



RESEARCH NUTRITION & PRECISION ANALYTICAL PRESENT

HORMONAL DYSREGULATION

CASE STUDY DISCUSSION



PRESENTED BY DR. CARRIE JONES, ND, MPH

Dr. Carrie Jones' passion and expertise lies in the areas of hormonal, adrenal, and thyroid health. She recognises that imbalance can occur at any age and believes it is important to look at the big picture such as the appropriate use of lab testing. Dr. Jones graduated from the National University of Natural Medicine (NUNM) in Portland, Oregon then went on to complete her residency in women's health, endocrinology and hormones. Later she graduated from Grand Canyon University's Master of Public Health program with a goal of doing more international work and health empowerment. Dr. Jones is an adjunct professor at NUNM and regularly consults, lectures, and writes on the topic of hormones, thyroid, adrenals, autoimmune and more both nationally and internationally. As the Medical Director for Precision Analytical, Inc., her goals are to provide ongoing cutting edge integrative clinical education to the large network of providers paving the way of healthcare with functional medicine.



SIMPLY. BETTER. TESTING.

Going Beyond the Basics of the DUTCH Test!

Clinical Pearls in PCOS, Fertility, Thyroid, Perimenopause/Menopause and Cases

By: Carrie Jones, ND, MPH
Medical Director– Precision Analytical, Inc.



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Realities in Australia (and the World)



- The World Health Organization states 74% of Americans and 67% of Australians are overweight.
- The Centers for Disease Control in the USA states 36% of Americans are obese. That's over 1/3 of Americans.
- The 2012 Australian Health Survey states 28.3% are obese.
- Australian, Diabetes, Obesity and Lifestyle study: in 2005 it cost \$21 billion for overweight/obese health related concerns.
- About 1 in 6 couples in Australia have fertility challenges
- The Australasian Society of Clinical Immunology and Allergy state autoimmune disease affects 1 in 20 people
- There are about 60,000 new cases of thyroid disease each year

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The take home message?

You will not be out of a job for a long while so let's help people get healthy!

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What questions do you need answered?

- Why is my patient having these symptoms?

- Women: Fatigue, PMS, Fertility, PCOS, hair loss, acne, mood swings, weight
- Men: Fatigue, mood swings, low motivation, hair loss, erectile issues, fertility

- What are my patient's hormone levels?

- Baseline versus treatment

- How is my patient processing their hormones?

- Androgen alpha vs beta pathway
 - Estrogen metabolism

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What questions need answered: Adrenals?

- How much is made by the glands and cleared in total?

- Cortisol Production/Clearance

- How much is free and available to bind to receptors and be active?

- Free Cortisol

- What is the diurnal (up and down) rhythm

- through the day?

- Cortisol Pattern

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Reviewing the DUTCH test (from top to bottom)

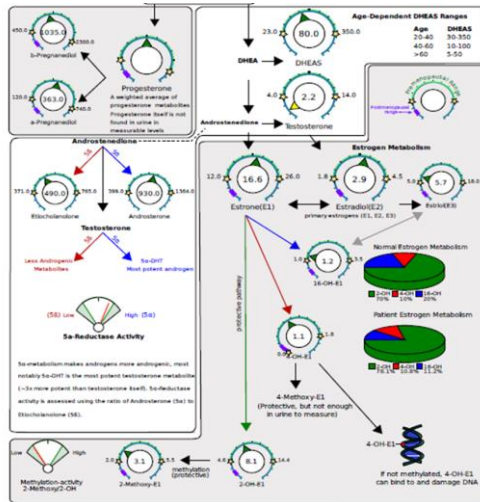
So we're all on the same page

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The DUTCH test

- Estrogen
- Estrogen Metabolites
- Progesterone
- Testosterone
- DHEA-s
- DHEA metabolites
- 5a-DHT
- 5a-reductase activity



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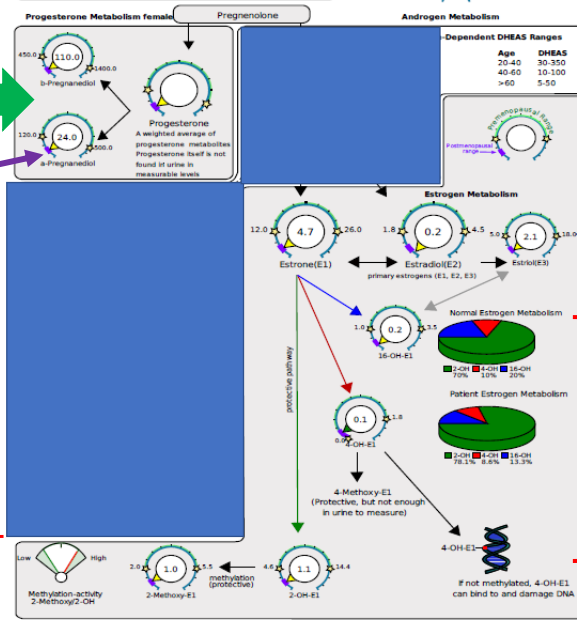
Let's break it down:

Menopausal Female

Progesterone →

Menopausal range is the purple rectangular box

Part of phase 2 estrogen detox



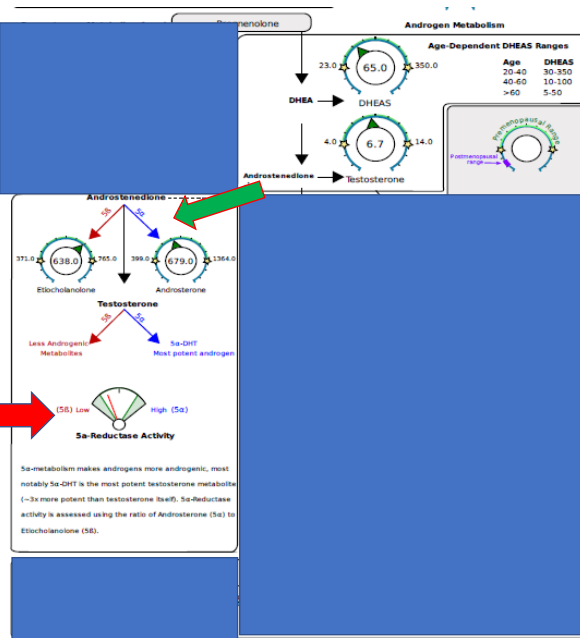
Estrogens: E1, E2, E3

Phase 1 Estrogen detoxification



Androgens:
DHEAS
Etiocholanolone
Androsterone
Testosterone

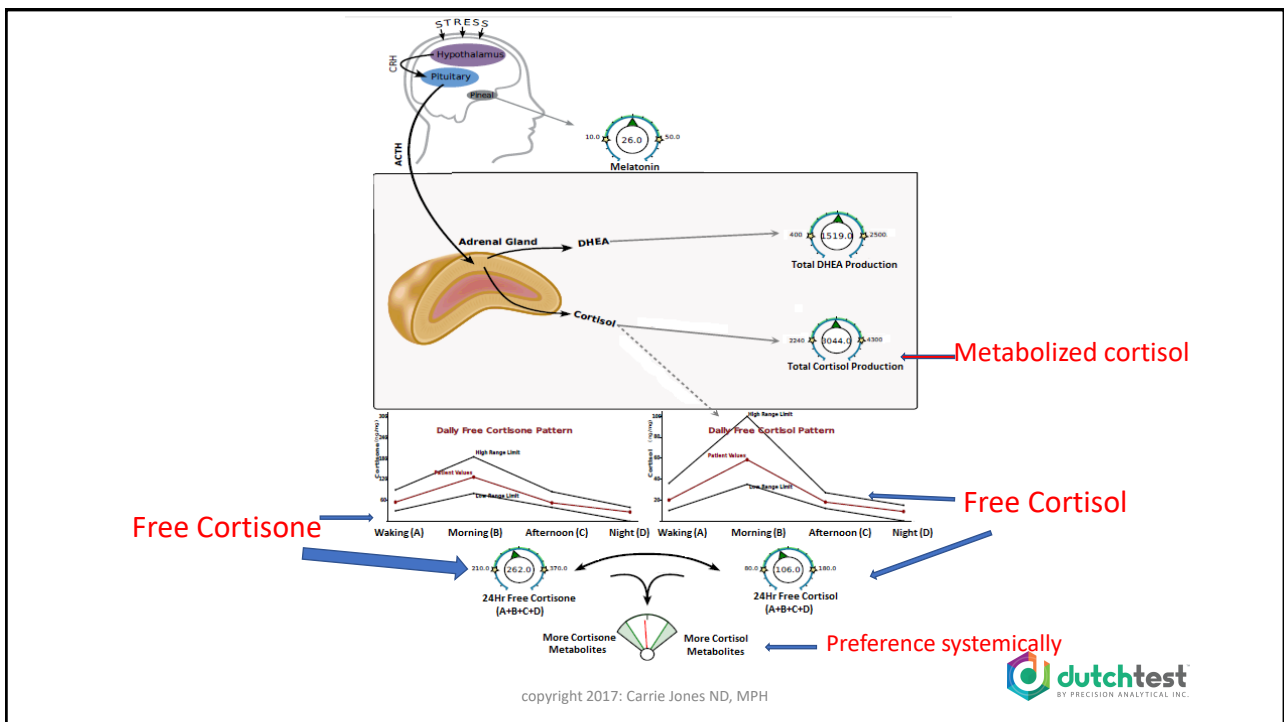
If high 5a = more androgenic side effects (hair loss, facial hair, acne, mood swings, prostate issues)



Read the DUTCH test following the steroid pathway

- Start at the top with pregnenolone (serum)
- Pregnenolone → DHEA and Progesterone
- Progesterone → alpha and beta metabolites
- DHEA → DHEA-s/etiocholanolone (beta)/androsterone (alpha)
- Testosterone → alpha and beta metabolites
- 5-alpha reductase/5a-DHT activity = androgenic?
- Testosterone → Estrogens
- Estrogens → phase 1 detox (2, 4, 16 OHE1)
→ phase 2 detox = methylation/COMT

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New Marker: 8-hydroxy-2-deoxyguanosine (8OHdG)



***Our newest addition on page 4 of a DUTCH Complete test!**

DUTCH Complete Extras					
Category	Test		Result	Units	Normal Range
Melatonin (*measured as 6-OH-Melatonin-Sulfate)					
	Melatonin* (Waking)	Within range	30.0	ng/mg	10 - 50
Oxidative Stress / DNA Damage, measured as 8-Hydroxy-deoxyguanosine (8-OHdG)					
	8-OHdG (Waking)	Within range	2.3	ng/mg	0 - 4.5



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What is it?

8-hydroxy-2-deoxyguanosine (8OHdG)

- A marker used for estimating DNA damage due to oxidative stress (ROS creation)
- Considered pro-mutagenic as it's a biomarker for various cancers and degenerative disease initiation and promotion
- Used to estimate DNA damage after exposure to cancer-causing agents: tobacco smoke, asbestos fibers, ROS, heavy metals, benzene, radon, arsenic, Nickel, toluene, toluene, and polycyclic aromatic hydrocarbons
- Sensitive enough to evaluate even mild chronic effects in ROS in the body of adults and children

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What increases it?

8-hydroxy-2-deoxyguanosine (8OHdG)

- Chronic inflammation
- High stress/high cortisol
- Increased cell turnover/Cancer
- Hypertension
- Hyperglycemia/pre-diabetes/diabetes
- Kidney disease
- IBD
- Chronic skin conditions (psoriasis/eczema)
- Depression
- Atherosclerosis
- Chronic liver disease
- Parkinson's (increasing levels with worsening stages)
- Diabetic neuropathy
- COPD
- insomnia

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Treatment:

8-hydroxy-2-deoxyguanosine (8OHdG)

- Address the cause (of course!)
- Increased fruits and vegetables from “a diverse number of botanical families”
 - Study showed an increase of 5.2 servings to 12 servings/day reduced 8OHdG
 - Brassica family veggies studied
- Increased antioxidants: carotenoids (beta carotene/Vitamin A), Vitamin C, Vitamin E, melatonin, selenium, lutein, lycopene
- Increase B vitamins and zinc (co-enzymes)
- Assess/evaluate glutathione, N-Acetyl Cysteine – look at GST gene

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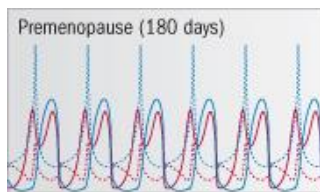


Stages of life:



- **Pre-menopausal/cycling woman** – a woman who is in the age range that she should still have regular menstrual cycles
 - FYI by 30yo only 10% of her non-growing follicles remain (fertility)
 - It takes about 70-80 days for a follicle to go from pre-antral to the selected dominant follicle (that's almost 3 menstrual cycles)
- **Peri-menopausal woman** – typically between 39-55yo where the HPO axis is not as regular, the communication is changing resulting in irregular cycles, skipped cycles, anovulation, hormonal swings and menopausal type symptoms.
- **Menopause** – once a woman has gone 12 consecutive months without a period, she is considered menopausal, the HPO axis has greatly slowed to the point where she makes low levels of steady state hormones, she may still be symptomatic. Typical age is 45-55yo.
- **Post-menopausal** – the point when all menopausal type symptoms have stopped. Typically, older than 55yo however many women experience symptoms for many years.

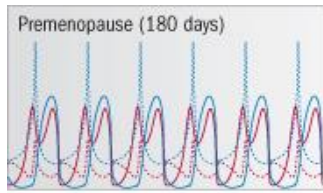
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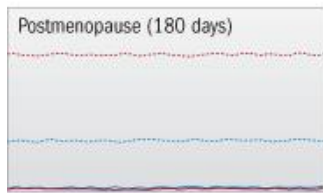
Normal regular rise and fall of hormones every 26-30 days

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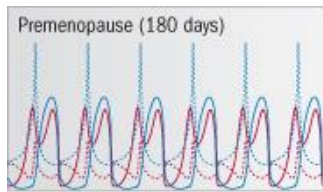
Normal regular rise and fall of hormones every 26-30 days



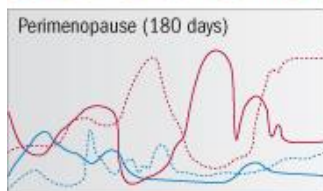
Very low levels of estrogen and progesterone due to no cycles

— Estrogen - - - FSH
— Progesterone - - - LH

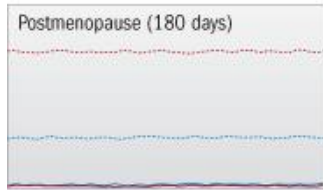
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Normal regular rise and fall of hormones every 26-30 days



Mad chaos – hormones spike up and down causing symptoms



Very low levels of estrogen and progesterone due to no cycles

— Estrogen - - - FSH
— Progesterone - - - LH

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The Common Concerns

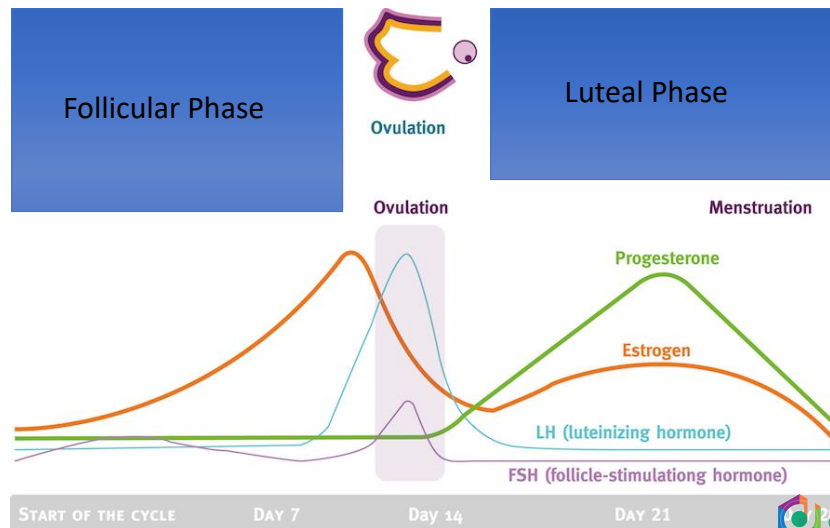


- Examples:
- Luteal phase defect
- PMS
- PCOS
- Menstrual migraines
- Fertility
- Libido issues
- Hot flashes/night sweats
- Weight gain
- Mood swings
- Cognition
- Bone loss

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Normal Menstrual Cycle



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Let's talk about Estrogen and Progesterone

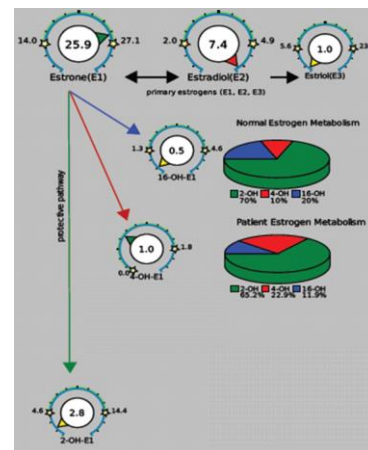


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Estrogen Dominance

- Common causes:
 - SNP issues
 - Ie. CYP1B1, CYP1A1, CYP3A4, COMT
 - Estrogens in environment
 - Supplementation
 - Relatively low Progesterone
 - Phase 1 detox issues
 - Phase 2 detox issues



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What about the infamous ratio with progesterone?

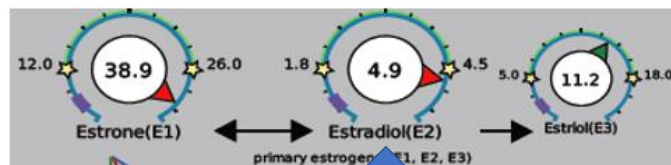
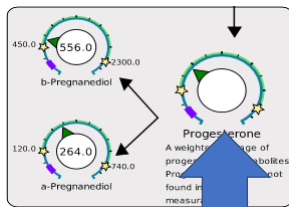
- Harder to do with the DUTCH test as we look at E1, E2 and E3
- Then you might be Estrogen dominant at the phase 1 level
- And/or you might Estrogen dominant at the phase 2 level

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What about the ratio with Progesterone?

***Superficial Level: Compare arrow directions**

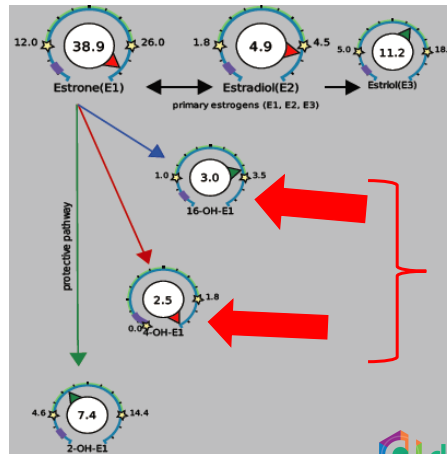
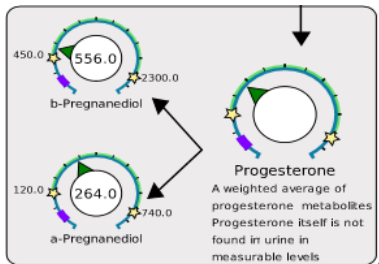


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What about the ratio with Progesterone?

*Next level down: look at the phase 1 Estrogen metabolites



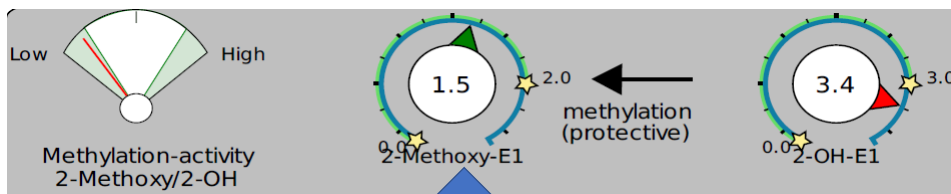
Remember: these get recirculated

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What about the ratio with Progesterone?

*Finally, look to see if estrogen is clearing out of the body through phase 2 detox.

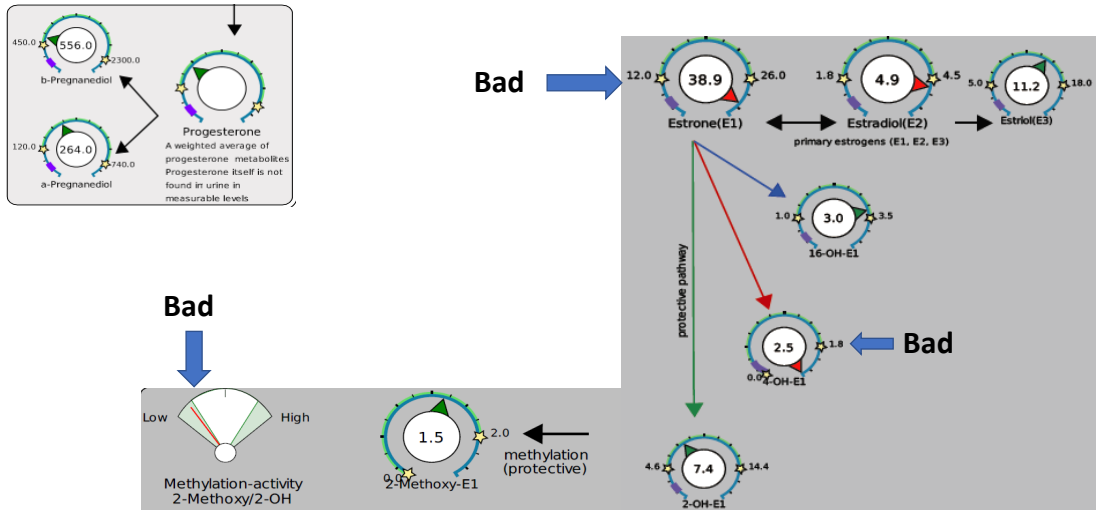


Sluggish phase 2 = E build up

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Worse Case Scenario: Estrogen



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Knowing estrogen metabolism in men and women allows you to evaluate phase 1 vs. phase 2 treatment (They are different)

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As you know, Phase 1 and Phase 2 treatment differ

- **Phase 1:**
 - DIM
 - I3C
- **Phase 2:**
 - Magnesium
 - P5P
 - TMG, Choline, Methionine, SAMe
 - Methyl B12/Folate
 - Calcium-D-glucarate
- **Overall Estrogen support to stop the Quinone pathway:**
 - Sulforaphane/Glucoraphanin (Broccoli Sprouts)
 - Glutathione/NAC

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What about the androgens?



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Where are Female Androgens Made?

The Ovaries produce roughly:

- 25% of the Testosterone
- 50% of the Androstenedione
- 20% of the DHEA (not DHEA-s)

The female 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 in women is made in adipose tissue via androstenedione conversion

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Where are Male Androgens Made?

Adrenals

• In Men:

- all DHEAs
- 80% DHEA,
- <10% androstenedione
- <5% testosterone

In the Gonads:

- 20% of the DHEA
- >90% androstenedione
- >95% testosterone

Men aromatize Testosterone into Estrogen in Adipose tissue via the aromatase enzyme.

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Let's look at PCOS

- 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
 - like the nipple area, top lip, chin area
 - put on Spironolactone and/or Accutane as a result
- Started gaining weight around the middle despite trying a "good diet" and regular exercise
- By the twenties and thirties hair started thinning/falling out
- Wants to get pregnant so stopped the pill and never got her period back

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What is the typical presentation?

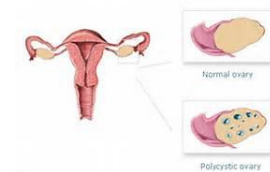
Androgen Excess

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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Diagnosis: 2 out of 3

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

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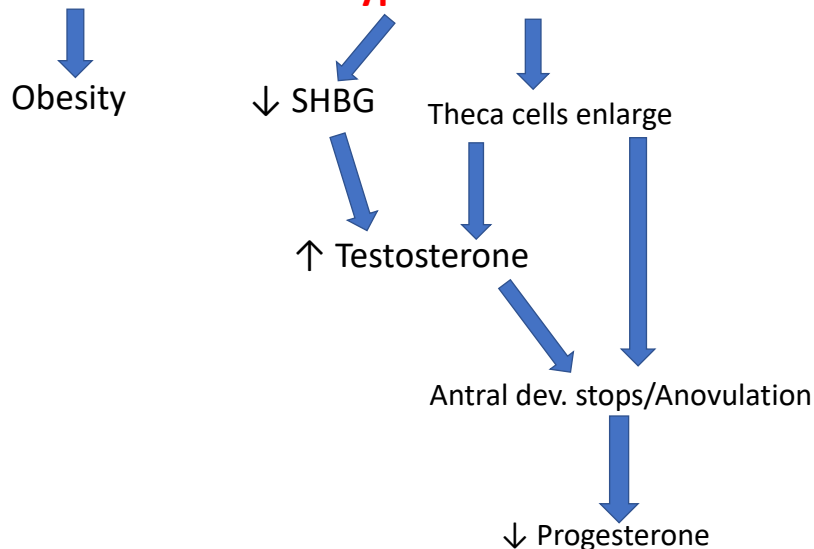
Is obesity part of the diagnosis?

Not always → 30%-75% are obese

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Insulin resistance → hyperinsulinemia



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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

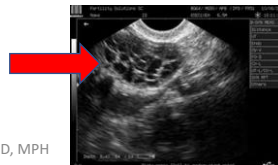
The other 50% of Testosterone is made in adipose tissue via androstenedione conversion

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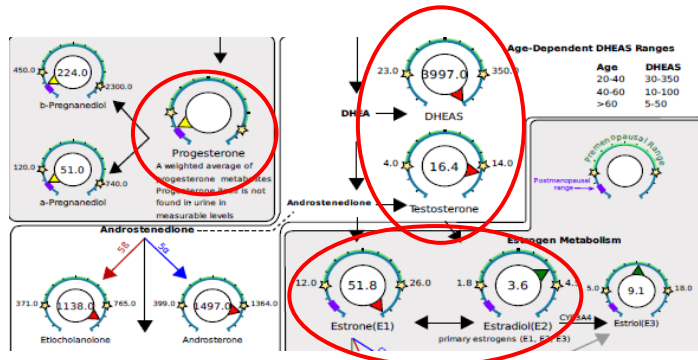
Commonly run labs:

- Fasting glucose/Fasting insulin (Hemoglobin A1c, 2hr glucose insulin tolerance test)
- Thyroid panel with antibodies
- Prolactin (ideal <20ng/ml)
- FSH/LH
- Cardiac markers: lipids, homocysteine, fibrinogen, CRPhs
- 17, hydroxyprogesterone
 - (>80 ng/dL in follicular phase or >285 ng/dL in luteal phase = suspect CAH, cortisol will be low too)
- Anti-mullerian hormone
 - (>4ng/ml suspect PCOS)
- *Consider a pelvic u/s



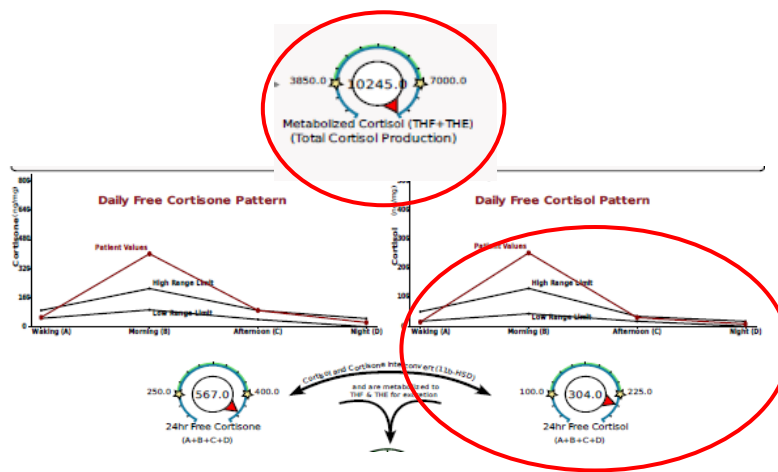
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- Progesterone = low
- Estrone = high
- Estradiol = upper end of the range
- DHEA-s = high
- Testosterone = high

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She's making a ton of cortisol = everything in the red!

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What do you do?
Where do you start?

Is it really PCOS?



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Goals:

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

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Address diet/blood sugar and 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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Address the stress/cortisol:

- Address the cause, meditation, acupuncture, journaling, counseling, finding joy/happiness, proper sleep hygiene
- Adaptogens
- Calming support:
 - 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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Improve ovulation/raise progesterone:

- Vitex agnus-castus (Chaste Tree berry) – 250mg-500mg daily
- Vitamin B6 (P5P) – 25-50mg P5P
- Chamaelirium luteum (False Unicorn Root) – be aware this is considered threatened by some herbalists
- Maca (be aware this could also raise androgens and estrogen) – 1000-2000mg/day
- Evening primrose oil – 500mg-1000mg/day
- 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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Reduce androgen 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) – 500-1000mg/day
 - Pygeum africanum (bark) – 500mg/day
 - Reishi mushroom

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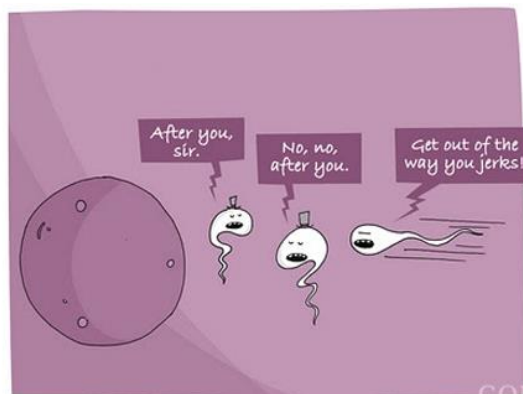
How did I treat the patient a few slides back?

- She was under VERY high stress and had a gut infection
- This, I am assuming, drove up her cortisol thus also increasing her adrenal androgens
- I focused on the gut infection and stress reduction methods
- Added 500mg of Chaste tree berry/Vitex daily and 20mg P5P
- In 3 months her periods resumed normally and she felt much improved

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What about fertility & DUTCH?



How the gentlemen died out.

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Fertility Statistics:

- Definition: inability to become pregnant in 12 mo with unprotected intercourse. For a woman over 35yo, it's the inability after 6mo, and 3mo of trying after 40yo.
- Healthy couples without complications have a 20-25% of becoming pregnant with each month of trying around ovulation
- Healthy couples without complications have an 85% chance of becoming pregnant in 12 months (if actively trying at ovulation)
- Infertility is about 30% male issues, 30% female issues, 30% both of their issues, and 10% unexplained

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Common Causes of Female Infertility

- Structural abnormalities
- Endometriosis
- Luteal Phase Defect
- Thyroid disorders
- PCOS
- Hyperprolactinemia
- Diabetes (type I and 2)
- Hypothalamic/Pituitary dysfunction
- Adrenal disease
- Celiac and other Autoimmune
- Age related/Premature Ovarian Insufficiency

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Fertility labs to consider for her:

- DUTCH Complete + Cycle mapping
- Day 2 or 3 FSH (Follicle stimulating hormone)
- AMH (Anti Mullerian Hormone)
- Full thyroid panel with antibodies and rT3
- Prolactin
- Nutrients: Vitamin D, Ferritin, Zinc, B12, Folate (MTHFR)
- Fasting glucose/insulin
- Cholesterol panel
- Ultrasound (maybe Hysterosalpingogram (HSG) to check tubes)
- Sexually transmitted infection check, general vaginal infxn check
- Gluten/gliadin markers for celiac and/or intolerance
- SIBO/Gut testing
- Other autoimmune testing such as for Lupus

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Fertility labs to consider for him:

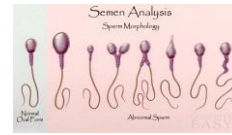
- DUTCH Complete
- Full thyroid panel with antibodies and rT3
- Semen analysis
- Nutrients: Vitamin D, Ferritin, Zinc, B12
- Cholesterol panel
- Fasting glucose/insulin
- Sexually transmitted infection testing
- Gluten/gliadin markers for celiac and/or intolerance
- SIBO/Gut testing
- Varicocele exam by doctor

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Semen Analysis FYI

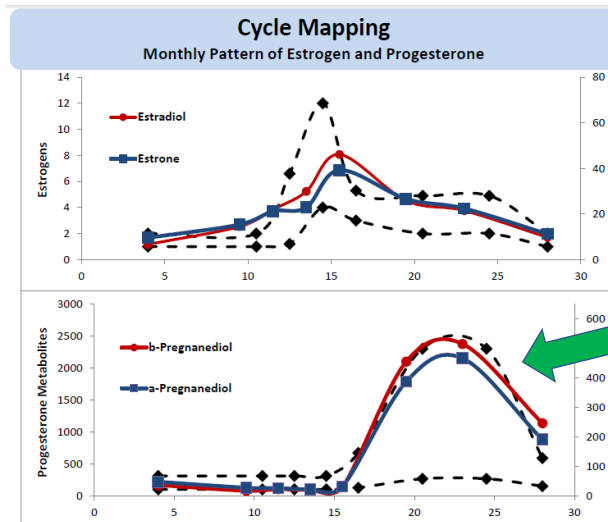


- Collecting one alone isn't accurate, most specialist centers collect 2-3 over 3-6 months
- Must abstain from ejaculation for 2-3 days
- Collection on site is ideal
- A varicocele is the most common finding in infertile men – 20% of the average man has one, 40% of infertile men have one
- Volume, Count, Motility, and morphology are looked at the most
 - Agglutination and viscosity often tested but not always
 - White blood cells often tested but not always
- There is a lot you can do naturally to support a poor sperm analysis

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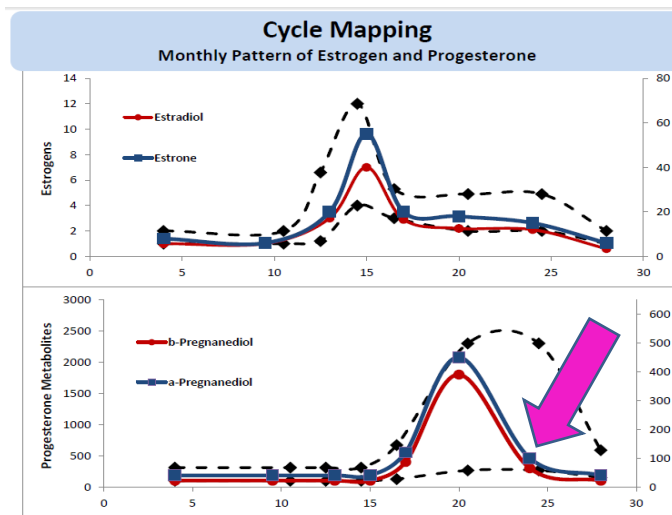
Normal Progesterone Curve



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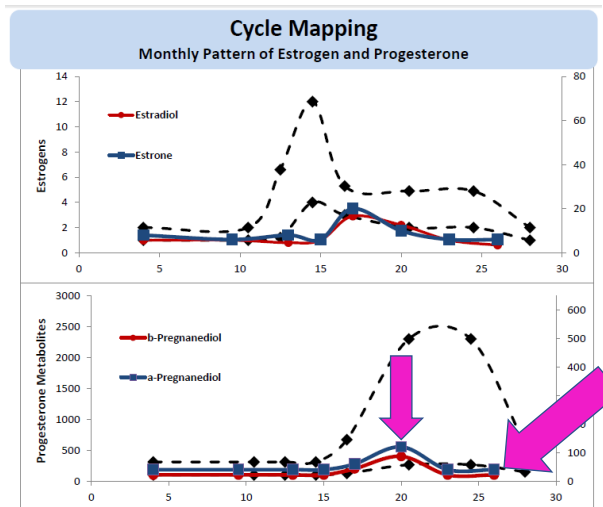
Normal Progesterone Curve???



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Long Follicular/Short Luteal phase



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Low P and Low E Treatment Suggestions for Women:

This applies to both cycling women and menopausal women

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Progesterone Deficiency:

- Address the cause (ie. PCOS, hypothyroid, stress, underweight, overtraining...etc)
- Chaste tree berry (Vitex)
 - helps HPO communication to improve ovulation
 - 250-500mg daily in the morning
- Ovarian glandulars to encourage ovulation
- Brain support like glandulars, Maca, cordyceps
- Vitamin B6/P5P –
 - helps the estrogen/progesterone ratio
 - regulates FSH and LH by helping serotonin and dopamine
 - P5P – 20mg-50mg daily
- Evening Primrose Oil
 - For fertility purposes perhaps don't take after ovulation as can interfere with implantation by causing uterine contractions in some women
 - 1000-4000mg/day
- Borage Oil –
 - Has more GLA than evening primrose oil has in it
 - 1000-2000mg/day
- False Unicorn Root (Chamaelirium luteum)
 - Ovarian adaptogen it's called
 - 100-200mg/day
 - Be careful as it is a threatened/over harvested herb – only use from reputable sources that grow and wild harvest it themselves.

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Using Progesterone:

- Bio-identical progesterone supplementation
- Usually done from a positive ovulation until menses
- In peri-menopausal and menopausal women: can do 6 days on/1 day off or 3 weeks on and 1 week off or 5 days on and weekends off...etc
 - Oral: 100-200mg daily at night
 - Sublingual: 20-60mg at night
 - Topical: rubbed into thin skin, be careful of transfer to other people,
 - 20-60mg daily
 - Vaginal: 10-50mg (do not use as a lubricant)
 - Pellet: must be inserted by someone who is trained

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Estrogen Deficiency:

- Address the cause (ie. PCOS, hypothyroid, underweight, overtraining, stress...etc)
- Chaste tree berry (Vitex)
- Ovarian glandulars
- Brain glandulars like Maca and cordyceps
- DHEA if warranted
- Phytoestrogenic herbal:
 - Black Cohosh (cimicifuga racemose)
 - Dong Quai (Angelica Sinensis)
 - Red Clover
 - Rhaponticum Rhubarb (Rheum rhaponticum L.)
 - Maca – 1000-2500mg/day
 - Tribulus (Bulgarian) (modulates testosterone and can increase estrogen) – 750mg days 5-14 of cycle, menopausal women take 4 weeks and 1 week break
 - Genestein and Daidzein (isoflavones)
 - Shatavari – 250mg bid

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DUTCH Case Studies



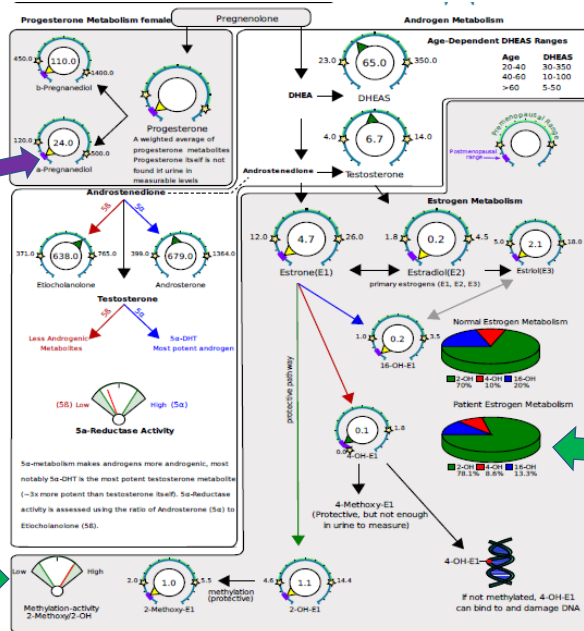
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**“Ideal”
menopausal
woman**

**Hormones mostly
in the menopausal
range (purple
rectangular box)**

**Methylation
activity healthy**

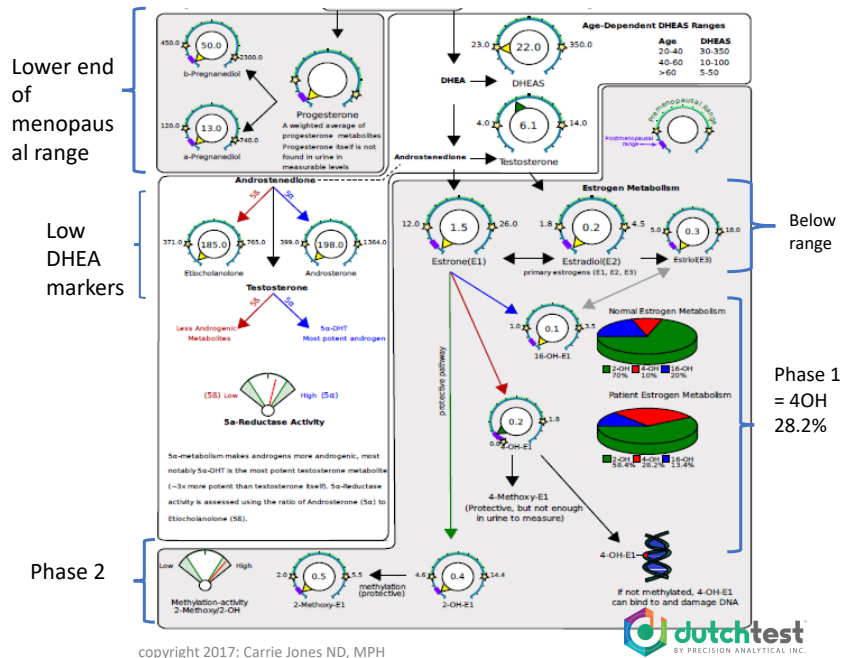


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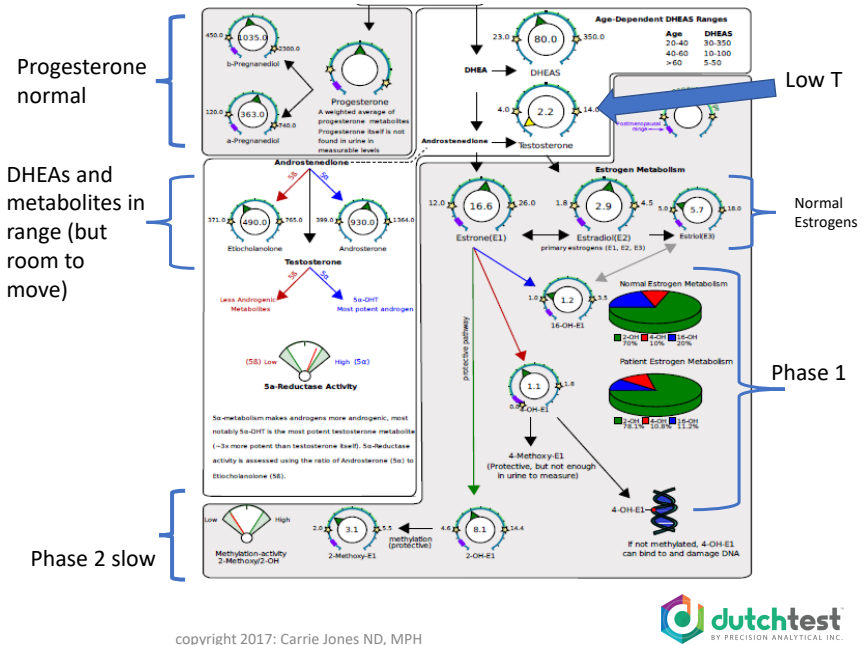
52yo menopausal woman (8 months no menses):
hashimoto's, fatigue,
severe hot flashes,
weight gain, mild
anxiety

What would you do?



Relatively "normal" 42yo with regular cycles. Minimal complaints. Wants to simply optimize health.

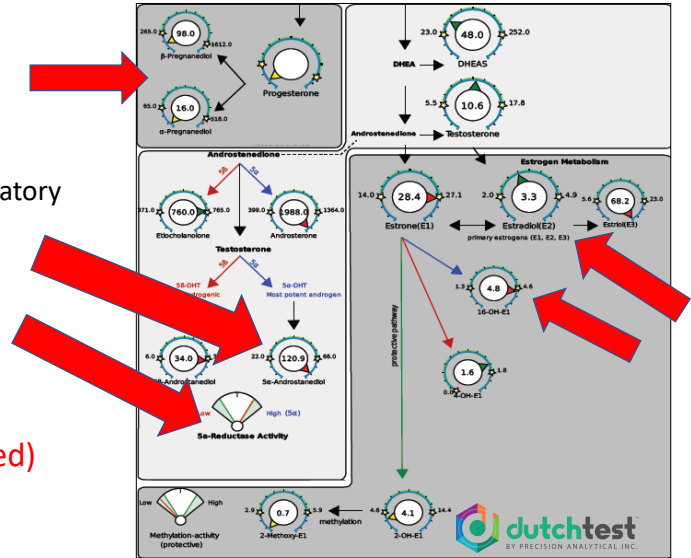
What would you do?



PCOS Evaluation

COMMON SYMPTOMS:

- **Ovulatory issues**
 - Low progesterone
 - No cycle, irregular cycle, anovulatory
- **Androgenic symptoms**
 - 5a dominant
- High estrogens
- Poor estrogen metabolism
- **Multiple cysts on U/S**
- **(Dx PCOS: need 2 out of 3 in red)**



39yo female with regular cycles, hair loss, migraines, anxiety, heavy bleeding, and >75lbs overweight

Not ovulating = low progesterone

Incr. T, etio & androsterone

Estrogen dominant

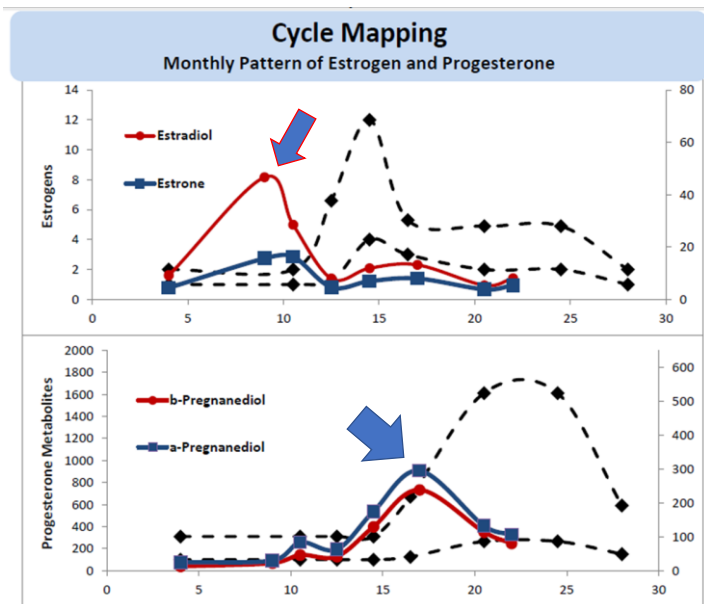
What would you do?

Phase 2 slow

Phase 1

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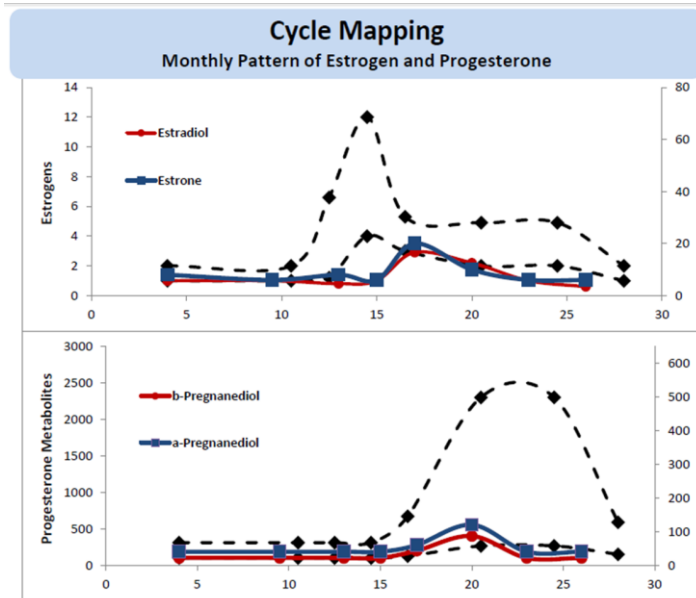


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28yo with short cycles (<25 days) trying to get pregnant.

What would you do?



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48yo woman with irregular cycles wanting to know if she is near menopause/does ovulate. Having hot flashes, night sweats, brain fog, low energy, depression

What would you do?

Let's not forget our men!

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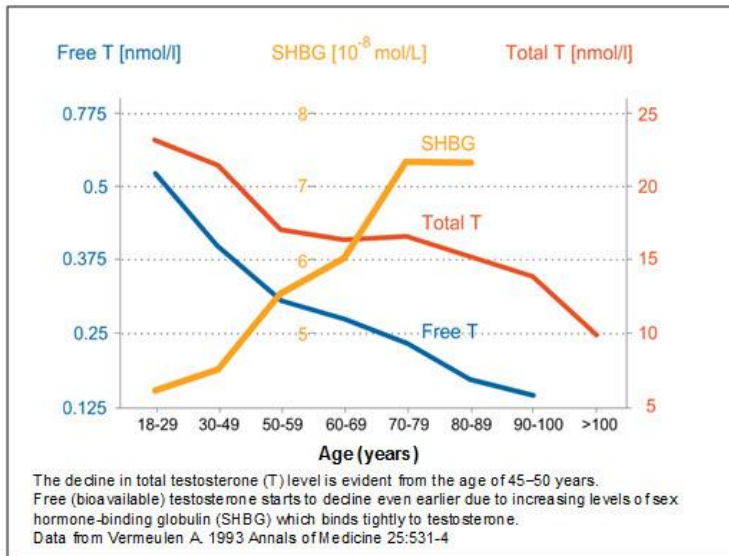


Quick Facts:

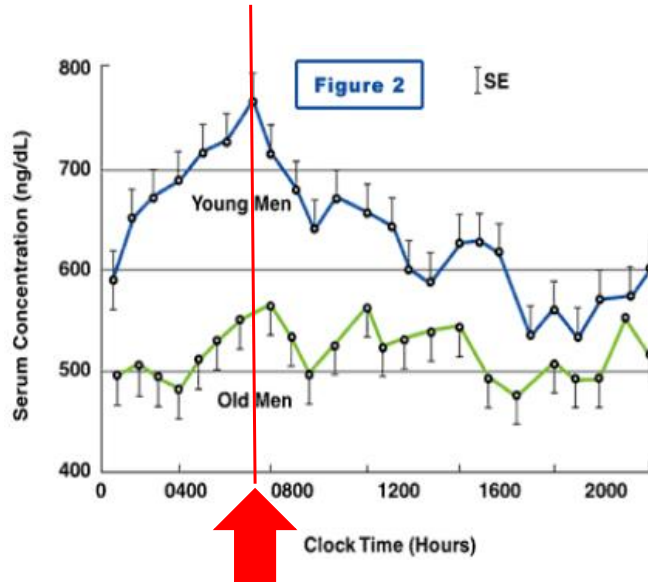
- Testosterone is highest at puberty then starts to decline 1-2% yearly at 30yo
- Unfortunately, this process can be sped up through poor lifestyle habits, dietary choices, exposures, lack of exercise and increased stress resulting in men in their 20's and 30's experiencing the fallout of a low testosterone level.
- Male factor infertility is 30% of the cause of infertility between couples
- Prostate cancer is 2nd most common cancer in men after non-melanoma skin cancer
 - In 2013, 176,450 men were diagnosed with prostate cancer
- According to the CDC, about 34-35% of men are obese (not overweight) with the most obese age range at 40-59yo.

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Review of testosterone pathway and sperm production:

- Hypothalamus releases gonadotropin releasing hormone (GnRH) in a pulsatile manner
- GnRH stimulates LH and FSH
- **LH** binds to Leydig cells in the testes → Testosterone, androstenedione and DHEA
- **FSH** binds to Sertoli cells in the seminiferous tubules to nurture developing sperm cells through the stages of spermatogenesis
 - There are 6 stages to seminiferous development and going from stage 1 to stage 6 is called a Cycle.
 - Each Cycle takes about 16 days and most sperm need 4.6 cycles to mature = 74 days
 - Sperm are then shuttled to the epididymis for maturation, storage, then transport out through the vas deferens to the prostate and out the penis on ejaculation.

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The Common Concerns:

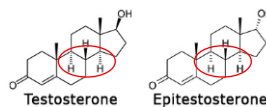


- Common complaints:
 - Fatigue
 - Weight gain
 - Sexual dysfunction
 - Low motivation
 - Low mood, more down lately
 - Loss of muscle strength
 - Male pattern baldness
 - Enlarged prostate
 - Fertility issues

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What is Epi-Testosterone?



Testosterone/Epitestosterone Ratio

1:1 - Ideal

<4:1 - Acceptable

>4:1 - Testosterone Doping

- It's an epimer of testosterone
- Weak competitive antagonist to the androgen receptor (anti-androgen)
- Most males have an endogenous production of epitestosterone to testosterone ratio of 1:1
 - Meaning it's produced about the same as regular testosterone
- **It does not increase with testosterone replacement**
 - It is a good marker to see how replacement is working
 - It used to be used to test for doping in sports

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Low Testosterone: Natural Treatment

- First, Address any known causes!
- Resistance training/HIIT
- Improve GH (resistance training, 7+ hours sleep...etc)
- Zinc – 15-100mg/day
- Maca – 750-3000mg/day
- Tongkat Ali (Eurycoma) root extract at least 100:1 – Indonesian is best
 - Supposed to 'knock' free testosterone off SHBG
- Horny Goat Weed (Epimedium)
 - Icaritin: PDE5 inhibitor
 - PDE5 is an enzyme that breaks down the result of nitric oxide with cGMP pathway, causing the erectile tissue to lose its blood flow
 - Shown to raise testosterone in animal models
 - Take before sex to help
- Pine pollen
 - Gibberellins – Structurally very similar to testosterone.
- Tribulus (Bulgarian) modulates testosterone – 500-750mg testosterone cycled
- Suma (Pfaffia paniculata) – amazon vine
 - Root has beta ecdisterone that act anabolic and immune supportive

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Estrogen and Men

- Made in adipose tissue (mainly) via aromatase enzyme
 - Testosterone →aromatase→estrogen



- **Increased levels:** excess insulin, excess adipose tissue, increased stress, alcohol
- **Symptoms of increased estrogen:** fatigue, low mood, low libido, weight gain, breast development, erectile dysfunction

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High estrogen treatment

- Address the causes as listed above
- Make sure it's not being transferred by someone in his house on topical estrogen
- Decrease aromatization by addressing insulin, stress, alcohol and weight
 - Anastrozole/Arimidex (medication)
 - Topical chrysin applied right to adipose tissue (weak to moderate activities in studies)
 - Oral difficult to absorb
 - Oral damiana: 400-500mg/day – moderate (limited study)
 - Agaricus (white button mushroom – high activity in studies)
 - Fatty acids in Urtica dioica (stinging nettle) – moderate activity in studies
 - Viscum album (careful this can be toxic)
 - Mangosteen – moderate to high activity in studies
 - C. Sinensis (tea) EGCG – weak activity in studies
 - Theobroma cacao – weak activity in studies
 - Apigenin and Quercetin – weak to moderate activity in studies
 - Resveratrol from Vitis L. – no activity to moderate activity depending on study

• Balunas M, Su B, Brueggemeier R, and Kinghorn A. Natural Products as Aromatase Inhibitors. Anticancer Agents Med Chem. 2008 Aug; 8(6): 646–682.

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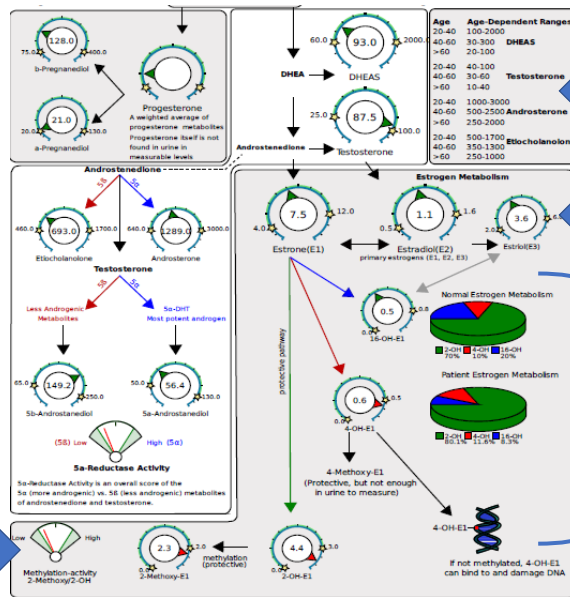
DUTCH Male Case Studies



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64yo male, no HRT, no real concerns



Phase 1 favors too much 4OH

Phase 2 a little sluggish

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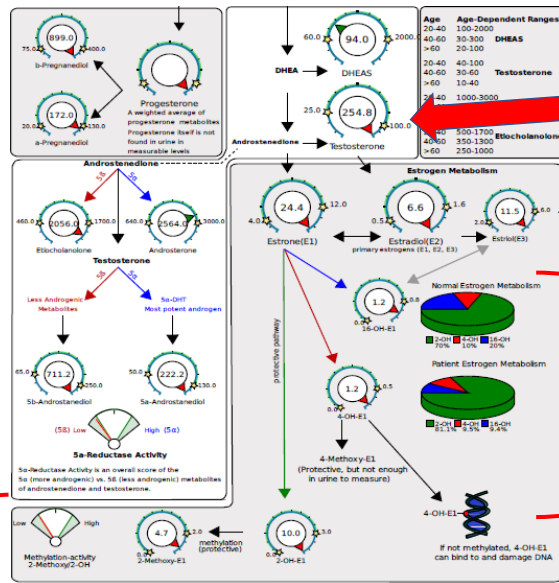


56yo with testosterone injection 4 days prior. Complains of low libido, weight gain, fatigue

What would you do?

Favors beta pathway overall but alpha high too

Sluggish phase 2



Elevated T.

Elevated estrogens

Upregulated phase 1

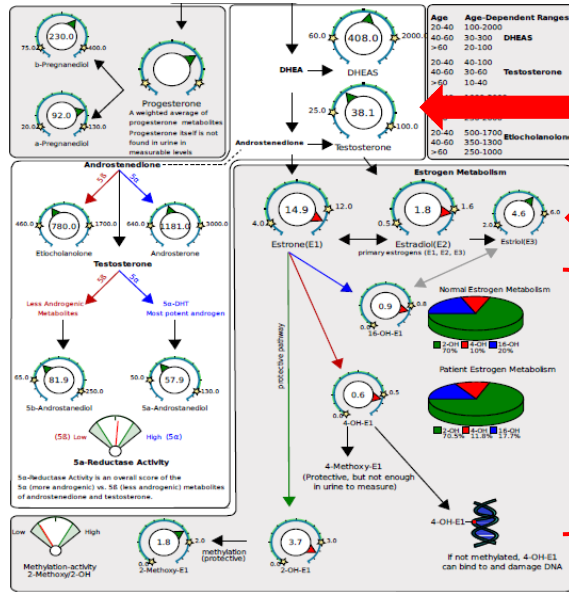


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40yo with fatigue, weight gain, borderline diabetic, low libido, depression

What would you do?

Sluggish phase 2



Borderline low T

Estrogens too high – why?

Phase 1 elevated



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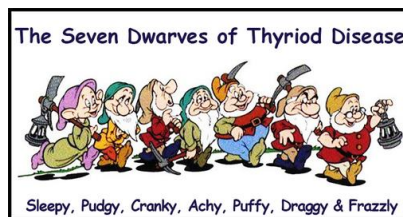
Lastly, let's talk about the thyroid!

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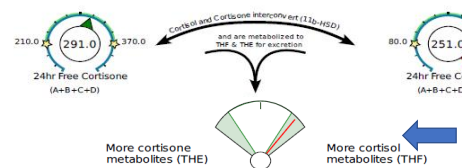
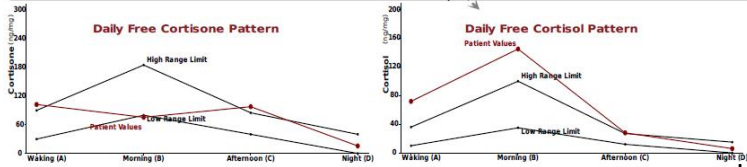
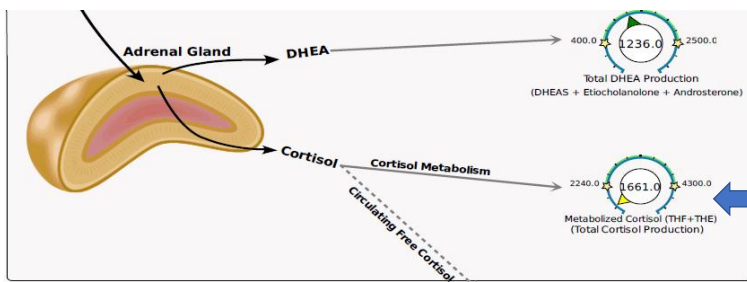


Hypothyroid and metabolized cortisol

- When the thyroid slows down OR if there is peripheral hypothyroidism due to deiodinase activity, it slows everything down
- Production of cortisol (in total) can slow down
- Liver enzymes that metabolize cortisol slow down



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THYROID
Volume 3, Number 3, 1993
Mary Ann Liebert, Inc., Publishers

Urinary Cortisol Metabolites in the Assessment of Peripheral Thyroid Hormone Action: Application for Diagnosis of Resistance to Thyroid Hormone

MATSUO TANIYAMA,¹ KEIKO HONMA,² and YOSHIO BAN¹

ABSTRACT

Urinary cortisol metabolites are altered both quantitatively and qualitatively in thyroid dysfunction. This study was conducted to elucidate the usefulness of urinary cortisol metabolites in the assessment of peripheral thyroid hormone action, particularly in the patients with inappropriate thyrotropin secretion. Twenty-four hour urinary 17-hydroxycorticosteroid (17-OHCS) level and gas chromatographical steroid profile were studied in 25 hyperthyroid, 18 hypothyroid, and 24 euthyroid control subjects. Five patients with generalized thyroid hormone resistance and two patients with thyrotropin secreting pituitary tumor were also studied. The ratio of urinary tetrahydrocortisone to tetrahydrocortisol (THE/THF) was significantly elevated in hyperthyroidism (4.58 ± 1.49) and depressed in hypothyroidism (1.31 ± 0.55) compared to control (1.93 ± 0.35). There were good correlations between THE/THF and serum thyroid hormone levels, especially in hypothyroidism. THE/THF can be a good biochemical indicator for deficiency of peripheral thyroid hormone action. Two patients with thyrotropin-secreting tumor showed high THE/THF, which reflected thyroid hormone excess. In contrast, THE/THF in the patients with generalized thyroid hormone resistance was low as compared to high serum thyroid hormone levels. Similar findings were demonstrated with 17-OHCS but discrimination of thyroid hormone resistance was insufficient. Thus, the ratio of the urinary concentrations of cortisol metabolites, THE/THF, appears to be a good marker for peripheral thyroid hormone resistance.

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Altered Equilibrium Between Cortisol and Cortisone in Plasma in Thyroid Dysfunction and Inflammatory Diseases

Yoichi Ichikawa, Koichiro Yoshida, Mitsuhiro Kawagoe, Eizo Saito, Yoshibumi Abe, Kazumi Arikawa, and Mitsuo Homma

The radioactivities of cortisol and cortisone in plasma were determined following simultaneous injection of ^{14}C -cortisol and ^3H -cortisone. The plasma concentrations of ^{14}C -cortisol and ^3H -cortisone decreased as a first-order function of time after an initial rapid drop, while there was a prompt appearance of ^{14}C -cortisone and ^3H -cortisol in plasma, which also decreased as a first-order function. The biologic half-lives of these four isotopic steroids were essentially identical. The ratio of ^{14}C -cortisone to ^{14}C -cortisol and that of ^3H -cortisone to ^3H -cortisol in plasma were constant after 60 min following injection and were identical, which suggested that cortisol and cortisone in plasma were at dynamic equilibrium. This ratio was 0.36 ± 0.01 (SE) in normals; it was decreased in patients with hypothyroidism (0.21 ± 0.03) and

inflammatory diseases (0.18 ± 0.01) and was variable in hyperthyroid patients (0.42 ± 0.11). The ratio of the metabolic clearance rate of cortisone to that of cortisol was significantly increased in hypothyroid patients and in patients with inflammatory diseases, while urinary 11-ketonic metabolites of cortisol are known to decrease relative to its 11-hydroxy metabolites in these patients. These data and the decreased cortisone-to-cortisol ratio at equilibrium were consistent with the altered equilibrium between cortisol and cortisone, favoring cortisol, in these patients. It was suggested that the altered equilibrium between these steroids may be an important factor in determining the effectiveness of secreted or exogenously administered cortisol and the plasma concentration of cortisone in several disorders.

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doi: 10.1111/j.1365-0442.2016.05111.x

ORIGINAL ARTICLE

Comprehensive study of urinary cortisol metabolites in hyperthyroid and hypothyroid patients

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Journal of Clinical Endocrinology and Metabolism
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Dynamics of 24-Hour Endogenous Cortisol Secretion and Clearance in Primary Hypothyroidism Assessed before and after Partial Thyroid Hormone Replacement*

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ABSTRACT. Although various abnormalities of hypothalamic-pituitary-adrenal function have been reported in primary hypothyroidism, neither 24-h patterns of pulsatile cortisol release nor estimation of its endogenous secretion and clearance rates have been fully investigated in this clinical setting. We studied pulsatile and circadian patterns of cortisol secretion in six hypothyroid men (mean free T_4 index, 0.59 ± 0.22 (±SE); mean TSH, >50 mU/L) by sampling blood at 20-min intervals for 24 h before (unreplaced) and then after 5–7 months of partial replacement treatment with levo- T_4 . Compared to a normal group, hypothyroid men had significantly elevated 24-h mean serum concentrations of cortisol (419 vs. 254 nmol/L; $P < 0.001$), with no change in serum cortisol-binding globulin concentrations. Cluster analysis of cortisol time series revealed a normal pulse frequency, with significant increases in mean peak amplitude (527 vs. 331 nmol/L; $P = 0.001$), mean interpulse valley concentrations (384 vs. 204 nmol/L; $P < 0.05$), and mean prepeak nadir concentrations (298 vs. 166 nmol/L; $P < 0.05$). Cosinor analysis showed preserved circadian rhythmicity (i.e. normal mean circadian amplitude of cortisol release) in hypothyroidism, with a significant delay in the timing of circadian acrophases and an increase in the mesor (mean). Analysis of data by a multiple

parameter deconvolution method demonstrated a normal 24-h endogenous cortisol production rate in the presence of significantly prolonged subject-specific half-life of cortisol disappearance (155 vs. 73 min; $P < 0.05$). Partial replacement therapy with levo- T_4 caused significant decreases in 1) mean 24-h serum cortisol concentrations (419 vs. 323 nmol/L; $P < 0.05$); 2) mean cortisol peak amplitudes (527 vs. 375 nmol/L; $P < 0.05$); 3) mean prepeak nadir concentrations (298 vs. 221 nmol/L; $P < 0.05$); and 4) mean half-life of cortisol disappearance (155 vs. 112 min; $P < 0.0019$).

In summary, the present study of cortisol secretory dynamics in hypothyroid men has shown elevated mean 24-h serum concentrations of cortisol with preserved circadian rhythmicity and normal endogenous production rates, but prolonged half-lives of cortisol disappearance. In conjunction with normal serum cortisol-binding globulin concentrations, these largely reversible findings suggest that significant hypercortisolemia in primary hypothyroidism is primarily due to decreased metabolic clearance of cortisol and a presumptive decrease in the negative feedback effect of cortisol on the hypothalamo-pituitary axis. (*J Clin Endocrinol Metab* 70: 155, 1990)

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**Having the most comprehensive,
easy to collect
adrenal and hormone test available
allows you to make
a greater impact on your patients
at a deeper level.**

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...and that
concludes our
talk

Thanks for listening!
drjones@dutchtest.com



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