



Metabolism of Steroid Hormones

Dr. Joe Klassen, ND

Meet Joe Klassen, ND



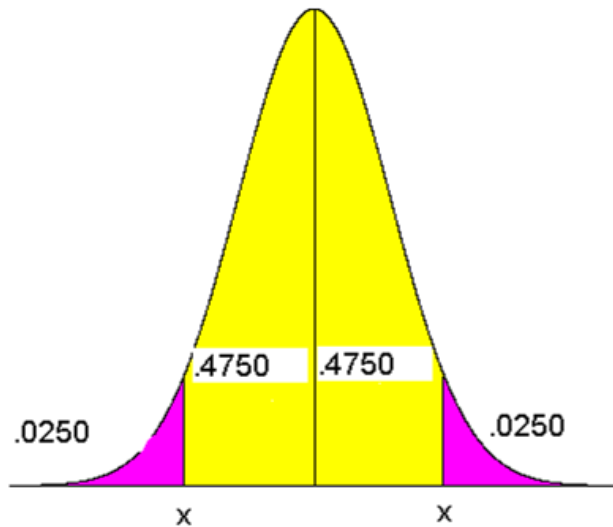
Naturopathic Training & Experience

- Graduated from Bastyr University of Naturopathic Medicine in Seattle, WA in 2005;
- A licensed Naturopathic Doctor in Alberta and a council member of the College of Naturopathic Doctors of Alberta;
- Started his practice at Fish Creek Naturopathic Medicine in 2006;
- Trained in prolotherapy and intravenous therapies;
- NBCHT Certified Colon Hydrotherapy Instructor.

Business History

- Graduate of the University of Saskatchewan with a Bachelor of Commerce degree;
- After starting a career in the stressful world of Fortune 500 companies, he decided to make a radical change and enter the field of medicine with an eye to natural health.

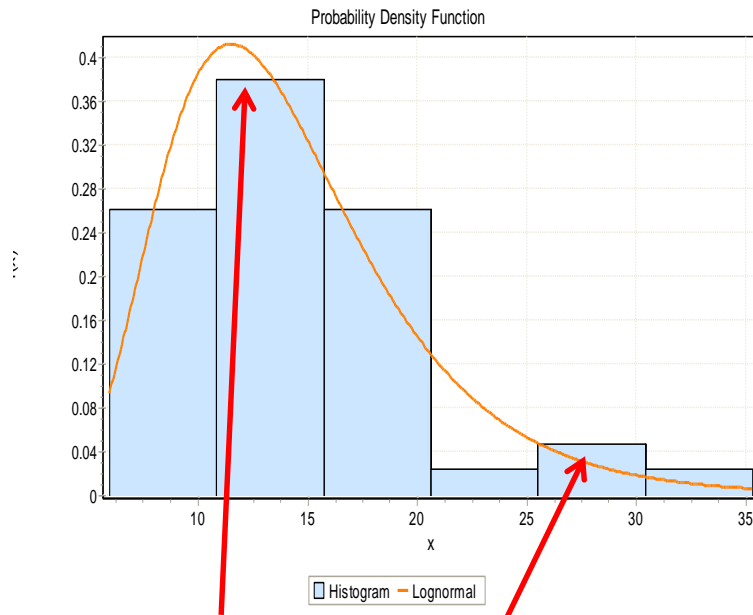
Lab Testing 101: Reference Values



Reference values for each test include age-specific and gender-specific variations, when indicated. Normal ranges of laboratory tests can vary significantly, depending on the method of testing and the particular laboratory.

- Reference values for laboratory tests are given in conventional and/or standard international (SI) units.
- Units of measure may vary by location
 - For example US blood sugar vs SI
 - mg/dl vs mmol/l
- 95% confidence interval
 - Population or sample norms?

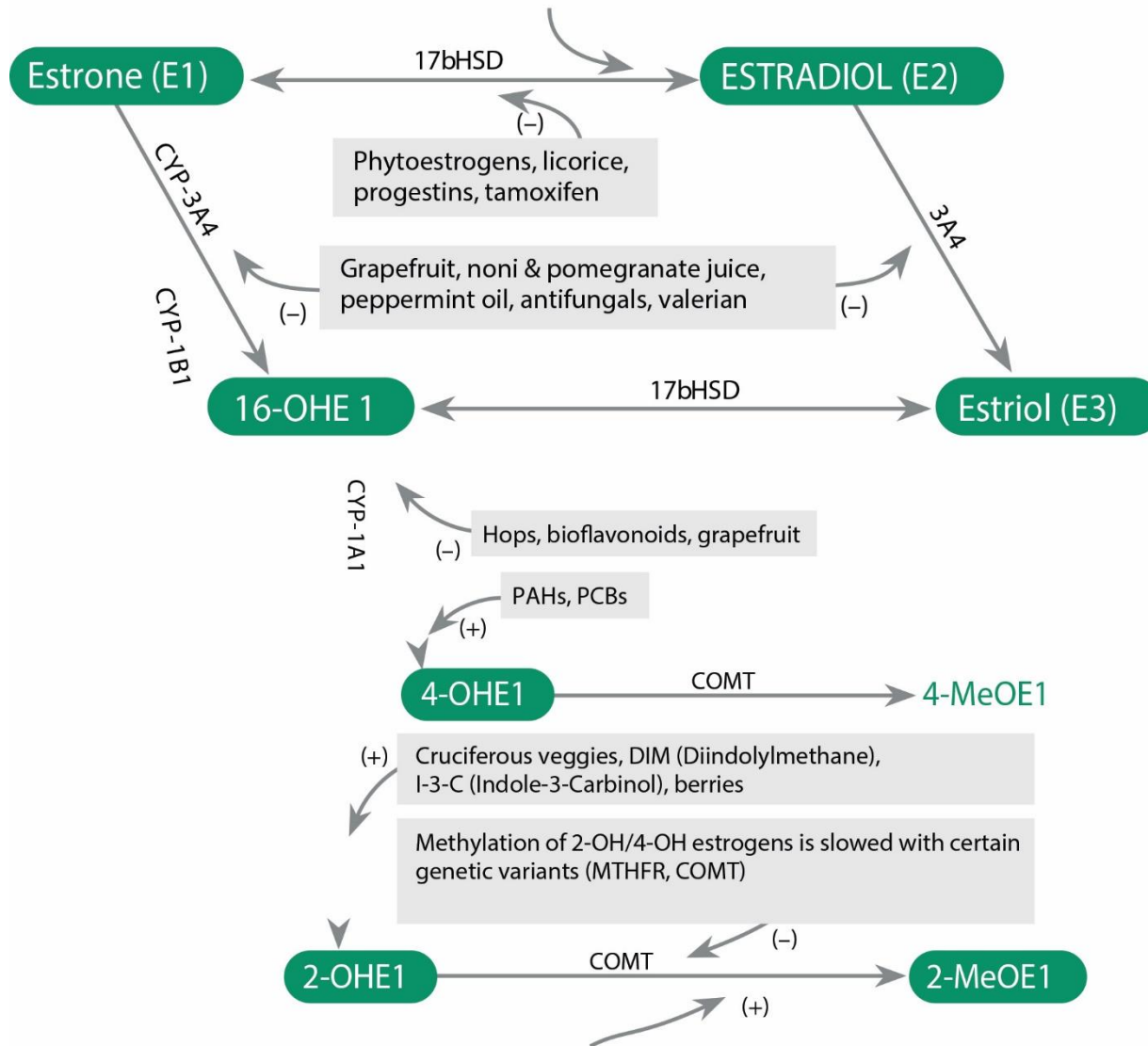
Lab Testing 101: Lognormal Distributions



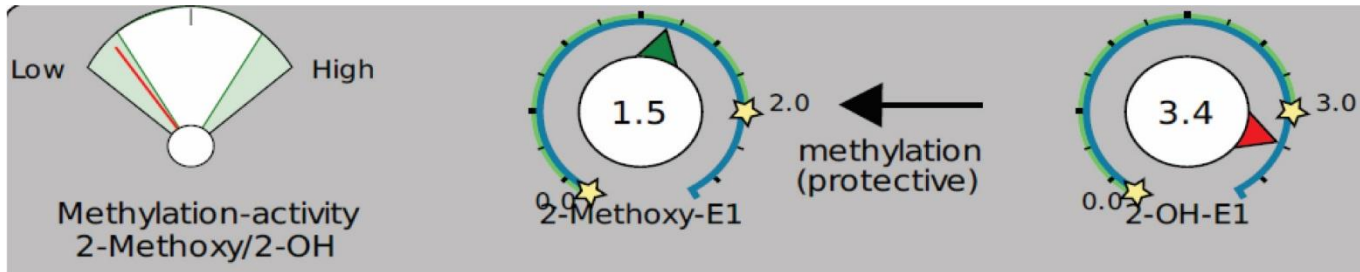
- Many biological variables, including urine steroid concentrations, respect a lognormal distribution (skewed distribution).
- The median is not in the middle of the range
 - If the quoted range is 5 – 35, the median is not 20.
 - It's less than 15
- You need to know the **percentile** of your result.

- Estrogen
 - E1, E2, E3, hydroxylation
 - Purpose
 - Fate:
 - 2-OH, 4-OH, 16-OH
 - 2-Me, 4-Me,

Estrogens



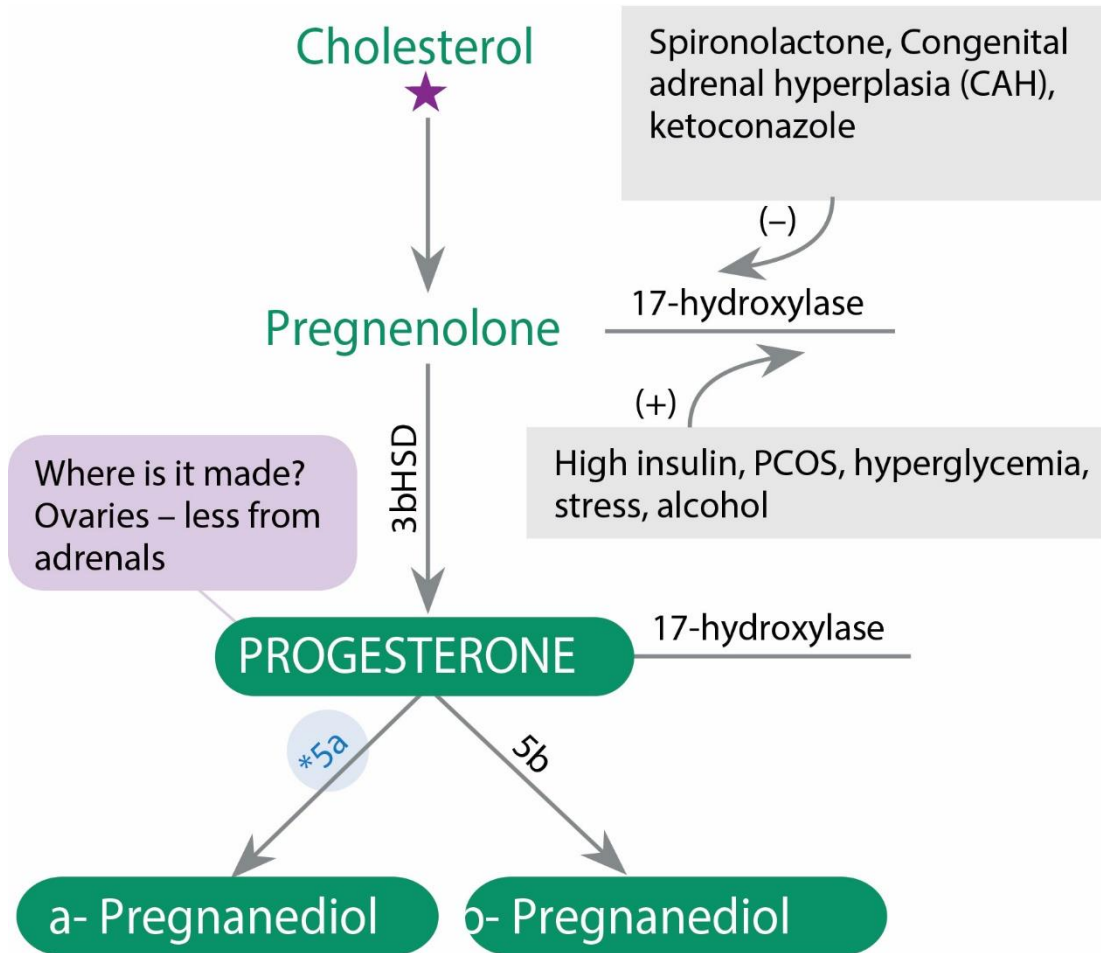
Estrogens



The final E1 and E2 pathway; COMT

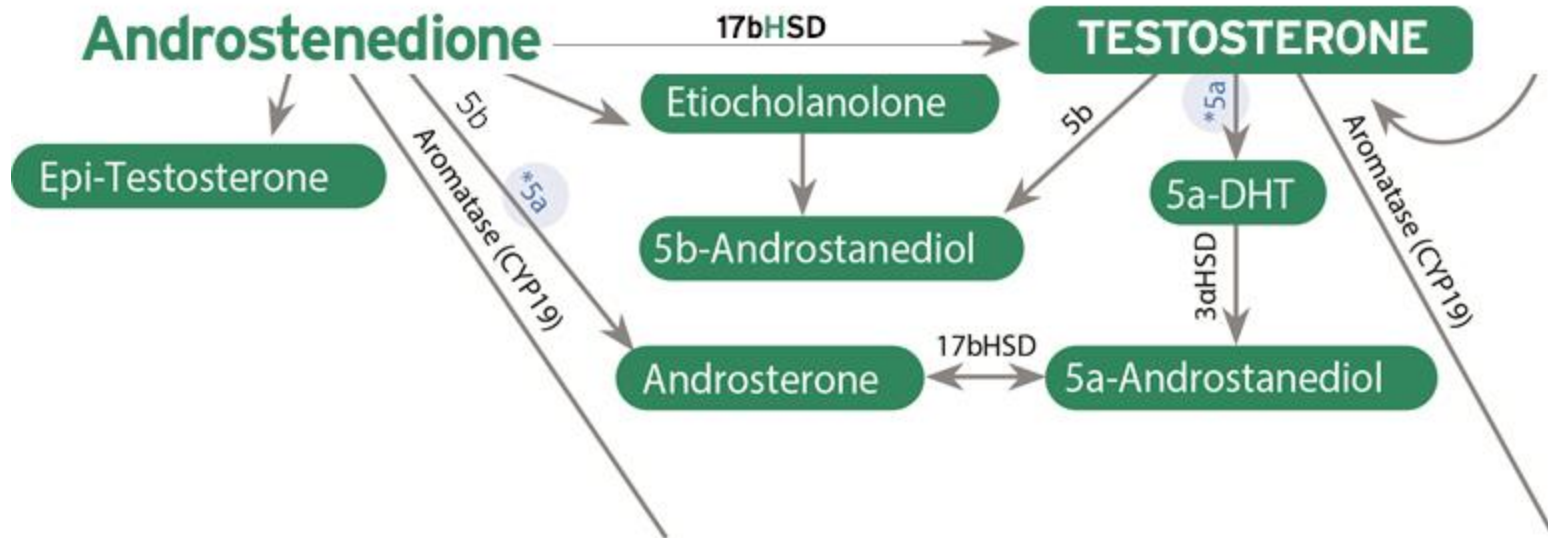
- Progesterone
 - A, B-pregnane diol
 - Urine, fecal release

Progesterone



- Testosterone
 - Epi-T, DHT, androgens,
 - Serve as precursor for estrogens
 - Urine, fecal release

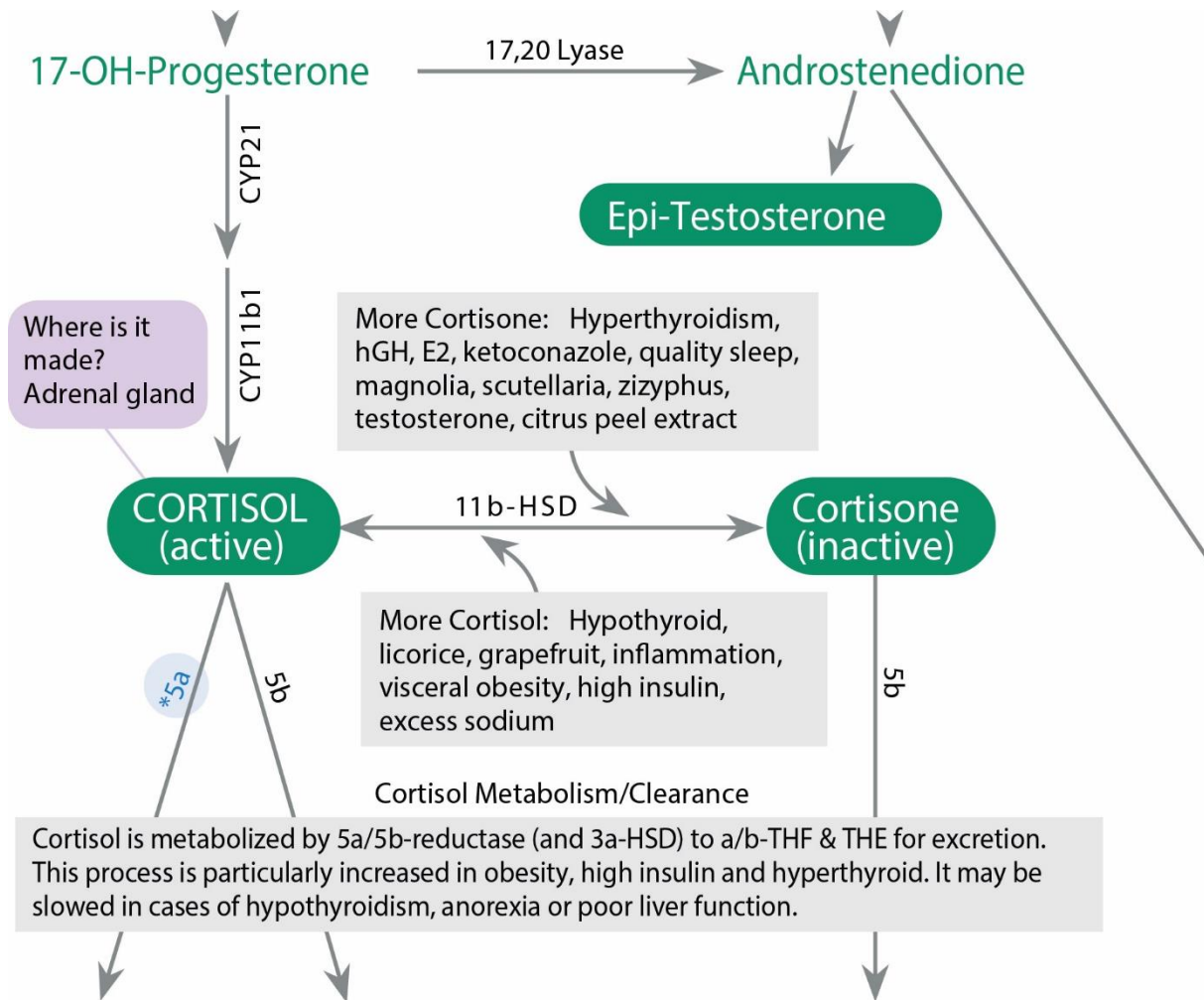
Androgens



Hormone Review

- Cortisol
 - A-THF, THF
- Cortisone
 - THE

Cortisol



- Metabolism in liver
 - Phase I
 - Oxidation/reduction
 - Phase II
 - Conjugation
 - Glutathione
 - Sulphate
 - Glycine
 - Glucuronide conjugation
- Biliary release, entrapment, defecation
- Gut deconjugation, enterohepatic recirculation
- Thyroid status

Parasympathetic activity

- Bile production
- Bile secretion
- Bile entrapment
- Fecal release

“In patients with obstructive disorders of the biliary tract significant increases in urinary pregnanediol may occur, suggesting that in biliary obstruction and interference with this pathway of excretion more pregnanediol is excreted correspondingly in the urine.”

Rogers J, Clinical significance of pregnanediol secretion. Fertil Steril. 1955 Nov-Dec;6(6):513-22.

Enterohepatic Circulation (EHC)

- Intestinal metabolism of bile-excreted hormones
- Intestinal conversion of exogenous molecules to endocrine active metabolites
- Pregnane X receptor
 - Sensor for steroid and xenotoxic substances upregulates detoxification, especially in situation of supraphysiological levels
 - “Innocent bystander” effect ie: supplemental estrogen leads to increased clearing of testosterone.

- Microbiome
 - “The second genome”

“The gut sterolbiome represents an important class of enzyme encoding genes that give gut microbiome the ability to act as an endocrine organ with far-reaching effects in the host. Perturbing effects of the sterolbiome, such as diet, antibiotics, probiotics, and so forth, have the potential to affect many physiological effects.”

Ridlon JM, Bajaj JS. The human gut sterolbiome: bile acid-microbiome endocrine aspects and therapeutics. *Acta Pharmaceutica Sinica B*. 2015;5(2):99-105. doi:10.1016/j.apsb.2015.01.006.

- Direct and indirect effects
- Gillson: “It’s like an accessory liver”

- Bacteria contain enzymes for degradation of unconjugated steroids
- Hydroxysteroid dehydrogenases can be found in normal gut bacteria, producing active steroid hormones and releasing into EHC
- Production and release of SCFA and LPS-bacterial cell wall lipopolysaccharide
- LPS elevates E2/P, increases CRH
 - Reduced fertility through suppressed LH
 - Reduced plasma T

- Lactic acid bacteria supplementation decrease fecal B-glucuronidase leading to increased fecal excretion and reduced plasma estrogens
- Interconversion of steroid derivatives
- Gingival bacteria can also metabolize sex hormones in fashion similar to intestinal bacteria
 - These may be the carbon source for *prevotella intermedia*. These will uptake E and P when K2 growth factor is not available (Korman & Loesche, 1982)
- Phytoestrogens
 - Lignans, isoflavones have little inherent estrogenic activity. They are altered by microflora

- Secondary bile acids can activate nuclear receptors that recognize host primary bile acid receptors exerting endocrine effects
- There is a role for UDCA therapy in improving secondary bile acids

- Smith (1982) – Early 1900's Sir Arbutnot Lane theorized that chronic constipation may lead to systemic dysfunction including “exophthalmic goitre” ...
- Harries (1923) – Graves from excessive absorption of tryptophan, goitre from excessive destruction of tryptophan
- LPS inhibits hepatic D1 (converts T4 to T3) and induces D2 in hypothalamus & anterior pituitary
 - Induces D2 in CNS, potentially causing suppression of TSH and TRH
- T3 glucuronide is major biliary excreted metabolite may be hydrolyzed by gut and returned via EHC

- Thyroid

“The metabolic clearance and secretory rates of the C-21 steroids (cortisol and aldosterone) are increased in hyperthyroidism and decreased in myxedema. In contrast, the metabolism of the C-19 and C-18 steroids (sex hormones) is decreased in hyperthyroidism and increased in hypothyroidism.”

Gordon GG, Southren AL. Thyroid-Hormone Effects on Steroid-Hormone Metabolism. Bulletin of the New York Academy of Medicine. 1977;53(3):241-259.

Case Study: Thyroid Health

Case study: Patient History

- 28 year old female, in no apparent distress
- Presenting for initial naturopathic consultation
- Chief complaints of fatigue, exhaustion, chronic and worsening hair loss
- Lack of energy, low libido, cold extremities, frequently cold body temp
- Often will wake with a night sweat of brief duration
- Patient reports that since age 16 clinicians have repeatedly commented on the visible swelling of the lower neck and have requested numerous thyroid lab evaluations. There have not been any findings to her knowledge and she is frustrated that there does not seem to be any diagnosis made from this effort.

Case Study: Physical Exam

- Gross examination shows a visible enlargement at base of anterior neck
- Scalp shows somewhat sparse dyed long hair with abundant downy recent growth.
- Palpation of the neck reveals an enlarged, boggy and non-tender thyroid, there are no enlarged or tender lymph nodes
- Eyes, ears, nose, throat are all within normal limits.
- Maxillary sinuses are without tenderness bilaterally.
- Patellar and Achilles reflexes are diminished bilaterally.
- Abdomen is somewhat guarded with tenderness in the right upper and lower quadrants with no palpable masses

Case Study: Physical Exam



- Thyroid panel: TSH, T3, T4, anti-TPO antibodies.
- Thyroid elements: Selenium, Iodine, Bromine, Cadmium in first morning urine
- Food sensitivity: Food sensitivity assessment with Candida
- Probiotic, digestive enzyme, B-complex

Case Study: Results

- TSH: 0.53

- T4: 18.1

Free T3

5.0

Units

Units

Reference Range

Reference Range

3.5-6.5

Free T4

18.1

pmol/L

10.0-25.0

- T3: 5.0

Thyroid Peroxidase Antibody

10

kIU/L

0-34

Thyroid Stimulating Hormone

0.53

mIU/L

0.20-4.00

- Anti-TPO: 10

- Food Sensitivity: Egg, whey, walnut.

- Iodine: Below average

- Bromine: Very high

- Cadmium: Very low

- Selenium: Very low

Case Study: Results

Creatinine Normalized

Analyte	Result	Range	0%	20%	40%	60%	80%	100%	Percentile
Selenium AM	0.043	0.047 - 0.12							9.8%
Iodine AM	63	42 - 230							28%
Bromine AM	2,600	750 - 2,500							85%
Creatinine AM	1.3	0.53 - 1.6							73%
Cadmium AM	0.086	< 0.49							0.00095%

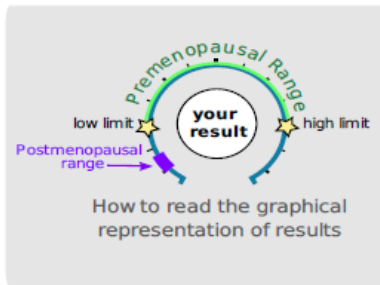
- GFCF diet
- Herbal thyroid support supplement including selenium and iodine
- Education on sources of exposure to bromine.
- Education on food sources of iodine and selenium

- Patient reports resolution of goiter.
- Energy has increased
- Hair loss has diminished
- Libido has returned

- Deficiency globally, with deficient cortisol
 - Low cholesterol
 - Dietary intake
 - Low pregnenolone
 - Cadmium
 - Toxic elements
 - Low thyroid

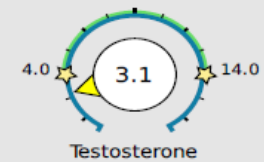
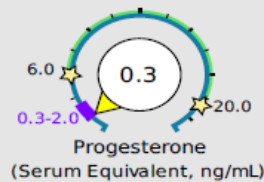
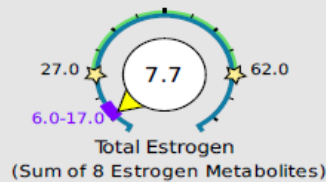
Common Patterns

- Adequate free cortisol with global hormone deficiency
 - This is typically a thyroid issue



Sex Hormones

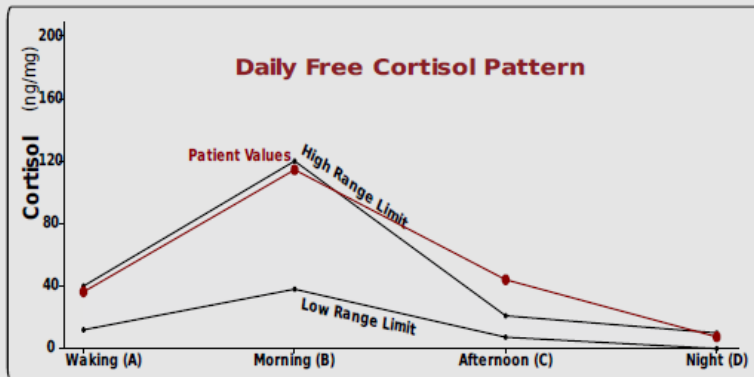
See Pages 2 and 3 for a thorough breakdown of sex hormone metabolites



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

Adrenal Hormones

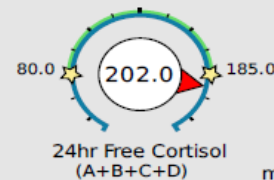
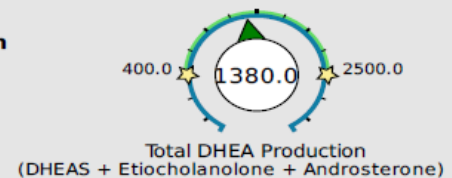
See pages 4 and 5 for a more complete breakdown of adrenal hormones



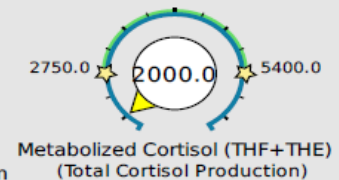
Free cortisol best reflects tissue levels. Metabolized cortisol best reflects total cortisol production.

Total DHEA Production

Age	Range
20-40	800-2500
40-60	530-1550
>60	400-1350



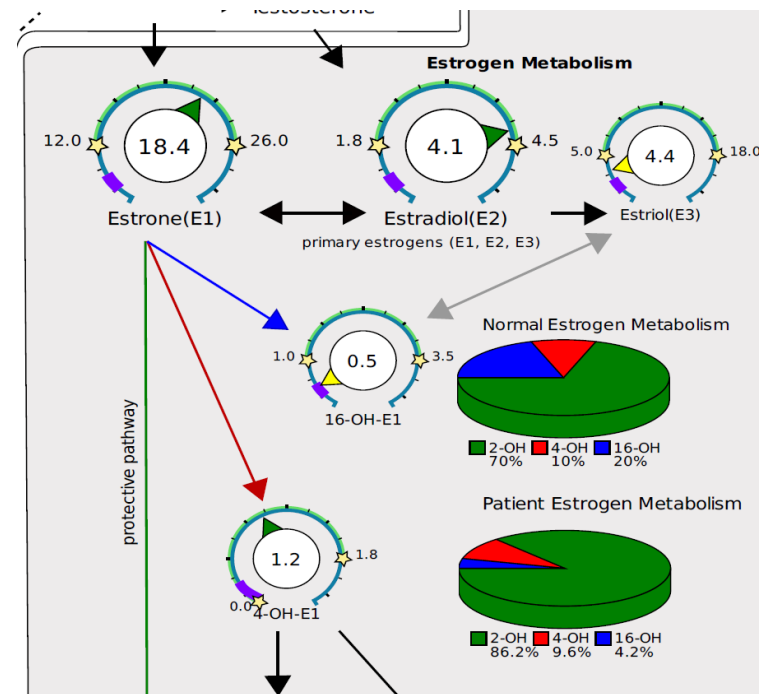
cortisol
metabolism



Common Patterns

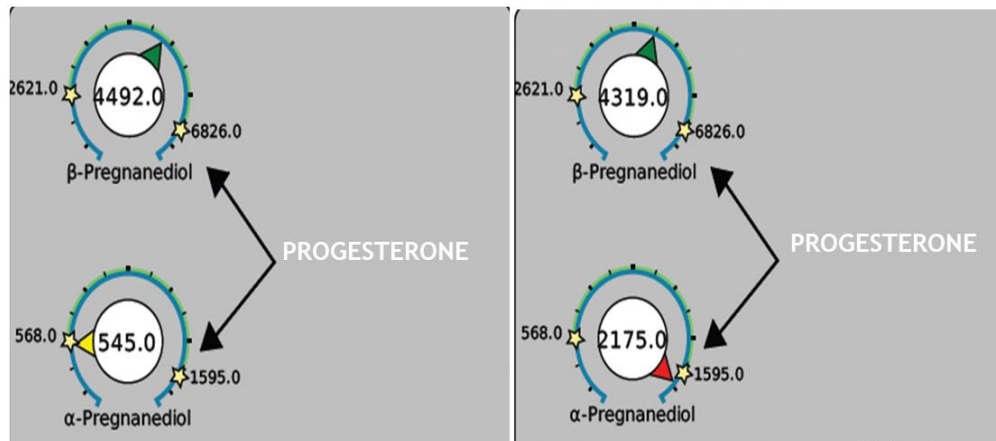
- Robust E1, E2 with deficient E3, 16OHE1
 - CYP 450 3A4 deficiency

This patient has known snp in this pathway



Common Patterns

- Symptoms of low progesterone in the presence of adequate progesterone.
 - The patient tends to the 5-b reductase pathway.
 - Total progesterone is adequate, but the α -pregnanediol is not sufficient
 - This patient would need higher dosing of BHRT progesterone or testosterone to achieve therapeutic effect.



- Metabolism of steroid hormones is multifactorial
- Role of enterohepatic recirculation and microbiome needs is important in hormone homeostasis
- Thyroid function plays a role in steroid hormone metabolism
- Understanding metabolic pathways helps to guide formation of effective treatment plans, increasing patient success

Thank You!

Questions?

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