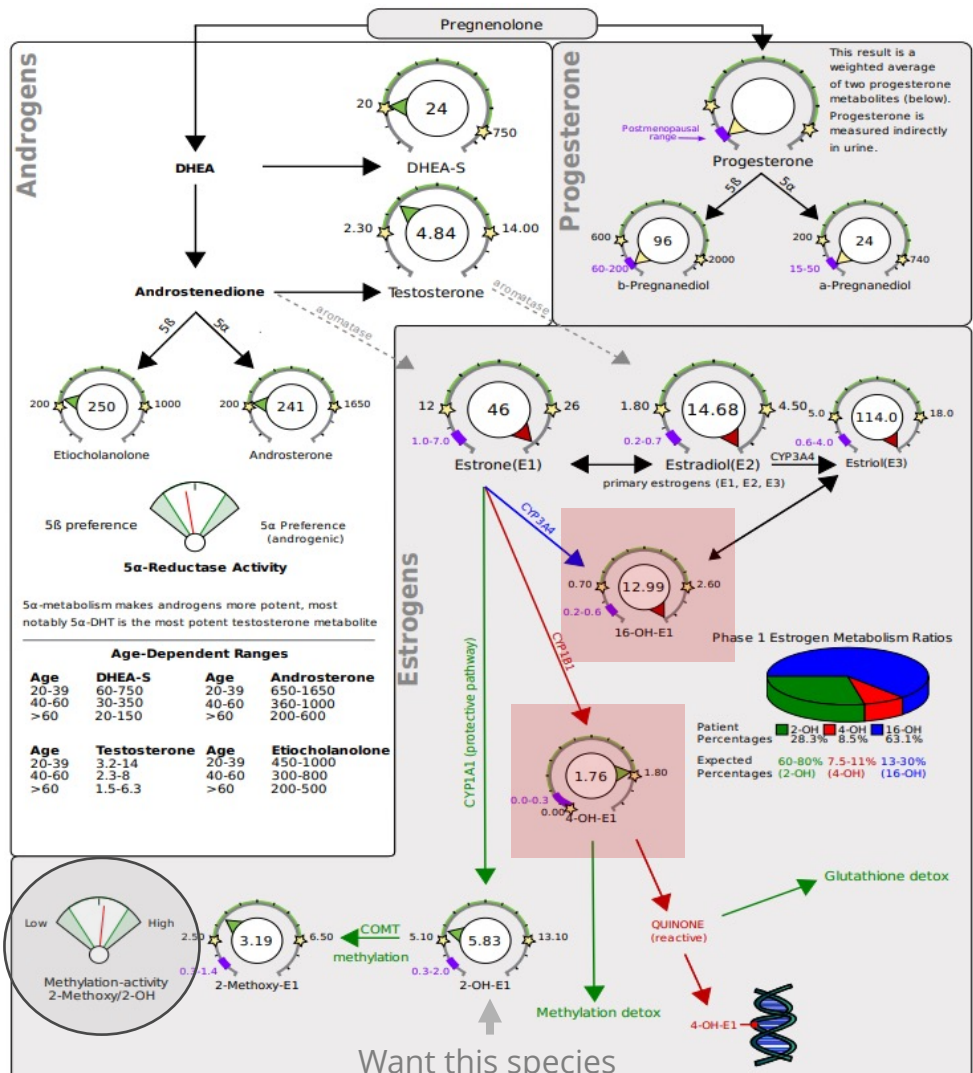


# 42yoF, Severe migraines, mood swings





# 44yoF – Heavy menses, regular cycles, bloating



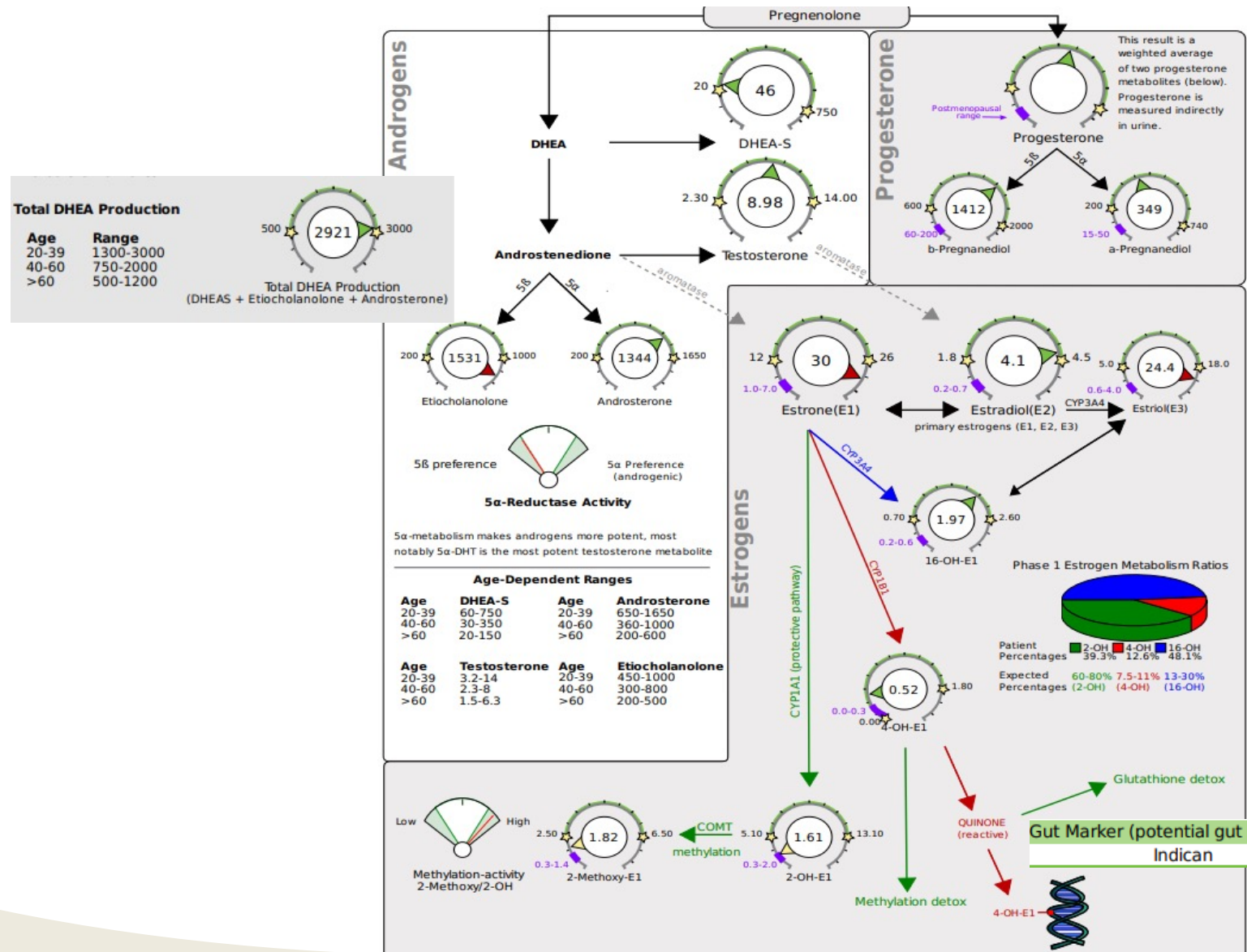
Want this species to be dominant

- Down-regulate 16OHE1
  - Nutritional supplement containing: DIM, I3C
    - Known to route metabolism away from 16OHE1 and increase SHBG
- Compare 16OHEs with SHBG (↓ in MetS), GGT (alcohol), prolactin, and glycemic markers on your serum panel to get more specific
- Support methylation to plan for increased 2OHE1 and 2OHE2 substrate
  - MTHF, Hydroxocobalamin, SAmE, Magnesium, B6, PhosCholine, TMG, MSM

# To DIM or Not to DIM?

That is the question

# 44yoF, Weight loss resistant



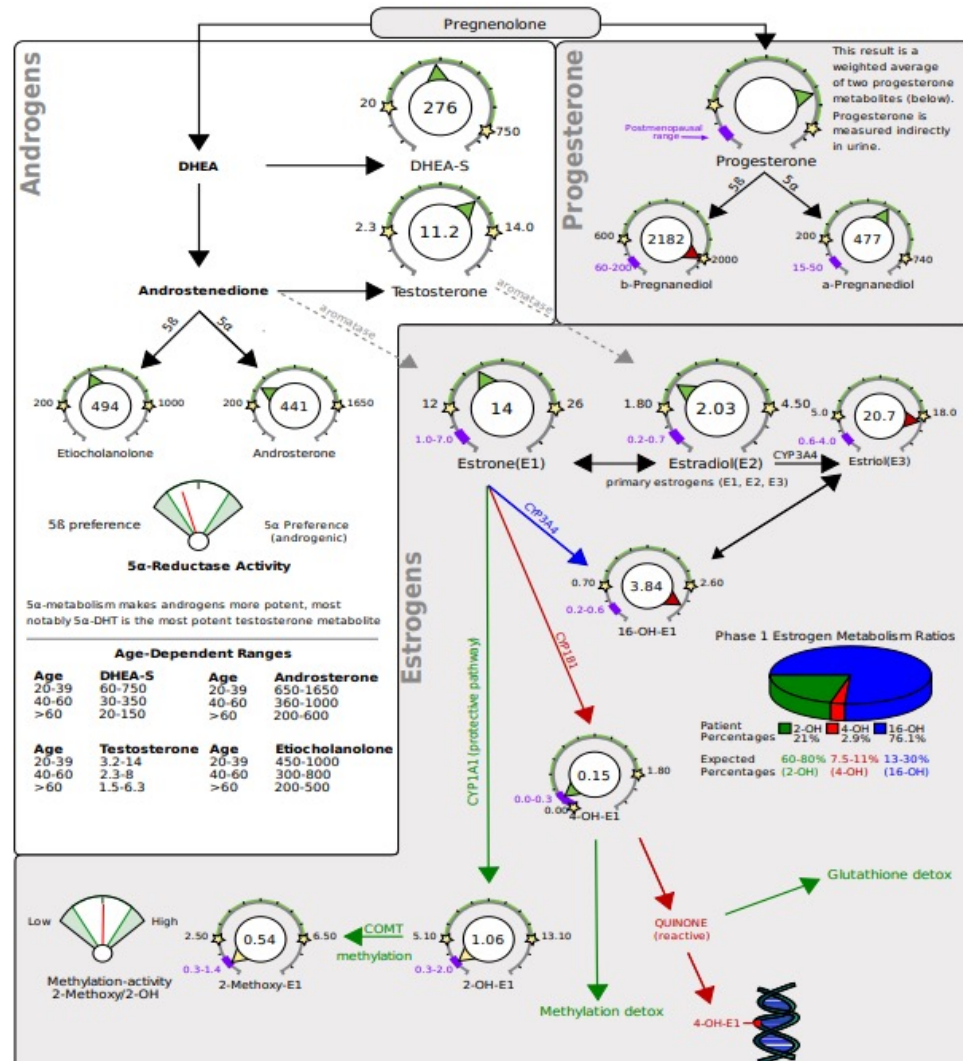
## Assessment:

- Estrogens recirculating from dysbiotic gut
- Low Phase One Activity
- High Methylation
- Consider gut inflammation as driver of poor sulfation and detox

## Example Plan:

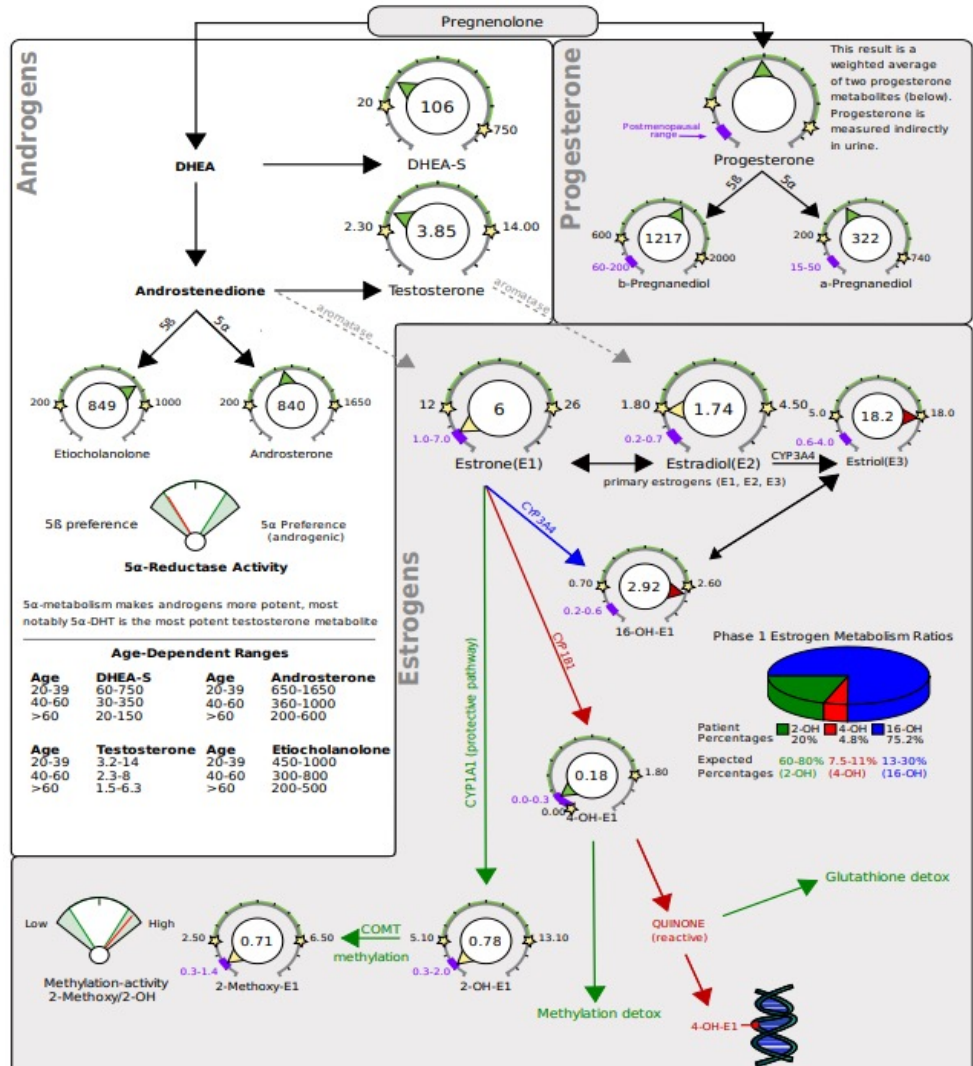
- Supplement with: 200 mg DIM + 1g CDG
- Myoinositol to address insulin sensitivity and high androgens
- NAC as a sulfation support and gut/systemic anti-inflammatory
- Order Comprehensive Stool test for tailored approach to gut healing

# 37yoF – Hair loss, acne (and only mild estrogenic symptoms)



- Check serum for high prolactin (prolactin induces androgen symptoms), LH, DHEA-S, and for low SHBG – Treat what you find!
- Gentle 16-OHE1 busters and 2OHE1 movers: Rosemary extract, Omega-3s, Ground flaxseeds, perhaps a low dose DIM product (<100mg/day)
- Support General Detox and **Sulfation**
  - Sulfur DONORS – Taurine, NAC, MSM, Methionine, Glutathione
  - Sulfation COFACTOR – Molybdenum
  - Support expression of SULTs – Thyroid supports that promote T3, SFN
  - Gallbladder supports – Bile Acids
  - Control inflammation
  - General liver support – Artichoke, Milk thistle
- Rationale: Sulfated estrogens can't bind receptors

# 20yoF – heavy menses, mood swings, night sweats



Overall:

- Parent estrogens are low-end
- Androgens low-normal for age
- DIM is not first choice – low E symptoms
- Instead, support sulfation (liver/gall bladder supports, sulforaphane, NAC, taurine, molybdenum)
- Check out that Indican – gut relationship

Category	Test	Result	Units	Normal Range
<b>Nutritional Organic Acids</b>				
Vitamin B12 Marker (may be deficient if high) - (Urine)				
	Methylmalonate (MMA)	Within range	1.3 ug/mg	0 - 2.5
Vitamin B6 Markers (may be deficient if high) - (Urine)				
	Xanthurenate	Above range	1.48 ug/mg	0.12 - 1.2
	Kynurenate	Above range	6.1 ug/mg	0.8 - 4.5
Glutathione Marker (may be deficient if low or high) - (Urine)				
	Pyroglutamate	Within range	42.1 ug/mg	28 - 58
Biotin Marker (may be deficient if high) - (Urine)				
	b-Hydroxyisovalerate	Above range	21.6 ug/mg	0 - 12.5
Gut Marker (potential gut putrefaction or dysbiosis if high) - (Urine)				
	Indican	Above range	105.7 ug/mg	0 - 100

# What about Sulforaphane?

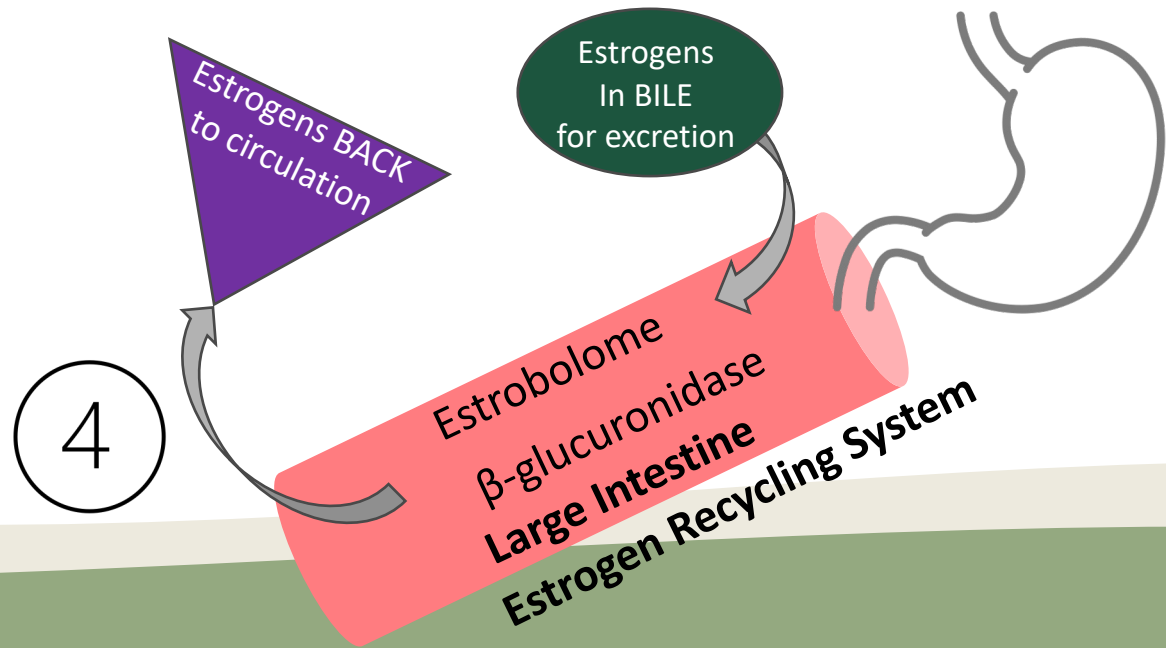
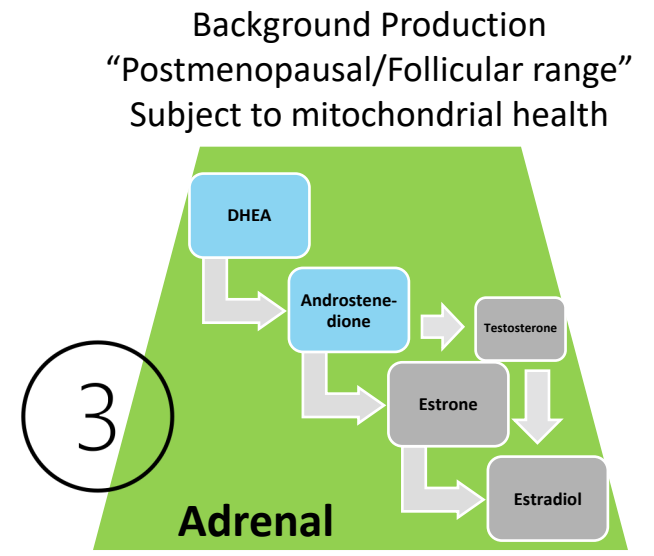
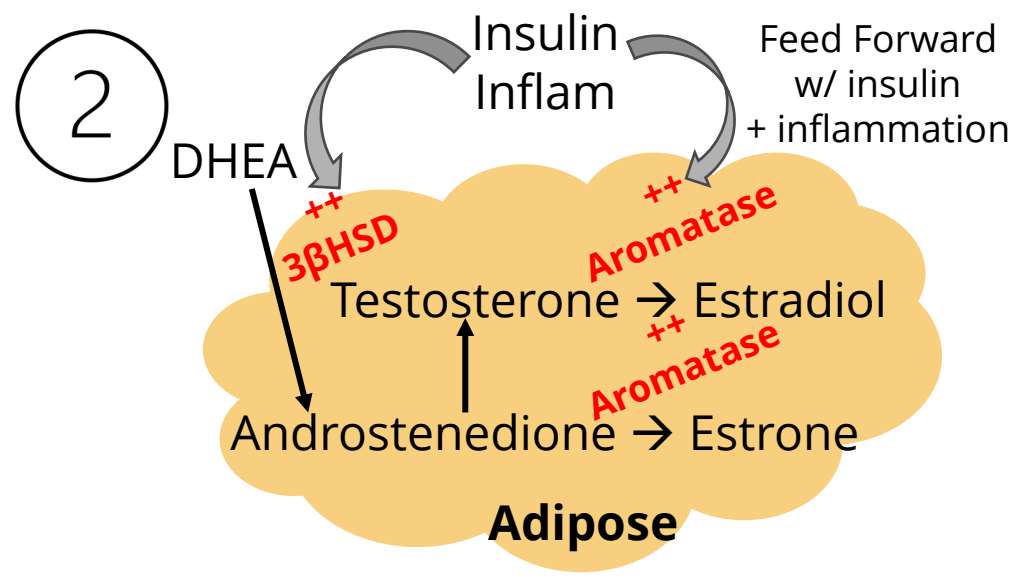
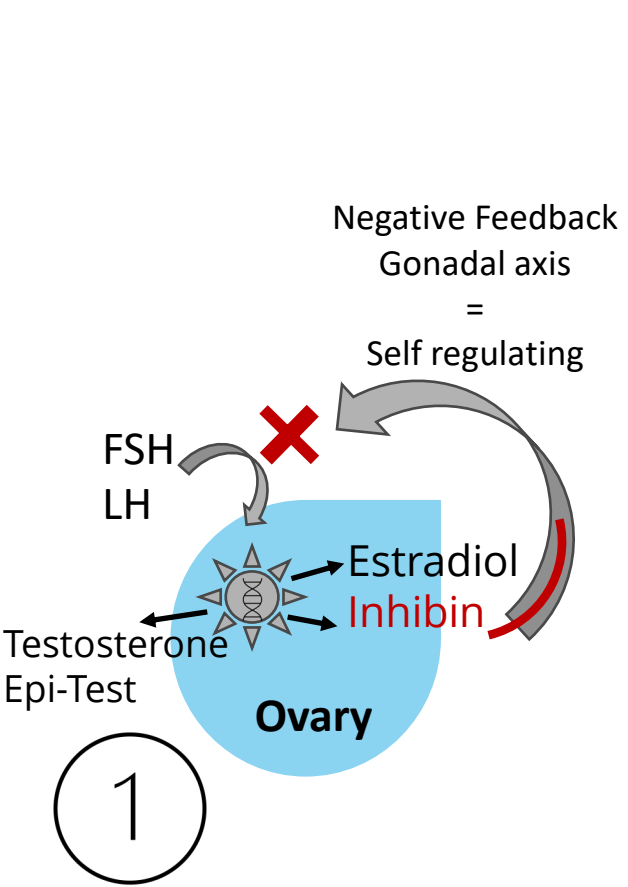
- SFN comes from broccoli sprouts
  - The marriage of glucoraphanin and myrosinase
- **Gentle Phase 1** Induction of CYP1A1 2-OHEs
- **Powerful Phase 2** Detox Support
  - Upregulates COMT expression
  - Increases Glutathione peroxidase activity
  - Supports expression of SULT genes for sulfation
- **Helps resolve high 16-OHE1 when estrogen production and SHBG aren't the problem**
- **Protects the DNA from 4-OHE1 and 4-OHE2 by up-regulating Quinone Reductase**



# Step 3: Identify the Source of Estrogen and Treat There

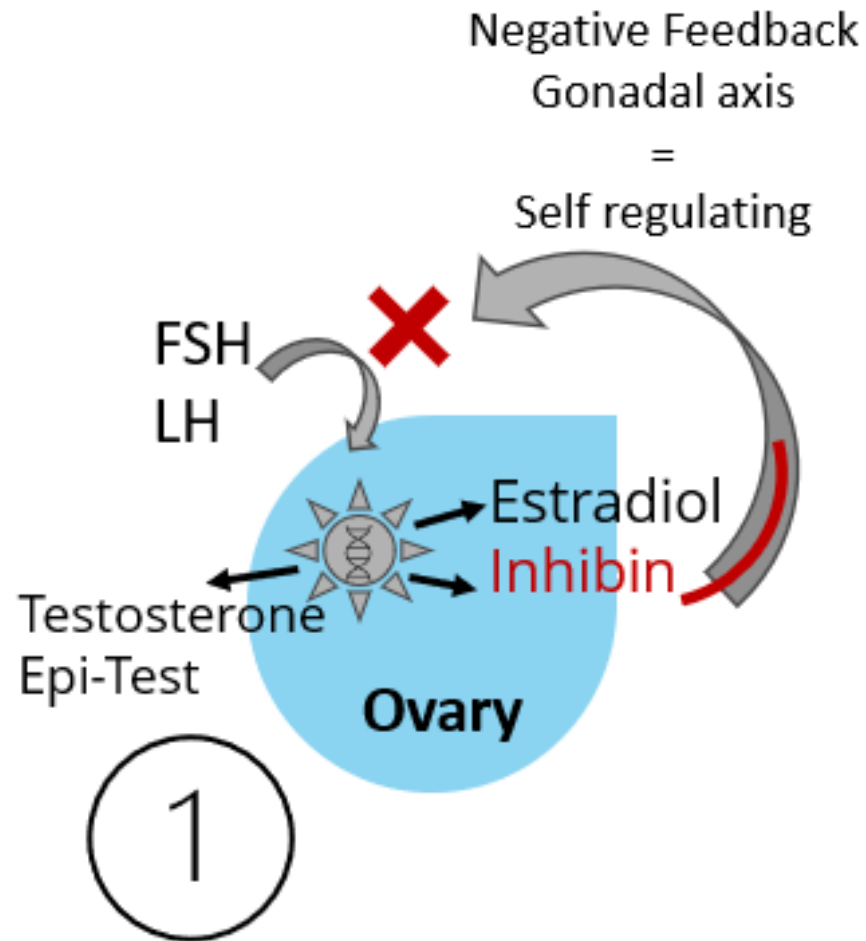
Target the Source  
Foundational Plans

# Where is Estradiol made?



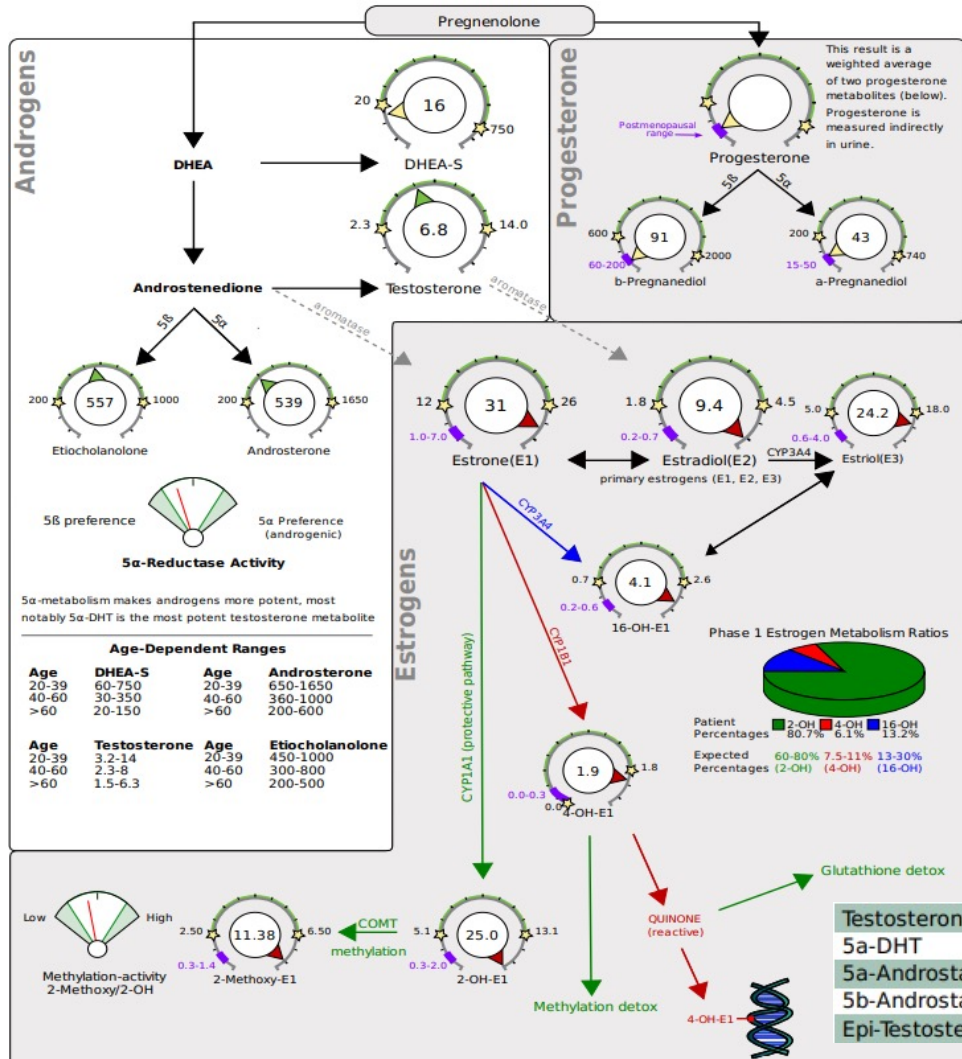


# Ovarian Source Estrogens



- Upregulators of Ovarian Es
  - FSH, LH
- Look for:
  - Age-range T *and* Epi-T
    - If Epi-T is low, ovaries might not be making that high estrogen!
  - High E1, E2, and metabolites
  - Pregnanediol levels to determine
    - ovulation,
    - anovulation,
    - luteal insufficiency, or
    - wrong collection timing (ovulatory phase estrogens can be quite high)

# Ovarian Source High Estrogens – 49yoF, irreg cycles



# Ovarian Source High Estrogens – Treatment

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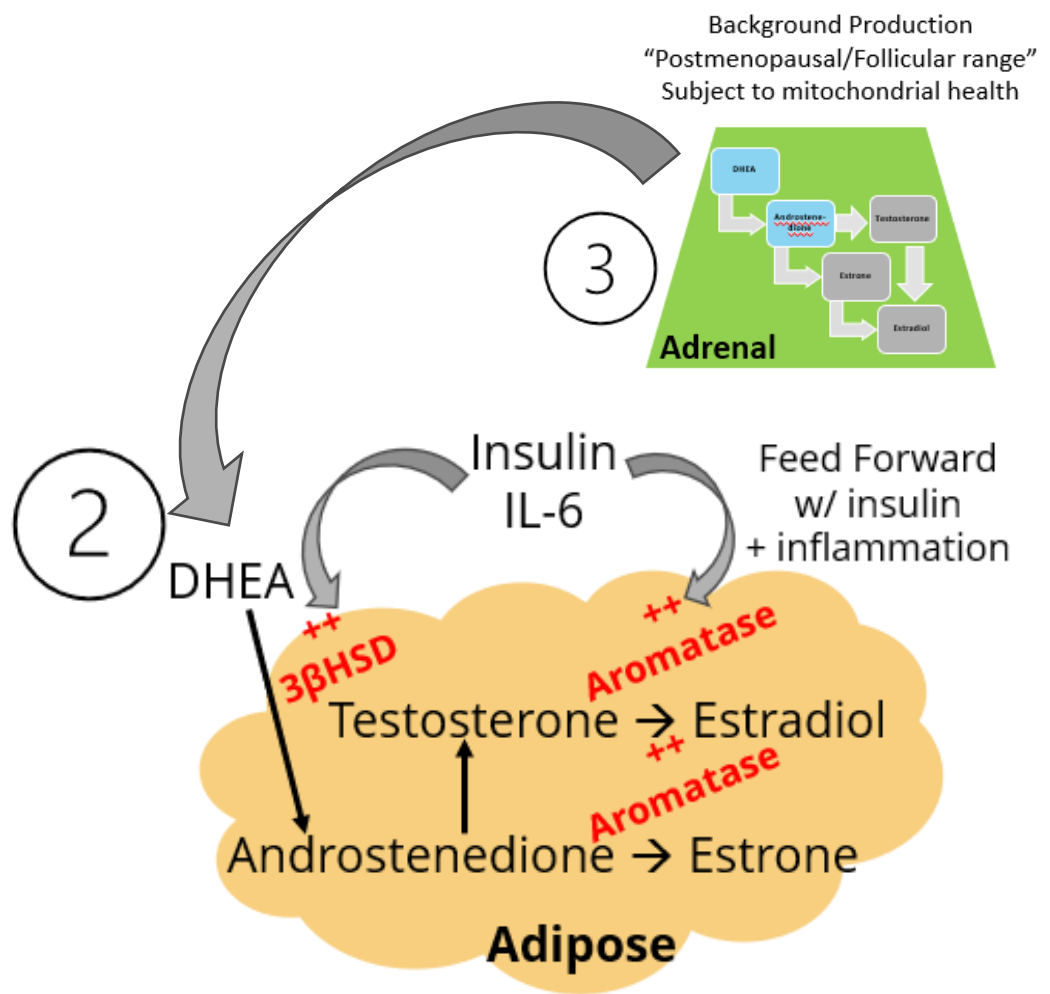
- Increase ovarian response to FSH
  - Myoinositol 1200-2000mg QD
  - Phytoestrogens: Maca, Dong Quai, Black cohosh, Yucca schidigera
  - Bovine Glandular Ovary
  
- Improve functional ovarian reserve
  - MTHF
  - Melatonin 3 mg QHS
  - NAC 600-1800 daily
  - Omega-3 intake
  - Trans-resveratrol
  - Mitochondrial Micronutrition: CoQ10, ALA, Carnitine, Antioxidants
  - Mediterranean style diet

# Adrenal-Source and Adipose-Source Estrogens Go Hand in Hand

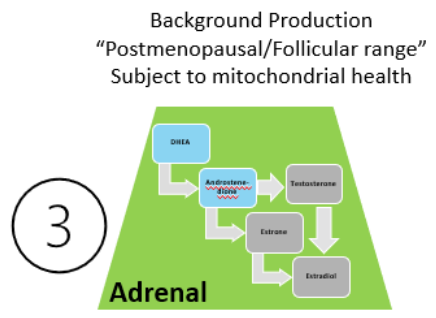
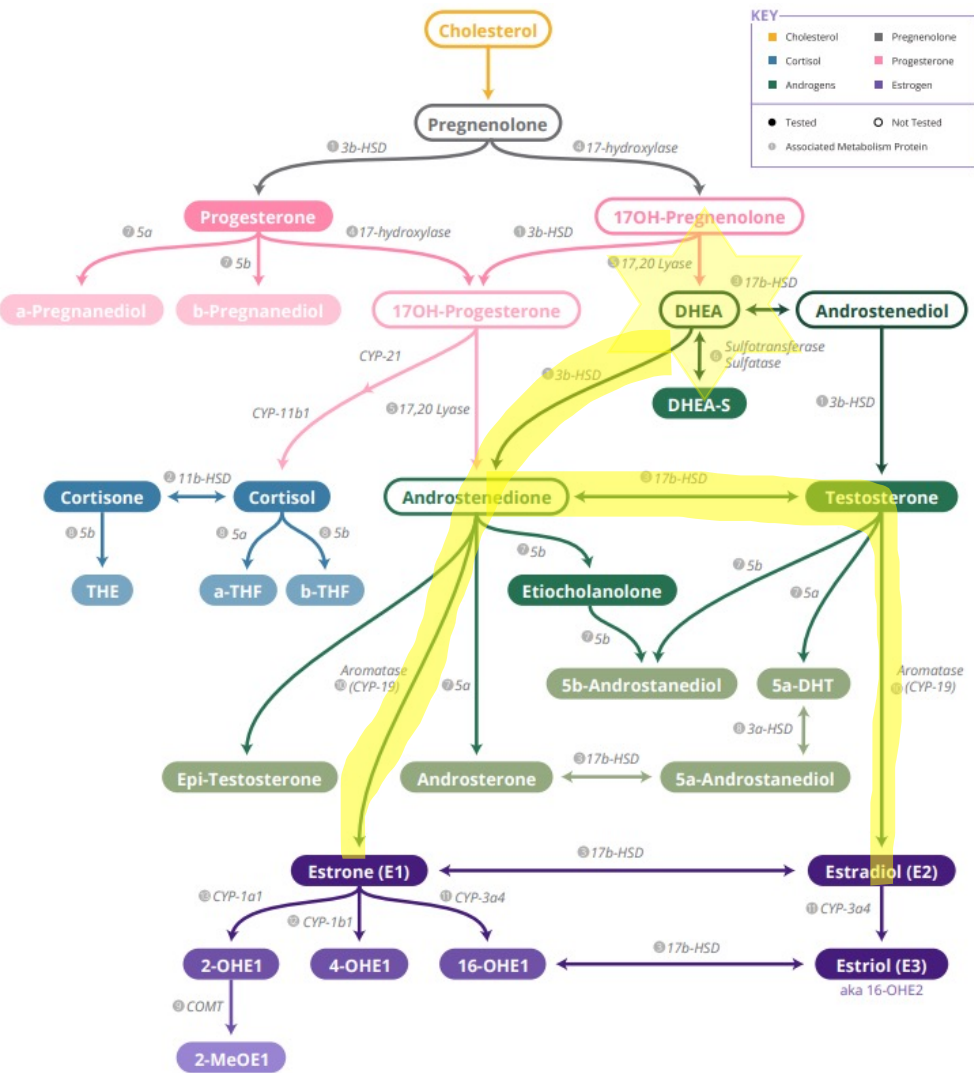
Adipose Estrogens come from Adrenal DHEA + locally produced TESTOSTERONE  
**Aromatase**

- Up-regulators of Adrenal DHEA production:
- ACTH (stress)
  - Insulin
  - Prolactin

- Look for:
- ↑ DHEA-S in serum (↑ adrenal androgen sum in urine)
  - ↑ Androsterone
  - ↑ 16-OHE1
  - ↑ Estriol
  - ↑ Testosterone
  - ↑ 5a-Androstanediol
  - ↓ Free Cortisols compared to ↑ TCMs
- } DUTCH test



# Adrenal-Source Estrogens – From DHEA!



Adrenal Estrogens come from **ANDROGENS**

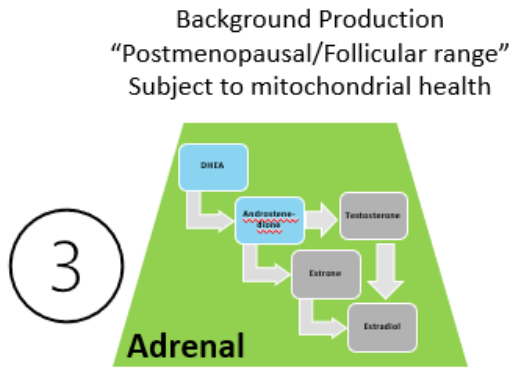
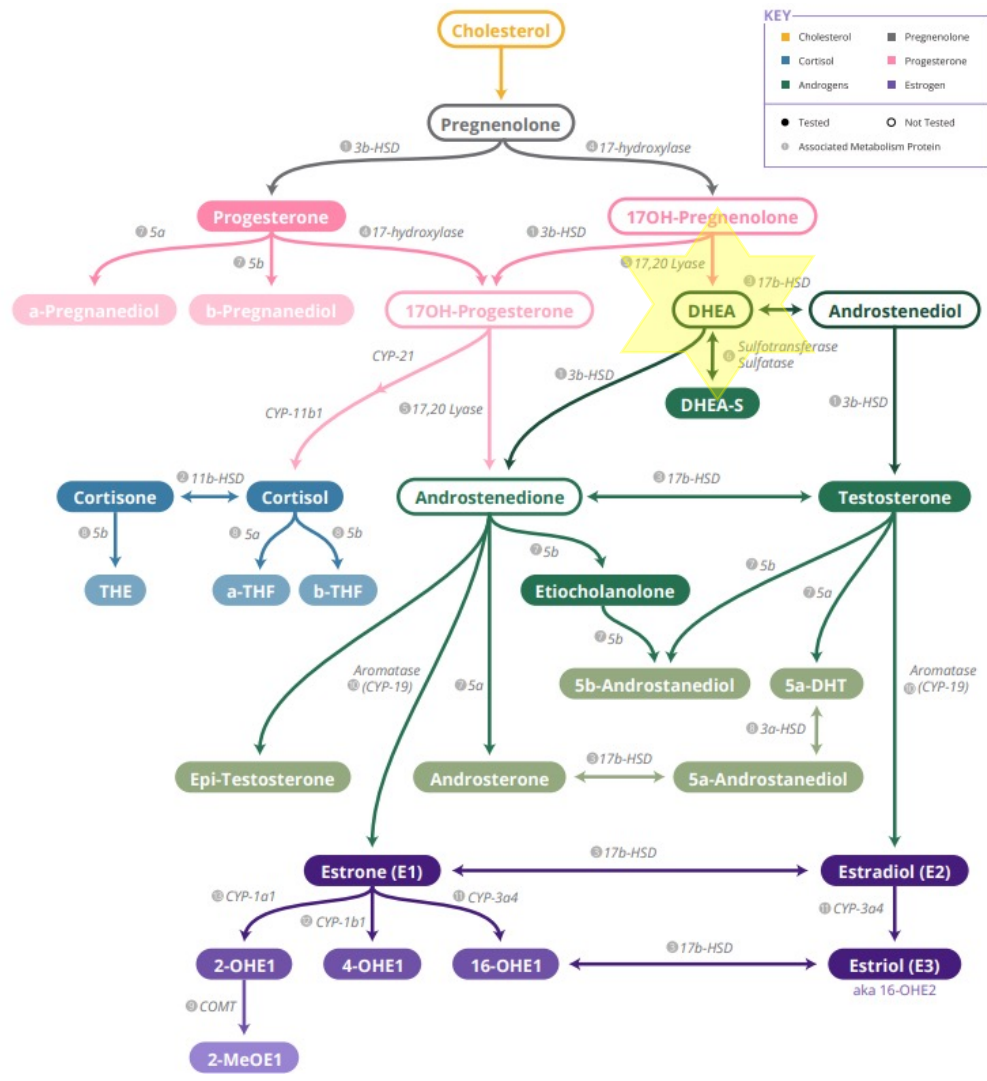
Up-regulators of Adrenal DHEA production:

- ACTH (stress)
- Insulin
- Prolactin

Look for ELEVATED

- DHEA-S\*
- Androsterone
- 16-OHE1
- Estrinol
- Testosterone
- 5a-Androstanediol
- ↑ Free Cortisols with matching clearance ↑ TCMs

# Adrenal-Source Estrogens – From DHEA!



**Remember:**  
DHEA is a PRO-HORMONE.

Because urine = post-tissue uptake and conversions have been made including through Androstenedione to **Estrone**, urine Total DHEA doesn't always correlate perfectly with serum DHEA-S in patients with high conversion to estrone and 16OHE1.

Serum represents DHEA-S in circulation to tissues.  
Urine represents what happened after tissue uptake.

# Is Estrone a “Bad Estrogen”?

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- Estrone
  - Higher affinity for ER $\alpha$  than ER $\beta$
  - But *overall lower affinity* for ERs than E2 has
  - May be considered “BAD” if it’s high because of high Androstenedione and a sign of formation of estrogens in adipose tissue

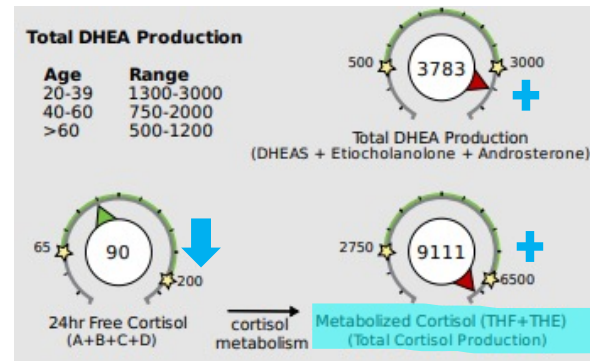
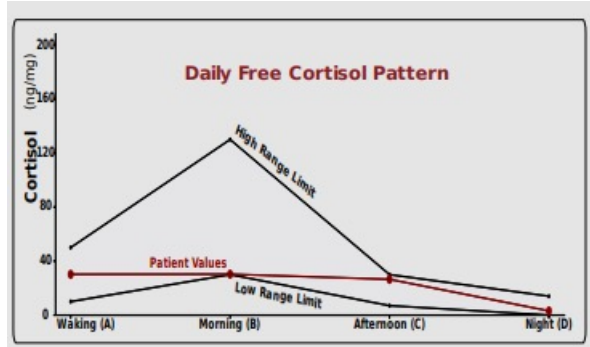
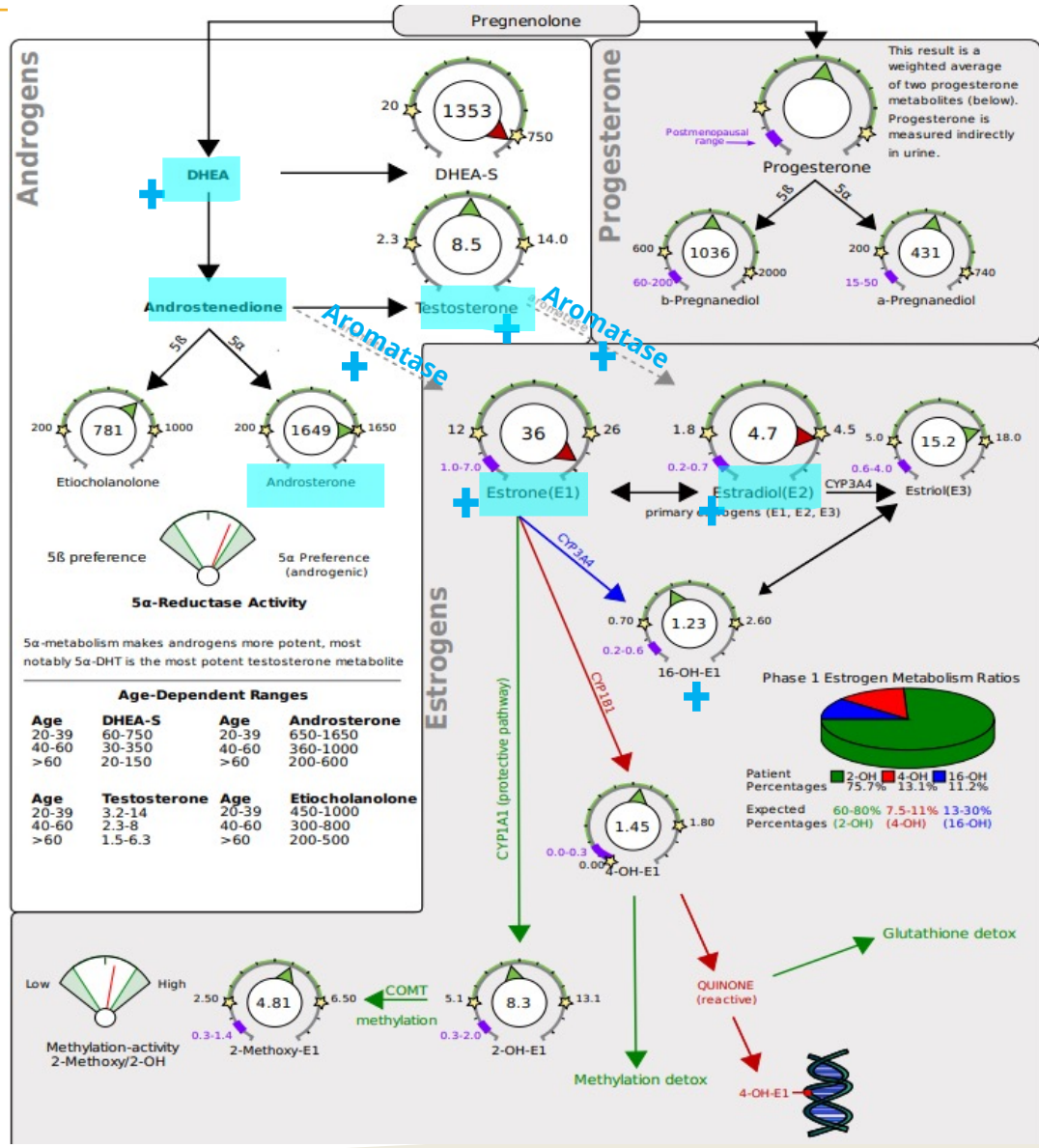
# Adipose-Source Estrogen Drivers

Adrenal Androgens → Adipose Estrogens

Insulin

↑ Estrone and Estradiol (often ↑ 16OHE1 also)  
High adrenal androgens

Also may find:  
↑ TCMs (compared to ↓ total free)  
Shift to THE





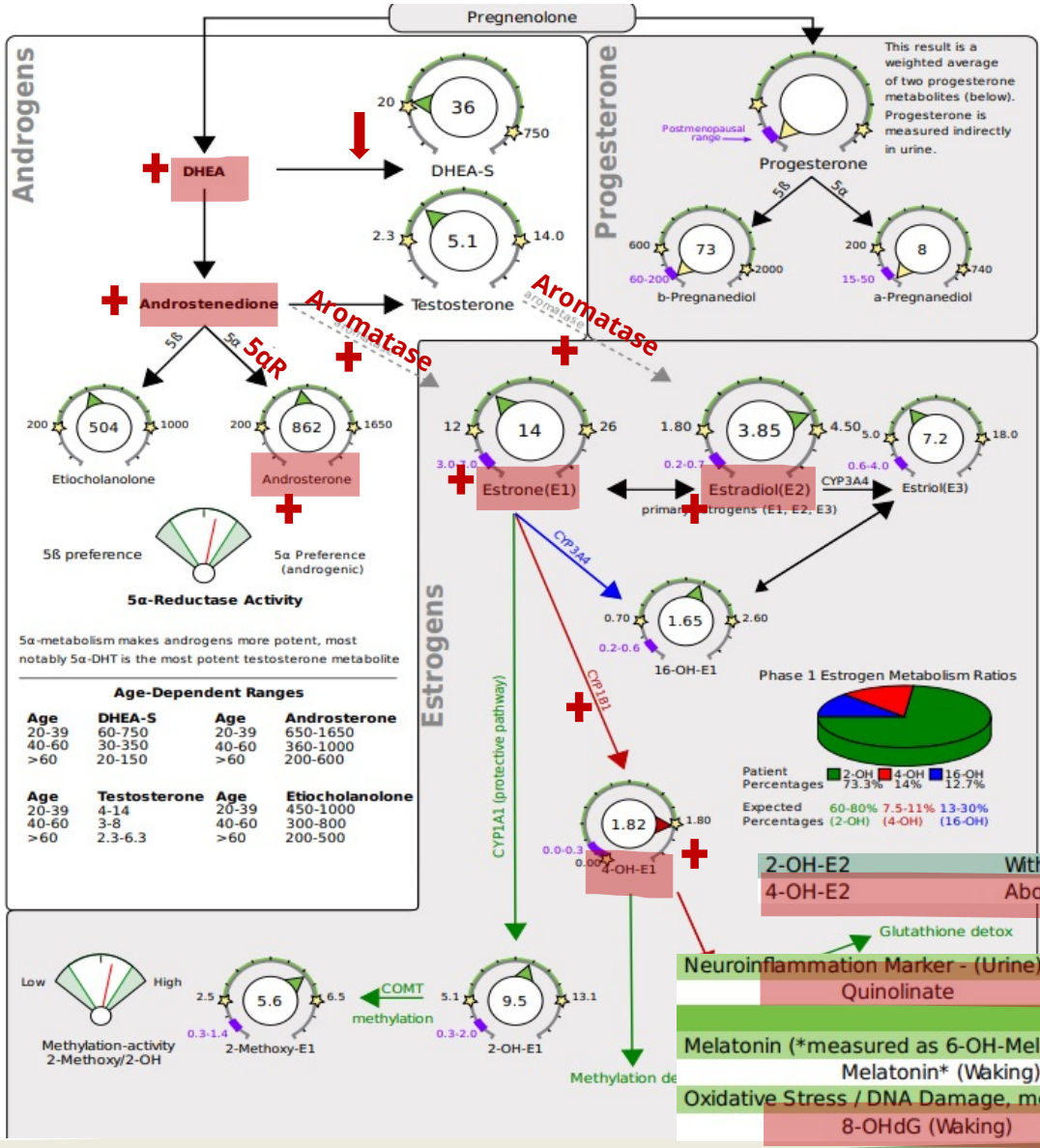
# Inflammation

Adrenal Androgens →  
Adipose Estrogens:

Driver:

## Systemic Inflammation

- ↑ Aromatase expression (low androgens, high estrogens)
- ↑ CYP1B1/4-OHEs
- May see high 16-OHE1 if inflamm is autoimmune or gut driven
- Low sulfated DHEA compared to metabolites
- ↑ 5aR activity – Androsterone
- ↑ Quinolinate
- ↑ 8OHdG (Oxidative stress/DNA)



2-OH-E2	Within luteal range	0.46	ng/mg	0 - 1.2
4-OH-E2	Above luteal range	0.6	ng/mg	0 - 0.5

<b>Neuroinflammation Marker - (Urine)</b>				
Quinolinate	Above range	11.6	ug/mg	0 - 9.6

<b>Additional Markers</b>				
<b>Melatonin (*measured as 6-OH-Melatonin-Sulfate) - (Urine)</b>				
Melatonin* (Waking)	Within range	32.1	ng/mg	10 - 85
<b>Oxidative Stress / DNA Damage, measured as 8-Hydroxy-2-deoxyguanosine (8-OHdG) - (Urine)</b>				
8-OHdG (Waking)	Above range	5.8	ng/mg	0 - 5.2

# Adipose-Source High Estrogens – Treatment Examples

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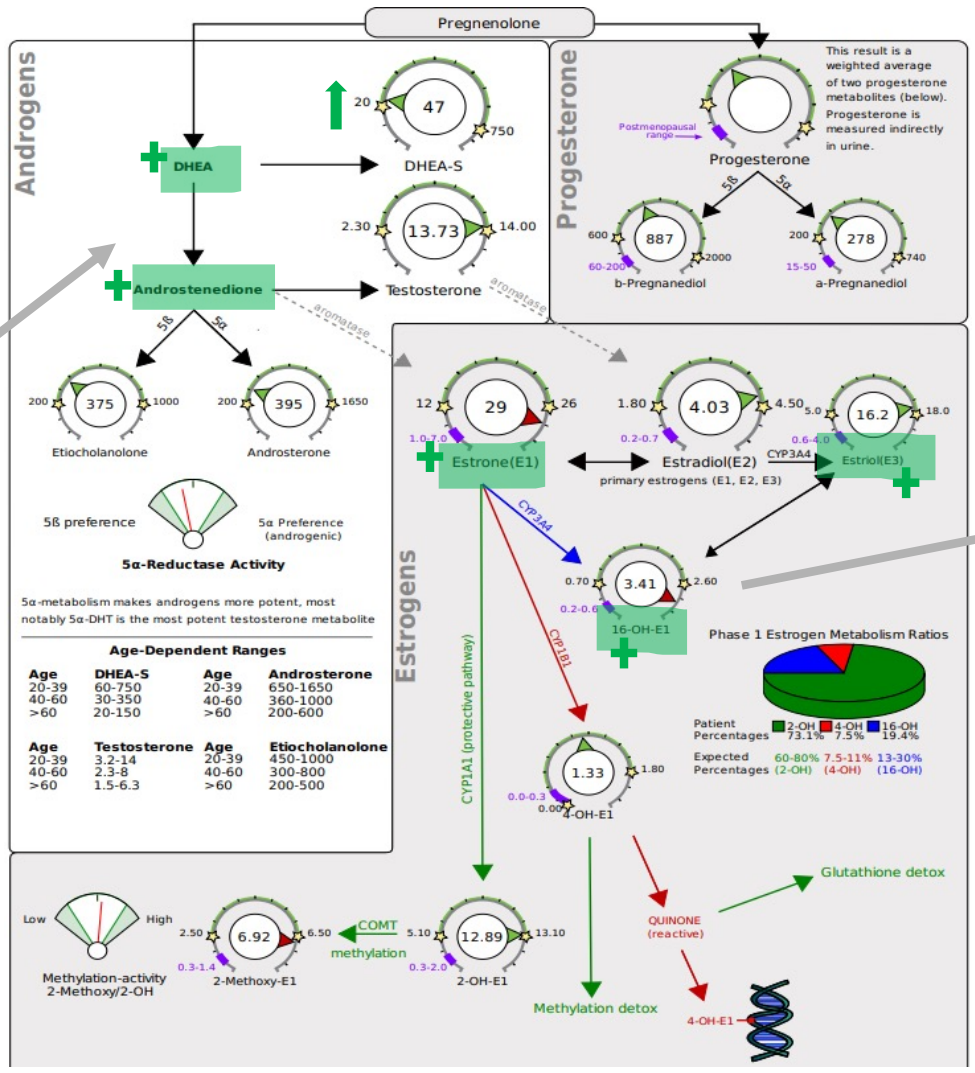
- Lifestyle supports:
  - Anaerobic exercise - Resistance training
- Insulin sensitizers:
  - Berberine 300-500 mg up to TID
  - Myoinositol 2-4g QD
  - R-ALA 300 mg
  - Minerals: Chromium, Zinc, Magnesium
  - Cortisol-controlling blood sugar herbs: Bitter melon, Cinnamon, Holy basil
  - Rx: Metformin, Thiazoladinediones
- Anti-inflammatories
  - Liposomal Curcumin 1-3 g daily
  - EGCG 800 mg daily
  - Rosemary – bottle dosing (depends on the extract)
  - Medicinal Mushroom therapeutics
  - Systemic enzyme therapies (Bromelain, empty stomach pancreatic enzymes, etc)

# Adrenal-Source Estrogen Drivers

Hormone/Pathway Drivers:

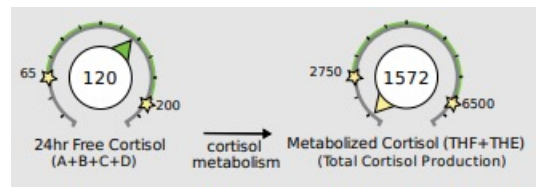
Prolactin

Prolactin stimulates Adrenal Androgen Production



16OHE1 makes this an estrogen dominant presentation

16-OHE1 stimulates Pituitary ERs → Prolactin



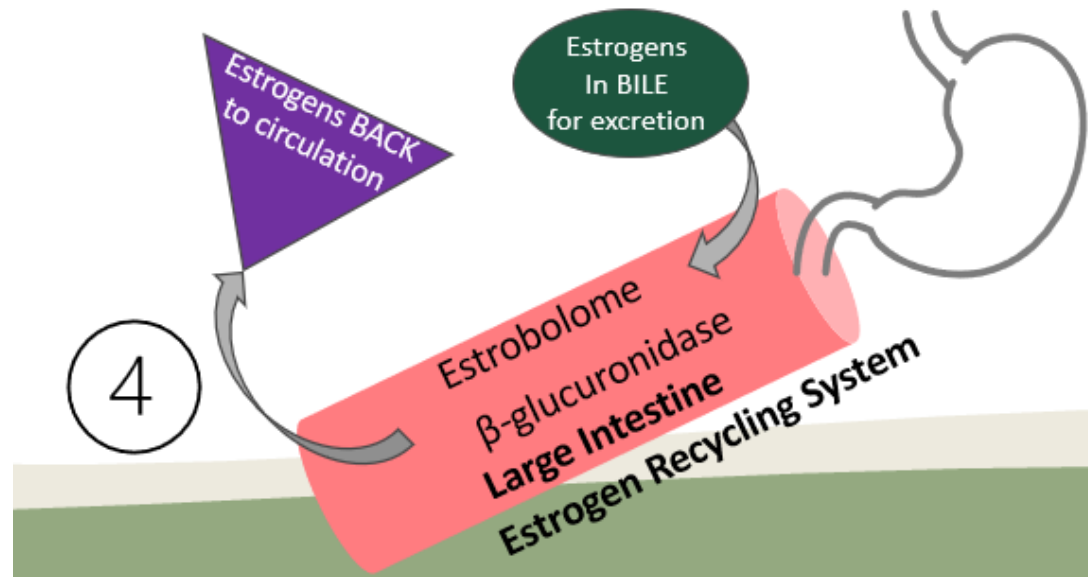
Note: When prolactin is high long term, GnRH is suppressed leading to LOW ovarian estrogen output (check for low LH and FSH)

# Prolactin as Driver of Adrenal DHEA → 16-OHE1 and E3

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- Sample Approach:
  - Rule out or treat hypothyroid (TSH is co-released with Prolactin)
  - Check HVA in OATs section and treat lows (if low, could be inadequate dopaminergic inhibition of PRL)
  - Refer for pituitary imaging if very high and confirmed
    - Prolactinomas can and should be managed medically or surgically
  - For idiopathic pesky high prolactin levels causing cycle irregularity and high androgen symptoms:
    - *Magic Combo*: Vitex + DIM (dosing will vary person to person, titrated/monitored)
      - Vitex increases dopamine centrally which opposes prolactin
      - DIM decreases 16-OHE1 formation cutting off estrogen up-regulation of PRL

# Gut-Source Estrogens

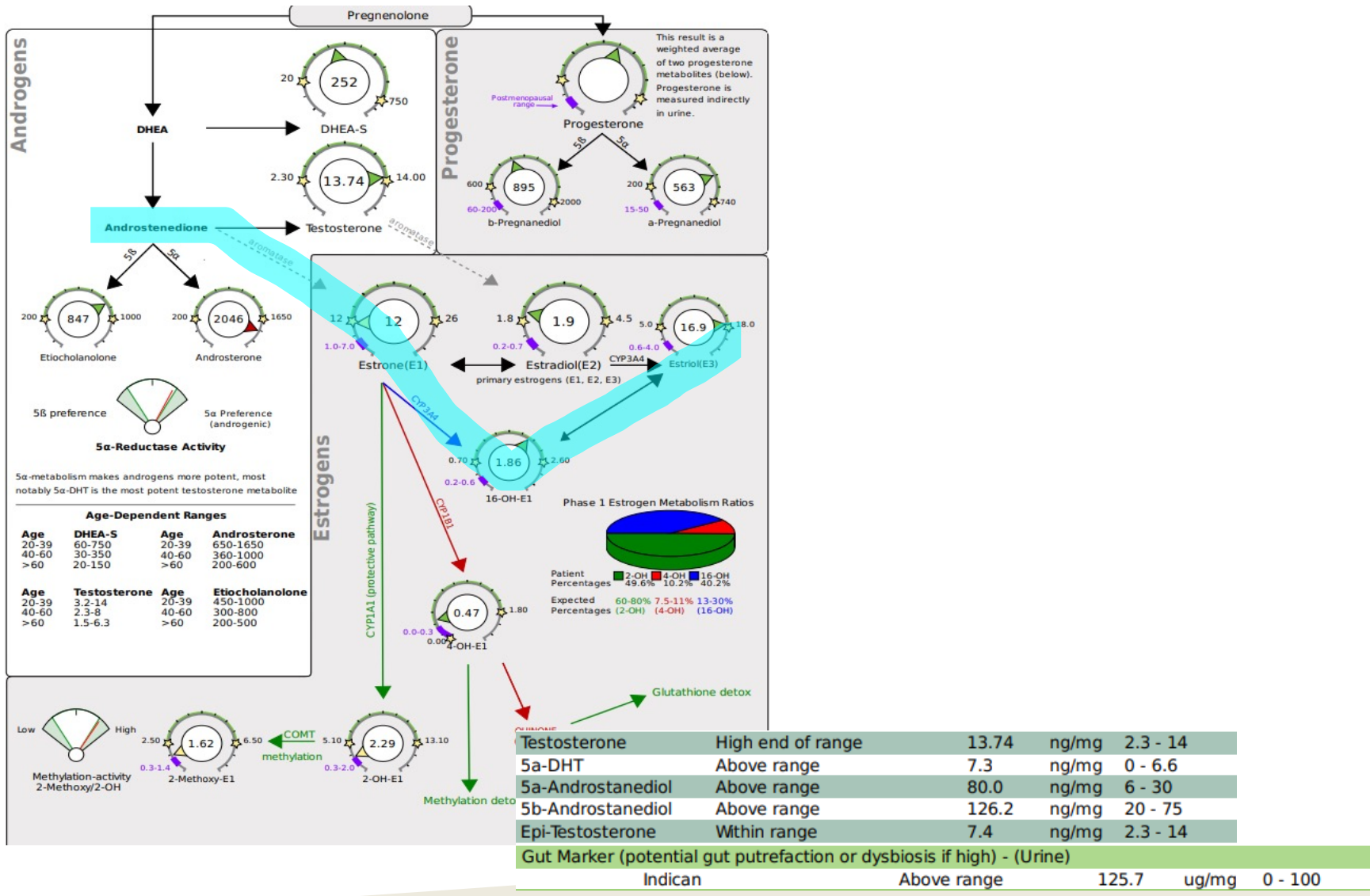


- On a GI Panel, look for:
  - High  $\beta$ -glucuronidase
- $\uparrow$   $\beta$ -glucuronidase producers:
  - Bacteroides fragilis
  - Clostridium perfringens
  - E. coli
  - Peptostreptococcus
  - Staphylococcus
- Not always a clear pattern on a DUTCH test alone, but look for:
  - High estrogens and metabolites
    - Often esp/only 16OHE1 and Estriol
  - Low DHEA-S compared to Androsterone
  - High Indican (dysbiosis marker)

# Gut-Source Estrogens – 26yoF PCOS, heavy menses, mood swings, BMI 25

Hierarchy:

Before rushing in to improve ovarian aromatase activity and increase androgen clearance through estrogen pathways, treat the gut.



# Gut-Source High Estrogens - Treatment

- Do some comprehensive stool testing
  - Test for  $\beta$ -glucuronidase activity and dysbiosis
- Address  $\uparrow$   $\beta$ -glucuronidase producers with anti-microbials:
  - Bacteroides fragilis
  - Clostridium perfringens
  - E. coli
  - Peptostreptococcus
  - Staphylococcus
- Correct digestive problems
  - Hypochlorhydria (HCl, ACV), Pancreatic insuff (digestive enzymes), Optimize diet (Mediterranean, AIP, etc)
- Consider **Calcium D-glucarate**
  - Keeps estrogens glucuronidated and on the “outs”
  - 1g – 1.5g in divided doses (it’s short-acting)
- Consider General Liver Detox Supports
  - Sulfury supports (NAC, GSH, Taurine, Methionine, SFN), humic/fulvic acids, butyrate
  - Herbs: Artichoke, Milk thistle, Reishi, etc
- Nourish the gut lining
  - Glutamine, DGL and other demulcents like okra and slippery elm,
- Recolonize
  - Pre-biotics and Pro-biotics
- Support Progesterone
  - Nourishes Bifidobacterium and L. reuteri
  - Decreases gut permeability
  - Offers enteric neuroprotection and is anti-inflammatory

# “OTHER” Drivers of Estrogens

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- Adenomyosis
- Cysts
- Endometriosis
- Fibroids
- Pregnancy

*Treat specifically.*



# Estrogen Dominance Assessment/Plan Sheet

## Estrogen Dominance Assessment Sheet for Approaching the Symptomatic Patient (Example)

### Step 1: Is Progesterone in balance with Estrogen?

PG/E2 ratios (DUTCH or Serum) – support progesterone if Low

- Luteal (Goal 100-500): \_\_\_\_\_
- Day 3 Follicular (Goal 50-300): \_\_\_\_\_

### Step 2: How does estrogen FEEL?

Estrogenic Detox Preferences (circle the one higher in its luteal range)

Treat pathways directly initially while working on Underlying Pathology (Step 3)

- 2-OHE1 vs 16-OHE1
- 2-OHE1 vs 4-OHE1

*If urine E1 and E2 are LOW and/or Total E2 in serum is LOW, consider avoiding DIM and I3C and choosing other detox supports that encourage sulfonation and phase one supports that downregulate expression of CYP1B1 and/or 16OHE1 formation, particularly. (Check out slides: 16-OHE1 Busters and 4-OHE Busters)*

### Step 3: Determine Underlying Pathology

#### Signs of Insulin and/or Inflammation as Driver

- 2-OHE1 vs 4-OHE1 favoring 4-OHE1
- 2-OHE2 vs 4-OHE2 favoring 4-OHE2
- Hypermetabolic Cortisol Pattern
  - Low(er) 24-hr Free Cortisol vs Total Cort Metabolites
- Low urinary DHEA-S (esp compared to metabolites)
- 5 $\alpha$ -Reductase elevated (Androsterone, 5 $\alpha$ Andro,  $\alpha$ -THF/ $\beta$ -THF)
- Quinolinic acid elevated

#### Signs of Dysbiosis/ $\beta$ -glucuronidase as a Driver

- 2-OHE1 vs 16-OHE1 favoring 16-OHE1
- Low urinary DHEA-S (esp compared to metabolites)
- High Indican
- Free Cortisols may be high

#### Signs of Impaired Egg Quality and Low Functional Ovarian Reserve

- Elevated serum LH:FSH ratio and high serum E2 on cycle day 3
- Total DHEA low in urine (DHEA-S low in serum)
- Melatonin metabolite low
- Pyroglutamate elevated and/or 8OHdG elevated
- Quinolinic acid elevated

# Step 1 from Estrogen Dominance Assessment/Plan Sheet

## Estrogen Dominance Assessment Sheet for Approaching the Symptomatic Patient (Example)

### Step 1: Is Progesterone in balance with Estrogen?

PG/E2 ratios (DUTCH or Serum) – support progesterone if Low

- Luteal (Goal 100-500): \_\_\_\_\_
- Day 3 Follicular (Goal 50-300): \_\_\_\_\_

### Step 1: Treatment Options for Low PG/E2 Ratio

#### Support Ovulation and Luteal Sufficiency

- LH modulators: (*I always use these pan-cycle*)
  - Myoinositol - 2-4g daily
  - Vitex agnus-castus - 200-600mg daily
- Adaptogens: (increase stress resilience)
  - Ashwagandha, Schisandra, Ginseng, Holy basil, Rhodiola

#### Treating Low Progesterone with HRT

- OTC USP Progesterone Transdermal Creams and Topical Oils
  - Large dosing range 10-50mg most common
- Rx Oral Progesterone
  - Orally delivered is more anxiolytic and sleep inducing
  - Dose at bedtime, can cause rapid relaxation and drowsiness;
  - 100-400mg QHS commonly used
  - Prometrium IR Micronized Progesterone 100mg increments (FDA approved)
  - Compounded SR Micronized Progesterone in E4M matrix
- Rx Vaginal Progesterone/Suppositories
  - Suppository dosing typically 100 – 800mg

# Step 2 from Estrogen Dominance Assessment/Plan Sheet

## Step 2: How does estrogen FEEL?

Estrogenic Detox Preferences (circle the one higher in its luteal range)

Treat pathways directly initially while working on Underlying Pathology (Step 3)

- 2-OHE1 vs. 16-OHE1
- 2-OHE1 vs. 4-OHE1

*If urine E1 and E2 are LOW and/or Total E2 in serum is LOW, consider avoiding DIM and I3C and choosing other detox supports that encourage sulfonation and phase one supports that downregulate expression of CYP1B1 and/or 16OHE1 formation, particularly. (Check out slides: 16-OHE1 Busters and 4-OHE Busters)*

## Step 2: Treatment Options for Detox Pathways

### 16-OHE1 Busters

- Direct down-regulators:
  - DIM/I3C (Diindolylmethane/Indole-3-Carbinol)
    - Therapeutic Dosing 100-300 mg daily
    - Some will d/c during menses and resume day 7
  - Trans-Resveratrol
    - Net effect: decreased 16OHE1 and 4OHE1/4OHE2
    - May compete/inhibit estrogenic activity at tissues, often used with Quercetin
    - Common dosing: 100-500 mg daily
  - Rosemary Extract
    - Net effect: decreased 16OHE1, increased 2OHE1/2OHE2
    - Often found in combinations with DIM or I3C, also anti-inflammatory
    - Follow bottle for dosing (can affect blood pressure in some people)
- If High 16-OHE1 is correlated with high Prolactin levels:
  - Rule out or treat hypothyroid (TSH is co-released with Prolactin)
  - Check HVA in OATs section and treat lows (if low, could be inadequate dopaminergic inhibition of PRL)
  - Refer for pituitary imaging if very high and confirmed
- Support SULFATION – a sulfated estrogen cannot bind its receptor
  - Use anti-inflammatories (Curcumin, Green Tea, Scutellaria, Rosemary, etc)
  - Sulforaphane, Taurine, Methionine, NAC, Glutathione, Molybdenum, bile acid supports
- Feed CYP1A1 2-OHE pathway:
  - DIM/I3C (hard core)
  - Sulforaphane (gentle)
  - Ground flax
  - Root veggies: Spanish black radish, carrot, turnips, etc
  - Andrographis
  - Omega-3s

### 4-OHE Busters

- Antioxidants
  - Foods:
    - Brassicas, Citrus fruit, Red pepper, Tarragon, Rosemary
  - Flavonoids/Polyphenols:
    - Quercetin, Citrus bioflavonoids, Rutin, Hesperidin, Apigenin, Resveratrol
- Optimize thyroid function
- Avoid toxic exposures
- Treat mold toxicities
- Support **Phase 2 Detox** to mitigate effects of high 4-OHEs (helpful for CYP1B1 snp carriers)
  - Support reduced glutathione
    - Liposomal glutathione, NAC, glycine, C, B6
  - Support quinone reductase (to cleave apart 4-OHcatechol-quinone complexes)
    - Sulforaphane (SFN), Soy isoflavones, Resveratrol
  - Support methylation
    - MTHF, Hydroxocobalamin, SAME, Magnesium, B6, PhosCholine, TMG, MSM, SFN

# Step 3 from Estrogen Dominance Assessment/Plan Sheet

## Step 3: Determine Underlying Pathology

### Signs of Insulin and/or Inflammation as Driver

- 2-OHE1 vs 4-OHE1 favoring 4-OHE1
- 2-OHE2 vs 4-OHE2 favoring 4-OHE2
- Hypermetabolic Cortisol Pattern
  - Low(er) 24-hr Free Cortisol vs Total Cort Metabolites
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- 5 $\alpha$ -Reductase elevated (Androsterone, 5 $\alpha$ Andro,  $\alpha$ -THF/ $\beta$ -THF)
- Quinolate elevated

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- 2-OHE1 vs 16-OHE1 favoring 16-OHE1
- Low urinary DHEA-S (esp compared to metabolites)
- High Indican
- Free Cortisols may be high

### Signs of Impaired Egg Quality and Low Functional Ovarian Reserve

- Elevated serum LH:FSH ratio and high serum E2 on cycle day 3
- Total DHEA low in urine (DHEA-S low in serum)
- Melatonin metabolite low
- Pyroglutamate elevated and/or 8OHdG elevated
- Quinolate elevated

## Step 3: Determine Underlying Pathology

### Insulin and/or Inflammation as Driver

- Lifestyle supports:
  - Anaerobic exercise - Resistance training
- Insulin sensitizers:
  - Berberine 300-500 mg up to T1D
  - Myo-inositol 2-4g QD
  - R-ALA 300 mg
  - Minerals: Chromium, Zinc, Magnesium
  - Cortisol-controlling blood sugar herbs: Bitter melon, Cinnamon, Holy basil
  - Rx: Metformin, Thiazolidinediones
- Anti-inflammatories
  - Liposomal Curcumin 1-3 g daily
  - EGCG 800 mg daily
  - Rosemary - bottle dosing (depends on the extract)
  - Systemic enzyme therapies (Bromelain, empty stomach pancreatic enzymes, etc)

### Dysbiosis/ $\beta$ -glucuronidase as a Driver

- Do some comprehensive stool testing
  - Test for  $\beta$ -glucuronidase activity and dysbiosis, Treat what you find
- Keep estrogens glucuronidated and on the "outs"
  - CDG 1g - 1.5g in divided doses (it's short-acting)
- Correct digestive problems
  - Hypochlorhydria (HCl, ACV), Pancreatic insuff (enzymes), Optimize diet (Mediterranean, AIP, etc)
- Consider General Liver Detox Supports
  - Sulfury supports (NAC, GSH, Taurine, Methionine, SFN), humic/fulvic acids, butyrate
  - Herbs: Artichoke, Milk thistle, Reishi, etc
- Nourish the gut lining
  - Glutamine, DGL and other demulcents like okra and slippery elm
- Recolonize
  - Pre-biotics and Pro-biotics
- Support Progesterone
  - Nourishes Bifidobacterium and L. reuteri
  - Decreases gut permeability, Offers enteric neuroprotection and is anti-inflammatory

### Impaired Egg Quality and Low Functional Ovarian Reserve as a Driver

- Increase ovarian response to FSH
  - Myo-inositol 1200-2000mg QD
  - Phytoestrogens: Maca, Dong Quai, Black cohosh, Yucca schidigera
  - Bovine Glandular Ovary
- Improve functional ovarian reserve
  - MTHF (dose to individual need)
  - Melatonin 3 mg QHS
  - NAC 600-1800 daily
  - Omega-3 intake
  - Mitochondrial Micronutrition: CoQ10, ALA, Carnitine, Antioxidants
  - Mediterranean style diet



Estrogen

Progesterone

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The screenshot shows a presentation slide titled 'Optimal Hormone Levels in Menopause' with bullet points: 'Conventional medical organizations do not recommend testing', 'Helpful in a comprehensive functional medicine plan', and 'Consider testing:'. Below the slide is a course interface for 'Module 2 - Hormones In Post-Menopausal Females' with 6 lessons. The current lesson is 'Estrogen in Menopause'. A 'Mark As Complete' button is visible, and a 'Downloads' section shows a file named '2.2\_Estrogen\_in\_Menopause.pdf'.

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