Estrogen Progesterone Testosterone
Part Two
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Testosterone

Estrogen

Progesterone

Triad 5

How do they inter-relate?
Progesterone ⇒ Testosterone

• Progesterone can convert to Testosterone if given too aggressively
• Complaints of acne or hair growth
Steroidogenic Pathway

Cholesterol → StAR → P450sc/f → Pregnenolone → 3β-HSD → Progesterone → 11-Deoxycorticosterone → Aldosterone

P450c17 POR

17OH-Pregnenolone → 17OH-Progesterone

P450c17 POR + b5

DHEA → 3β-HSD → Androstenedione

17β-HSD1, 17β-HSD2

Androstenediol

3β-HSD

Testosterone

5α-Reductase 1 & 2

5α-Androstane-3,20-dione

5α-Androstane-3α,17β-diol

Dihydrotestosterone

Androsterone

17β-HSD2

5α-Androstane-3α,17β-diol

17β-HSD1, 17β-HSD2

5α-Androstane-3,20-dione

17β-HSD6

17β-HSD3

AKR1C1-4

Estrone

17β-HSD1

Cortisol

P450c11β Fdx/FdR

11β-HSD1, H6PDH

Cortisone

P450c11β Fdx/FdR

11β-HSD2
Progesterone – Testosterone
Compete for 5-a-Reductase

5-alpha Reductase

Progesterone

Testosterone

DHT

5-Pregnanes
Cancer cells
Progesterone metabolites

4-pregnenes (normal) \[\xrightarrow{HSOs}\] progesterone \[\xrightarrow{5\alpha\text{-reductase}}\] 5\alpha-pregnenes (cancer)

(HSO – hydroxysteroid oxidoreductase)
Testosterone gets bullied

Testosterone

DHT

5-a-reductase

Progesterone (-) “blocker”

Aromatase

Cortisol +++

Estradiol

\[ T \]
Male under stress results in low T

Stress contributes to weight gain
Stress directly inhibits T production
Cortisol drives aromatase

Testosterone

5-a-reductase

Progestosterone (blocker)

Aromatase

Cortisol +++

DHT

Estradiol
Estrogen’s effect on Testosterone

- Estrogens: directly stimulate production of prolactin which \( \downarrow \) LH and thus \( \downarrow \) T
- This is part of the normal feedback mechanism that regulates T production.
  - Testosterone conversion to Estrogen and (-) feedback to the pituitary.
  - T & DHT have (-) feedback to the hypothalamus
Female Breast Cancer

Breast cancer pattern:
Low T (free 5-a-reductase)
Low Progesterone
Cortisol↑ so ↑E2

Testosterone

5-a-reductase

Progesterone (−) “blocker”

Aromatase

Cortisol +++

Estradiol

DHT
Menopause Symptoms

Peri-menopause loses the breaking effect of Progesterone so $\uparrow E2$

Exacerbates estrogen dominance
Low T levels

Testosterone

5-a-reductase

Progesterone (- ) “blocker”

Aromatase

Cortisol +++

Estradiol

DHT
Triad 5 + Triad 1

Testosterone

5

Estrogen Progesterone

Cortisol

1

Thyroid Pancreas
More Relationships – CORTISOL
Relating to Triad 1

Testosterone

Cortisol

DHT

5-a-reductase

Progesterone (-) “blocker”

Aromatas

Estradiol

= Opposes
Receptor Relationships

- **Progesterone** and **Cortisol** receptors only differ by 2 amino acids
  - Leads to cross reactivity and competition
  - A lack of progesterone can enhance cortisol expression

- **Testosterone** opposes **Cortisol**
  - Anabolic vs Catabolic
  - Compete at the DNA receptor site
  - Cortisol chronically will downregulate DHEA (precursor to T)
One more look . . .

Once Cortisol (stress) starts to rise it can get very lopsided. Low T

.opensquare= Opposes

Testosterone

DHT

5-a-reductase

Progesterone (-) “blocker”

Aromatase

Estradiol

Cortisol
In a high CORTISOL state we see low T and estrogen dominance.

- **↓T**: C directly suppresses production of T.
  - Competes with T at the receptor site.
  - Enhances aromatase thus converts T to E2.

- **↑E2**: C competes with Prog at receptor site.
  - Upregulates aromatase thus exacerbating E2 dominance.
Testosterone & Cortisol

- Testosterone is anabolic in nature
- Cortisol is clearly catabolic
- They are diametrically opposed and their relationship is predictive of degenerative disease including heart disease and cancer
Testosterone & Cortisol

- Sleep deprivation to 5 hours nightly reduced testosterone production in young healthy males.
  - 5 hours sleep per night led to a 15% reduction in Testosterone levels after just one week.

**Conclusion:** Stress (cortisol) adversely affects testosterone

[Leproult, Effect of 1 Week of Sleep Restriction on Testosterone Levels in Young Healthy Men, JAMA 2011]
Triad 5 & Triad 1

- This relationship translates into high risk for prostate cancer and breast cancer.
- T is protective for both prostate and breast
- Estrogen exacerbates risk for both
- Cortisol exacerbates risk for both
CANCER: Relationships to watch for

- ↑ Cortisol
- ↓ DHEA
- ↑ Estrogen
- ↓ Testosterone
- ↑ Estrogen
- ↓ Progesterone
Progesterone ➔ Cortisol

• Excess progesterone may convert into cortisol

• Progesterone and cortisol receptors differ by just 2 amino acids – competition.

• BHRT – Progesterone may cause anxiety
  – Paradoxical reaction from expectation
Hypothyroid Drives cortisone to cortisol
• Premenopausal women with estrogen dominance, can easily be hypothyroid
• Now aggressively add progesterone and it is conceivable that she may feel “anxious” due to progesterone’s excess drive to cortisol
  – Paradoxical response from expectation
Triad 5 + Triad 1

- Testosterone
- Cortisol
- Estrogen
- Progesterone
- Thyroid
- Pancreas
Testosterone Inverse to DM

- Among men with DM the frequency of lowT is 20-64%
- Study of 55 type 2 Diabetic men showed a low freeT in 54% of these patients and these men demonstrated higher fasting glucose levels than men with normal freeT levels.
  [Corrales, Partial Androgen Defic., Metab. 2004]
- Men with higher testosterone levels (range, 449.6-605.2 ng/dL) had a 42% lower risk of type 2 diabetes.
  [Ding, Sex differences in endogenous sex hormones, JAMA 2006]
Low T leads to DM

Six large prospective studies have shown that low testosterone levels predict development of type 2 diabetes in men

Inevitable conclusion

• Low T universally results in poor blood sugar and insulin function
• T2DM is secondary to low T 50% of the time

So does this predict Metabolic Syndrome and Heart Disease?
Low T = DM = MetS/CAD

• Non diabetic men were 4 fold more likely to develop MetS if they were hypogonadal.

[Laaksonen, sex hormones, inflammation, Eur.J.Endocrin 2003]

• Lowest quartile for T was twice as likely to develop DM and MetS

[Laaksonen, Testosterone and SHBG, Diabetes Care 2004]
Triad 5 + Triad 1 + Triad 3

Testosterone 5

Estrogen  Progesterone  Thyroid

Cortisol 1

Pancreas

Cardio 3

Neuro  Vascular
A 5-year follow-up study of disease incidence in men with an abnormal hormone pattern

R. Rosmond¹, S. Wallerius¹, P. Wanger², L. Martin², G. Holm¹ & P. Björntorp¹
From the ¹Cardiovascular Institute, Sahlgrenska University Hospital, Göteborg; and ²Department of Clinical Sciences, Huddinge University Hospital, Huddinge; Sweden


Monitored T level & Cortisol over 5 years
Tracked development of CAD, DM & HTN
All health parameters declined with ↓T & ↑Cortisol

Conclusions. These data suggest that an abnormal neuroendocrine secretory pattern is prospectively associated with increased disease incidence.
Coronary Heart Disease

Cortisol, Testosterone, and Coronary Heart Disease
Prospective Evidence From the Caerphilly Study

George Davey Smith, DSc; Yoav Ben-Shlomo, BSc, MBBS, MRCP, FFPHM, PhD; Andrew Beswick, BSc; John Yarnell, MBChB, DPH, MSCM, MD, MFPHM (Ire), FFPHM; Stafford Lightman, MBChB, PhD, FMedSci; Peter Elwood, DSc, MD, FRCP, FFPHM

Background—There is a popular belief that chronic stress causes heart disease through psychoneuroendocrine mechanisms. We have examined whether an elevated circulating cortisol-to-testosterone ratio increases the risk of ischemic heart disease.

Methods and Results—We undertook a prospective cohort study of 2512 men aged 45 to 59 years between 1979 and 1983 from Caerphilly, South Wales, with a mean follow-up of 16.5 years. Subjects underwent a clinical examination, and morning fasting blood samples were taken for analysis of cortisol levels, testosterone levels, and other cardiovascular risk factors. The ratio of cortisol to testosterone showed weak associations with potential confounding factors but strong positive associations with components of the insulin resistance syndrome (P<0.001). A positive linear trend was seen across quintiles of cortisol:testosterone ratio for incident ischemic heart disease (age-adjusted OR per z score change in ratio 1.22, 95% CI 1.07 to 1.38, P=0.003). This was markedly attenuated after adjustment for components of the insulin resistance syndrome (age-adjusted OR per z score change in ratio 1.10, 95% CI 0.96 to 1.25, P=0.18). There was no association between the cortisol:testosterone ratio and other causes of death (age-adjusted hazard ratio 1.24, 95% CI 0.82 to 1.88, P=0.29).

Conclusions—This is the first population-based prospective study that links cortisol:testosterone ratio and incident ischemic heart disease, appearing to mediate the insulin resistance syndrome. Whether this reflects the effects of chronic stress, behavior, or other factors remains to be determined. (Circulation. 2005;112:332-340.)

Quintile analysis shows a direct linear relationship: C:T ratio predicts CAD, HTN, DM, death.
Triad 5 + Triad 1 + Triad 3
Estrogen shows similar physiology
Estrogen & DM

• Estrogen regulates the insulin production capacity of the pancreatic islet cells
  [Choi, Jang, Estrogen and exercise may enhance β-cell function Endocrinology 2005]

• Estrogen regulates insulin sensitivity in the liver
  – Activates glycogen synthetase and glycolytic enzymes and advantageously modulates glucose uptake of peripheral tissues
  [Bryzgalova, Evidence that estrogen receptor-alpha plays an important role in the regulation of glucose homeostasis, Diabetologia 2006]

• Estrogen deficiency or alterations in ER signal transduction result in insulin resistance.
Estrogen Receptor – Alpha vs Beta

• ER-α and ER-β seem to have opposite actions on modulation of GLUT4 activities.
• **ER-α stimulation improves glucose control** in men and women.
• By contrast, **ER-β activation might have a diabetogenic effect** and opposes the action of ER-α. (Estriol)
• Presumably, a continuously adjusted balance between ER-α and ER-β maintains the ideal GLUT4 expression and glucose homeostasis. So is Estriol a good idea?

[Muraki, Estrogen receptor alpha regulates insulin sensitivity, Endocr J 2006]
Estrogen – overdose or “dominance”

- Higher concentrations of estradiol can inhibit insulin signaling by modulation of insulin receptor substrate-1 (IRS-1) phosphorylation in adipocytes
  - Lower doses of estradiol improved insulin receptor function as it augmented IRS-1 efficiency
  - Higher doses had the opposite effect leading to insulin resistance.
- Estrogen dominance contributes to weight gain

[Nagira, Altered subcellular distribution of estrogen receptor is implicated in estradiol- induced dual regulation, Endocrinology 2006]
Triad 5 + Triad 1 + Triad 3
Progesterone and similar physiology

Testosterone

5

Cortisol

1

Cardio

3

Estrogen  Progesterone  Thyroid  Pancreas  Neuro  Vascular
Progesterone & DM

• **Excessive** progesterone can contribute to IR
• Progesterone may alter production or translocation of the GLUT-4 protein

[Campbell, Effect of the ovarian hormones on GLUT4 expression, Endocrin & Metab 2002]
Triad 5 + Triad 2 + Triad 4
Hormones and Detox

Testosterone

Estrogen

Progesterone

Immune

Brain

Liver

Lymph

Kidney
Triad 4 – Detox & Hormones

- Conjugated hormones from Liver
- Bacteria break conjugated bonds
- Constipation
- Hormones Free to reabsorb
- Quinone estrogens levels rise
- Sluggish detox process

- 2.5 pounds of commensal flora
- Detox capacity of the liver
BHRT clearance

- Flax meal – lignans bind and remove
- DIM – benefits liver metabolism
- Probiotics – efficient detox, the second liver

“Constipation is ILLEGAL”
case studies
Barbara Hiltz

- 52 year old executive for a large insurance company who states that she is “losing her edge” at work.
- Her cognition, memory and creativity have been in decline for the past two years. She is experiencing night sweats that awaken her to drenched sheets and she struggles to fall back to sleep.
- Her waist has grown slightly and she can’t seem to shake the extra pounds like she used to.
- Barb has a history of fibrocystic breast changes but otherwise is very healthy and active. She used birth control pills throughout her youth but otherwise has not used hormones.
- Her relationship with her husband is flat, and carbs are her growing source of comfort. She admits to cravings, and has become a night eater.
- Overall energy and recovery have diminished. Occasional struggles with mood.
Pathologic Disturbances: Barb Hiltz

Testosterone

Other
- **Triad 1** – Cortisol, Insulin, ?Thyroid
- Triad 2 – Cognition & Sleep
- Triad 3 – ⌀
- Triad 4 – Clearing estrogen?

Sleep
Hot flash
Night sweats
Mood & Energy
Fatigue
Cognition
Weight Gain

Estrogen

Progesterone

Surges

<1

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Barbara Hiltz: Clinical Strategy

- Triad 1: Break insulin resistance and manage cortisol and evaluate thyroid
- Triad 2: Address gut-immune-brain axis
- Triad 4: Assess for toxicity

BUT . . .

- Balance estrogen:progesterone . . .

Before or After triads 1,2,4 ???
Which direction is best?

BHRT Now
- This is why she came to you
- It’s destroying sleep
- Estrogen improves IR

Cortisol Is King
- Cortisol driving aromatase → E2
- Stress can cause sweats and flashes
- Cortisol competes with progesterone
Barbara Hiltz: Insulin & Cortisol Tx

**Tx: ↑Cortisol**
- Adaptogen: Holy Basil, Phellodendron/Magnolia
- Multi-Vit or B complex support
- Adrenal glandular
- Medullary peptides

**Insulin Resistance**
- Chromium GTF 1000 mcg po BID x 60 days then 500 mcg po BID
- Berberine extracts – 1000 mg/day
- ALA 1 Tab (600 mg) po BID

**Dietary changes**
- Paliolithic diet
- Low glycemic whole food options
Barbara Hiltz: Thyroid Support

Hypothyroidism

Yes
Selenomethionine 400 mcg/Iodine 1 mg*
Sterols/Sterolins 20 mg
3 caps BID x 60 days, then 3/day
Give T4/T3 alone or in combination
AND work to rule out source of Antibodies

+TPO?

No
Selenomethionine 400 mcg/Iodine 1 mg
Tyrosine 500 – 750 mg BID
Thyroid gland or Armour Thyroid

*Consider Iodine up to 3 mg for 2 months then ↓ 1 mg qd
Avoid mega doses – contributes to thyroiditis
Barbara Hiltz: Thyroid Support

Subclinical Hypothyroidism
(Borderline high TSH/suboptimal T4 and T3)

Yes

Symptoms?

No

Selenomethionine 200 mcg/Iodine 1 mg*
Thyroid glandular OTC or Rx
If Antibody(+) then Rx, not gland

Selenomethionine 200 mcg/Iodine 1 mg
Manage cortisol/adrenal
Manage BHRT

*Consider Iodine up to 3 mg for 2 months then ↓ 1 mg qd
Key Concept

Presence of TPO antibodies indicate autoimmune process, seek causative factors:

- food allergies
- heavy metals
- chronic infections
- stress
Key Concept

If presence of TPO or ATA antibodies, do not use prescribed or over the counter glandulars
Key Concept

Ferritin is a transport molecule for T3 into the cell.

Ferritin

- 80-100: No Tx needed
- <80: Ferritin 5 mg 6 tabs daily x 60 days then 3 tabs daily
BHRT for Barb

• Discussed options and signed consent
  – Gave literature to read
• Started oral progesterone to aid sleep and reduce hot flashes
• Will assess at second visit for adrenal and sleep progress and determine if E2 appropriate
<table>
<thead>
<tr>
<th>Target Organ</th>
<th>Treatment</th>
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</table>
| Triad 1 – Adrenal, Thyroid, Glucose | MVI/Minerals  
Chromium & Magnesium (glucose)  
Adaptogen - Magnolia/Phellodendron  
Adrenal glandular  
Thyroid glandular  
Selenium/Iodine combination |
| Triad 2 - Gut               | Paliolithic Diet, flax meal  
Probiotic & Cats Claw                                                     |
| Triad 4                     | DIM  
Chlorella if detox indicated                                               |
| Triad 5                     | DIM  
Estrogen patch  
Progesterone - oral                                                        |
Peter Limpman

Peter is a 55 year old construction foreman. Lifetime of construction, building decks, small remodeling jobs, industrial welding and now oversees large construction projects. Peter grew up in a small farming community where he was the local football hero as the star linebacker.

Presents as a typical stoic male with few complaints but upon persistent questioning he admits to a general sluggishness that has become pervasive. He struggles on work assignments, as motivation and drive are low. He denies sexual problems but admits to a less than robust sex drive. His strength and endurance are not as good as they once where but he chalks that up to age. He has a growing back problem that nags him and now more diffuse joint issues have continue to affect his mood. He denies depression but you sense a general melancholy. He weighs 260 pounds but has always been a big guy. He struggles with an ever-expanding waist, again attributed to age.

His primary care doctor has told him that his cholesterol and blood pressure are high and he was started on a beta blocker and a statin. His doctor wanted him on an SSRI for his mood but Peter declined. The labs he provides you show a fasting blood sugar of 96 which his PMD regards as normal. Peter states that his favorite past time activity is wood working but he hasn’t been in the mood to do this for quite some time.
Pathologic Disturbances: Peter Limpman

Testosterone

Other
• **Triad 1** – Cortisol, Insulin Resist
• Triad 2 – Brain
• **Triad 3** – HTN, Chol, vascular
• Triad 4 – watch kidneys

Estrogen

Energy
Mood
Cognition
Weight Gain
Joint ache
HTN, Chol, Glucose
? Metab Syndrome?

Progesterone

214

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Where do we want to start?

• Do we jump right in with T replacement?
  – Preferred Tx option? Stimulate or Replace?
• Should we address CV & Cortisol first?
• What about toxins?
  – What if heavy metals are disturbing hypothalamic function?
• Should we get a heavy metal panel?
Pathologic Disturbances: Peter Limpman

Stacking
- Triad 1 – ↑Cortisol, ↑Insulin
- Triad 2 – (+)Food IgG, Auto-Immune
- Triad 3 – HTN, (+)LDL-P, (+)trigs
- Triad 4 – Mercury & Lead

Testosterone
- FBS 110
- Cortisol - flat
- BP 145/88, HR 82
- CRP 5.5, Trigs 230
- LDL-P 1860
- Mercury & Lead (+)

Estrogen

Progesterone

214

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1. Break insulin resistance and manage cortisol (Triad 1) This is the cause of #3
   • This will make Tx #3 easier
3. Cardiopulmonary Risk (Triad 3)
4. Treat toxicity (Triad 4)
Feeling Lost?

Basic Essentials that (nearly) always apply
1. Start with “sleep” and “gut”
2. Always Tx Adrenal before Thyroid issues
3. Move slow and steady on hormones
4. Pick elements with multiple impacts
   - Fish oil – brain, gut, insulin, inflammation
   - Probiotic – detox, digestion, brain, immune, yeast
Peter Limpman: Testosterone Options

Stimulate

- Clomifene – 50 mg twice per week
- Alternative = HCG subQ – 125 daily
- Alternative = pituitary peptides Bid
- Zinc & Protein support
- Check Prolactin and LH

Replace

- Topical T – 1% cream, 1/4 cc titrate up over 6 weeks
- Check a salivary or capillary level at 10 weeks

Replace

- SubQ T cypionate in ethyl olate base – twice/week
- Start 15 to 20 mg and titrate up
- Check lab 48 hours after last injection – serum or saliva
- Monitor Estrogen, DHT, SHBG, PSA, CBC
Peter Limpman: Stress Support

Adrenal Cortex Extract 1-2 caps BID
Do not use full gland in HTN cases

Hypocortisolism

Yes
Adaptogen 1 cap BID
Rhodiola or Holy Basil
Phellodendron/Magnolia

No

Hypertension?
Yes
RG3
Neural peptides
Vit B & C

No

Severe?
Yes
Vit B & C

No
Peter Limpman: Insulin Management

Basic Support
- Trace Minerals and Vitamins
  - Magnesium (bowel tolerance) 200-500 mg BID
  - Chromium GTF 1000 mcg BID x 60 days then 500 mcg BID thereafter
  - Vitamin D3 to serum 50-60

Direct Impact
- Impact insulin sensitivity
  - ALA 1 Tab (600 mg) BID
  - Berberine extract 1000 mg daily (divided)
  - Bitter Melon TID x 60 days then reduce to BID
  - Cinnamon 125 -250 mg TID

Repair Physiology
- Manage the T level – directly impacts mitochondrial mech.
- Manage Cortisol to restore insulin function
- Manage Thyroid – GLUT 4 channel responds to T3
Dietary Advice

Evening carb cravings?

Yes

Caveman Diet
No grain/dairy/gluten
Low carbohydrate
1-2 servings low GI carbs

No

Caveman Diet
No grain/dairy/gluten
Low carbohydrate
Key Concept

If patient reports difficulty sleeping, add Neuromedulla 2 caps at night to reactivate (reset) hypothalamus.
Dyslipidemias

LDL-P elevated

> 1000

Sterols 2.4 gm
Omega 3 fatty acid
Aged garlic

> 1300

Niacin - 500 mg BID – TID
Omega 3 fatty acid
Pantathine - 900 mg daily
Plant Sterols – 2.4 gm daily
Red Yeast Rice 600-1200 mg BID
Hypertension

Initial

Screen for heavy metals, IR & Cortisol evaluation

Weight loss & Dietary changes

>160/90

Quinapril 10-40 mg daily

>130/80

Arginine 3 caps BID, in 30 days
AGE 1200 mg BID
Add Hawthorn 450 mg BID or
Omega 3 fatty acid
CoQ10 50-200 mg daily
Taurine & Magnesium

>160/90
CRP-hs elevation

• Clear marker of CV risk, needs to be <1.0
• Reduce inflammatory diet
  – Get rid of carbs, sugars, processed foods
• Reduce inflammatory lifestyle habits
  – Poor sleep, sleep apnea, lack of exercise, etc
• Treat with: Aged garlic, Curcumin,
  Omega 3 fatty acids, EGCG, antioxidants
Angie Little

Angie is a 42 year old female with chief complaint of headaches for the past 5 years and is now experiencing PMS symptoms with mood change and breast tenderness.

• Long history of constipation with some occasional reflux.
• Sleep has deteriorated over past few months. It has been an unstable issues for 2 years now.
• She reported low libido to her OB/GYN and received a patch that contained some form of estrogen and testosterone.
• Medications include omeprazole for her occasional GERD.
Pathologic Disturbances: Angie Little

Other
- Triad 1 – Cortisol?
- **Triad 2** – GERD, Constipation, Sleep, headache
- Triad 3 – ø
- Triad 4 – Clearing estrogen?

Esterified Estrogen

Testosterone

Methyltestosterone

Estrogen

PMS
- Headache
- GERD
- Constipation
- Sleep
- Breast tenderness

Progesterone
Ongoing History: Angie

- She reports that initially the patch made her headaches better but now they have returned.
- Her doctor gave her progesterone cream to help with this but it made her feel anxious.
- Now she is craving and gaining weight. Going from bad to worse – not happy.

Thoughts?
Angie

- Constipation is recirculating estrogens
- Poor bowel flora unable to detoxify
- PPI is interfering with proper digestion so nutrient deficiencies are mounting
- Food allergies causing glial activation

Gut issues dominating her Hormone issue
Sleep Issues

• Low and high estrogen states can interfere with sleep

• Progesterone will facilitate sleep
  – Progesterone $\Rightarrow$ allopregnanolone $\Rightarrow$ GABA

• Oral progesterone
  – 90% liver conversion to allopregnanolone
Headaches

• Excess estrogen can cause headaches
  – Too stimulating. (Angie = Poor clearance, rising levels)

• Migraines - resolve with estrogen Tx
  – Effects neurotransmitters - the amines
  – Increases blood flow & oxygen delivery
  – Improves neuronal function
  – Reduced Alzheimer’s expression
Progesterone $\Rightarrow$ Agitation

- Progesterone in abundance can fuel conversion to Cortisol
- Occasionally, women report agitation as a result of stimulation of cortisol
- Check DHEA levels, if low then support with 25 mg at HS to slow this reaction
Progesterone Excess

- Increase cortisol and/or testosterone
- Cause insulin resistance
- Weight gain, fat storage (Angie)
- Increased appetite and carb cravings (Angie)
- Inhibits anti-candidal neutrophils in gut and slows GI transport
- Down regulates estrogen receptors in brain leading to depression
Soy

• Phytoestrogens -
  – Isoflavones: daidzein & genistein
• Weak estrogens - 1/1000 to 1/100,000 the activity of estradiol
• Decrease breast cancer? Fermented – Yes.
• Estrogen receptor modulator vs blocker
• Fermented vs whole vs fractionated supp
Stacey King

• 18 year old senior in high school
• Has had trouble with self esteem due to weight gain, acne and excess hair growth.
• She finds comfort in food and her 4 cats.
• Complains of foggy thinking, and painful heavy periods, when they occur, which is less often than not.
• Is not interested in college because she “just does not want to deal with making new friends.” Living at home is just fine with her.
Stacey King: Triad 1, 4, 5

Stacking
- Triad 1 – Stress, fatigue, wt gain
- Triad 2 – Celiac risk, Depression
- Triad 3 – Sympathetic overdrive
- Triad 4 – Exposures? Metals

Testosterone
- FBS 103
- Cortisol 22
- T3 1.9
- +TPO
- + Pb and Cd
- +HLA DQ2/DQ8

Progesterone
- Undetectable

Estrone 300
Stacey King: Clinical Strategy

• Break insulin resistance and manage cortisol and thyroid (Triad 1)

• Assess for toxicity (Triad 4)

• Balance estrogen:progesterone
  – Looks like PCOS
Key Concept

PCOS is reversed with weight loss and control of insulin resistance
Dietary Advice

Evening carb cravings?

- Yes
  - Caveman Diet
  - No grain/dairy/gluten
  - Low carbohydrate
  - 1-2 servings low GI carbs

- No
  - Caveman Diet
  - No grain/dairy/gluten
  - Low carbohydrate
Stacey King – Insulin & Cortisol

- As above with adaptogens and glandulars
- Berberine, ALA, Chromium, Mg, Omega 3
- Evaluate level of thyroid function
  - R/O antibodies
  - TSH in younger patient more reliable but check freeT3 to assess GLUT 4 performance
Elevated Cortisol

Yes: Anxiety and mind racing at night?

- Add L-theanine 1-2 caps 2-3x daily

No: Magnolia/Phellodendron Holy Basil (or if IBS sx)
- Phenyl-GABA
Stacey King: Thyroid Support

Subclinical Hypothyroidism (Borderline high TSH/low T4 and T3)

- Yes
- Symptoms?

Selenomethionine 200 mcg/Iodine 1 mg
- Thyroid glandular OTC or Rx

- No

Selenomethionine 200 mcg/Iodine 1 mg

*Consider Iodine up to 3 mg for 2 months then ↓1 mg qd
Chromium is required for conversion of T4 to T3
T3 needed to stimulate GLUT 4
Cortisol blocks conversion of T4 to T3
Hypothyroid Symptoms & ↑TSH

(+) TPO or ATA Ab’s

No

Yes

Rule out source:
- Heavy Metals
- Food allergies
- Chronic stress
- Chronic viral issue

Tx with T4 and T3

Treat with thyroid glandulars
Selenium & Iodine
Armour or T4/T3
Environmental Chemicals

Persistent Organic Pollutants?

Yes

No

Chlorella 2000 mg BID
Glycine 500 mg BID
Taurine 500 mg BID
Alpha Lipoic Acid 600-1200 mg BID
Degex Liquescence ½ tsp BID
Key Concept: POPs

If access to infra red sauna, utilize three times per week for 20-40 minutes.

Pre-load with niacin 500 mg, arginine 1000 mg and green drinks 30 minutes prior.
<table>
<thead>
<tr>
<th>Target Organ</th>
<th>Treatment</th>
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</table>
| Triad 1      | Caveman diet  
Chromium & Magnesium  
ALA or Berberine  
Vitamin D3  
Mangnolia/Phellodendron  
Selenometh-Iodine  
Liothyronine (T3) |
| Triad 4      | Chlorella  
Multi-vitamin & Minerals  
Degex liquescence  
Chelate metals when appropriate |
| Triad 5      | DIM  
Progesterone topical 20 mg days 7-25  
Saw palmetto |
Libido

• Testosterone 2% cream - topical cream
  – Apply pearl sized dab to clitoris 3x/week
  – If too intense then apply to labia

• Scream Cream - aids climax
  – Viagra + Aminophylline + Arginine + peppermint (tingle factor)
  – Apply to clitoris pre coitus