The Next Generation of Hormone Assessment

Applying The Correct Tool for The Question

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Director of Product Innovation

Objectives:

- Distinguish the pros and cons of serum, salivary, and urinary hormone testing options
- Discuss common assumptions around hormone testing
- Recognize which tests may best serve the specific needs of the patient
- Understand best practices around hormone testing

“It ain’t what you don’t know that gets you into trouble. It’s what you know for sure that just ain’t so.”

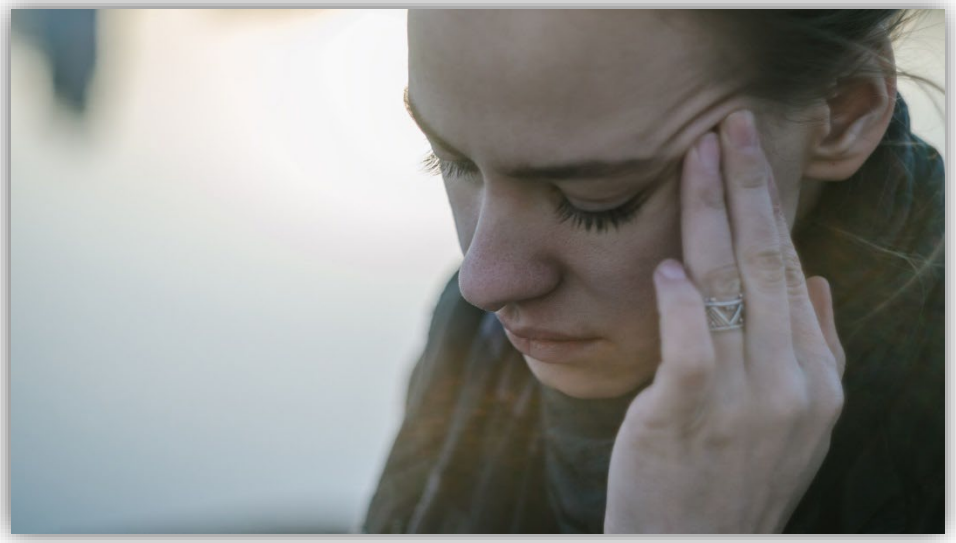
-Mark Twain

-Josh Billings

-Anonymous

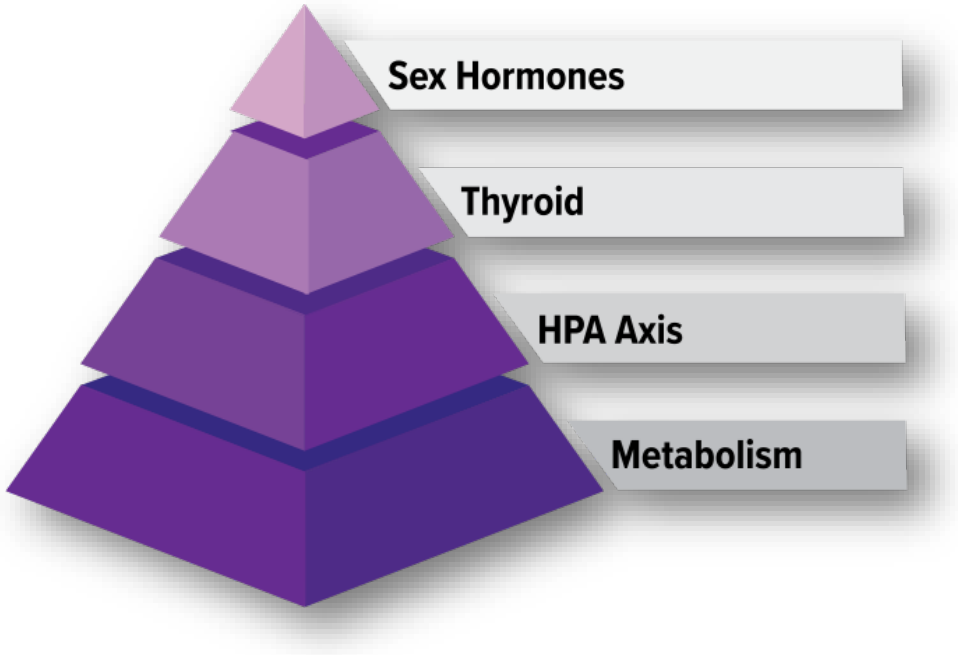
What are the Symptoms of Hormone Imbalance?

- Weight gain
- Anxiety
- Low libido
- Brain fog
- Vaginal dryness
- Hair loss
- Hot flashes
- Sleep disturbances
- Mood swings
- Breast tenderness……



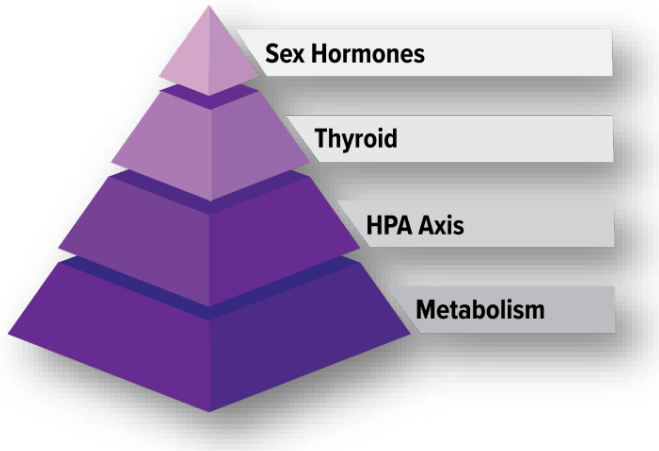
Hormones are about finding a balance…

- The list of symptoms goes on and on, testing provides greater insight
- The key is in reaching a state of balance for each individual patient
- Start slow, increase in small increments
- Monitor the clinical picture



Metabolic Flexibility

- Metabolic health is all about energy management
- Metabolic health is also about adaptability
  - The body was not designed to operate on the same percentages of macronutrients all the time
  - The body likes stress, it makes it more adaptable
- Key markers for metabolic health
  - TG/HDL ratio
  - Fasting insulin
  - Uric Acid
  - Inflammatory and Oxidative Stress Markers

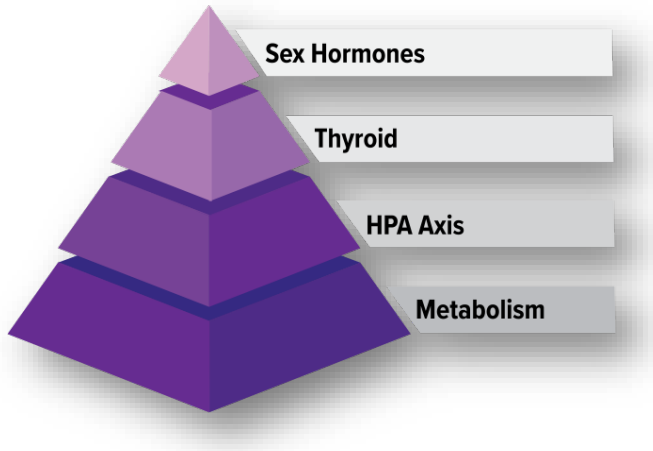


HPA Axis and Adrenal Function

- When you think of ”poor adrenal function” what do you think of?

Stress

- What is stress?
  - Stress = life events that are outside what our daily expectations have prepared us for
  - Inflammation
  - Infection

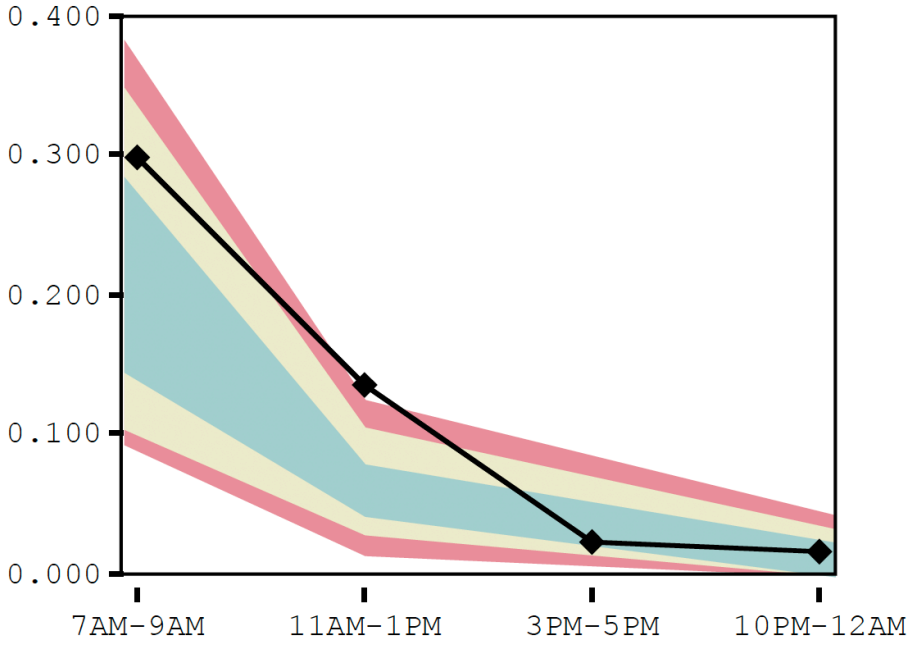


Routine

…As what’s the consequence of poor routine?

Anabolic/Catabolic Imbalance

- Stress signals lead to catabolic physiolog
  - Osteopenia
  - Sarcopenia
  - Immune suppression
  - Weight gain & water retention
  - Low libido
- Androgens serve the opposite role
- Try to see the picture of anabolic/catabolic balance
  - Don’t just look at these hormones in isolation



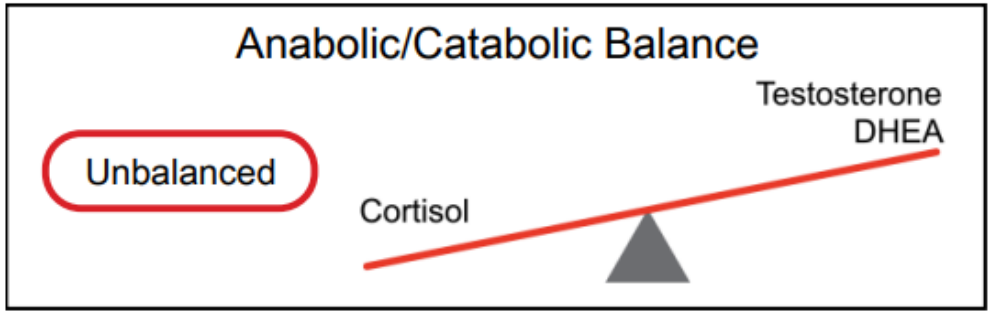
Need For HPA Axis Support

ADRENOCORTEX

2

Cortisol Curve	▼
Morning Cortisol	●
DHEA	●
DHEA:Cortisol	●

- Stress Reduction
- Mindfulness Training
- HRV Biofeedback
- Breathwork Training
- Exercise/Yoga/Tai Chi
- Herbal Adaptogens
- Lower Blood Sugar
- B-Vitamins
- Phosphoserine
- Glandulars

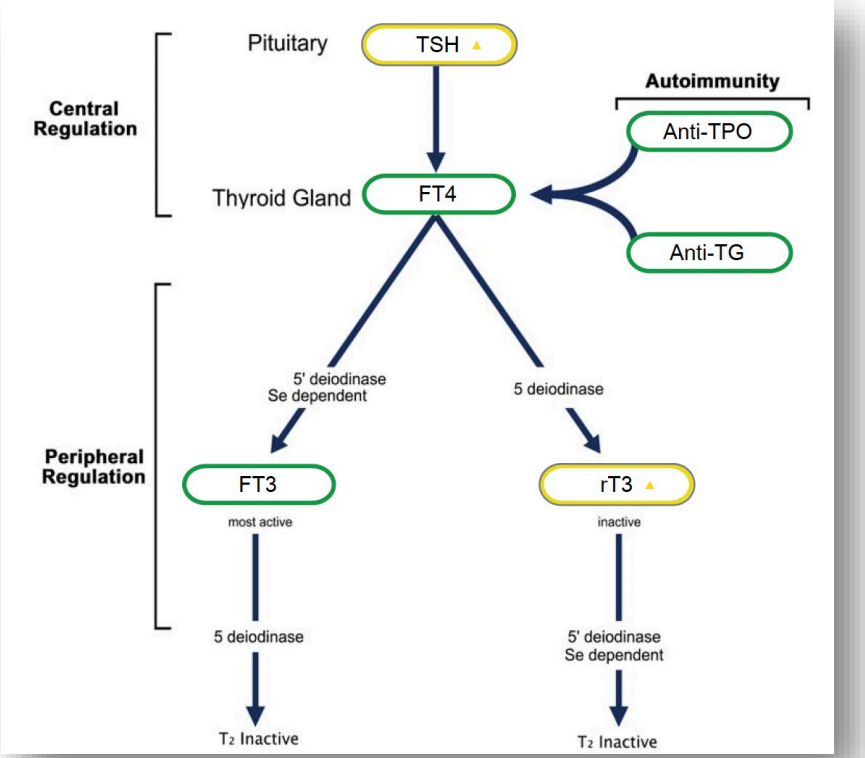


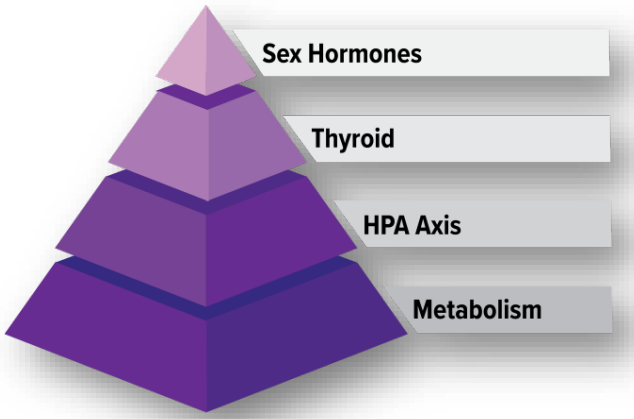
The Role of the Thyroid

- Big Picture: The thyroid gland is a cellular thermostat

- It serves as an upstream regulator of anabolic energy usage
  - Thermal regulation
  - Anabolic processes: Tissue growth and repair
  - Tissue sensitivity
  - Metabolic traffic cop

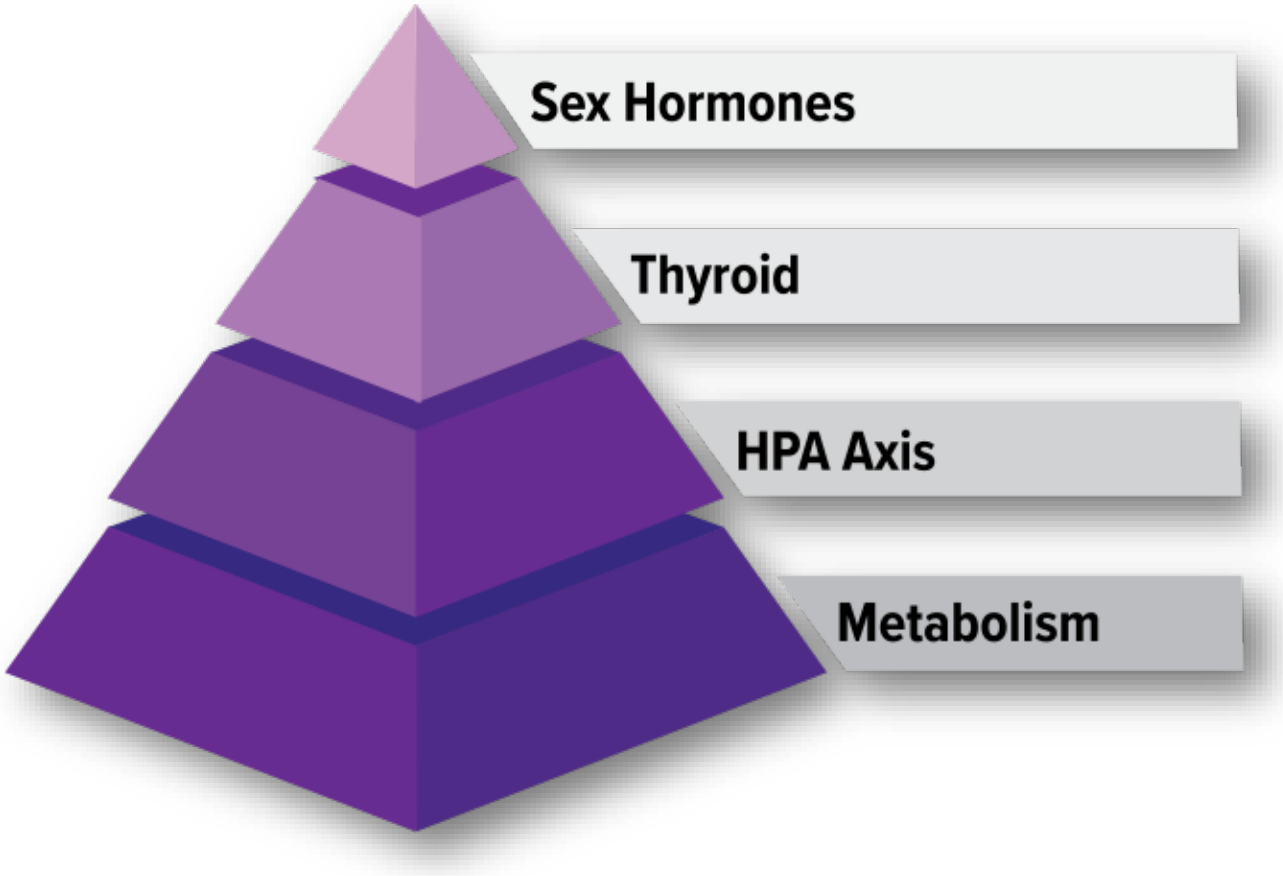
- Highly susceptible to cortisol and adrenaline



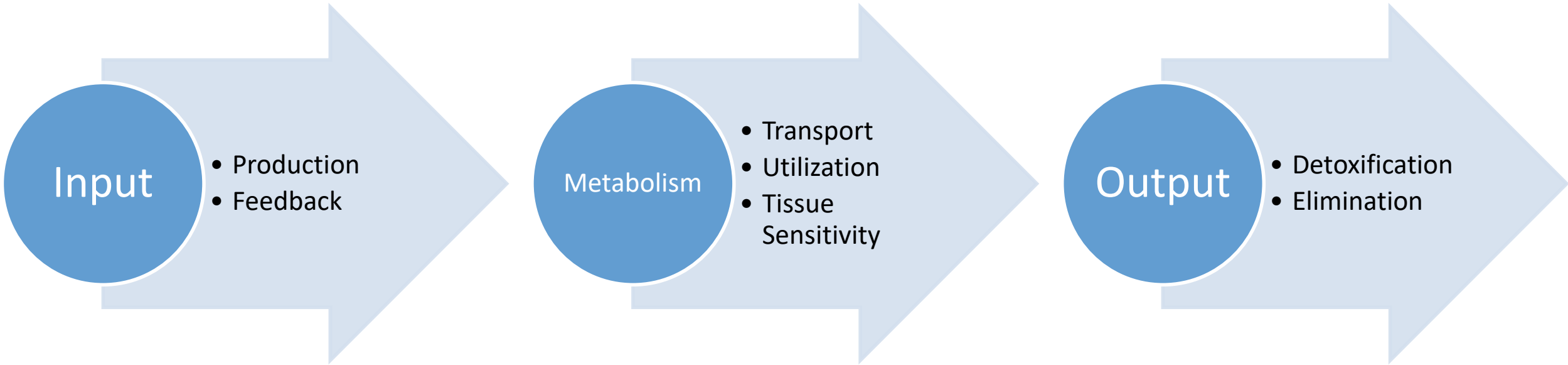


Sex Hormones

…and how to manage them!



Understanding Inputs vs. Outputs



Factors that Regulate the Hormone Cascade

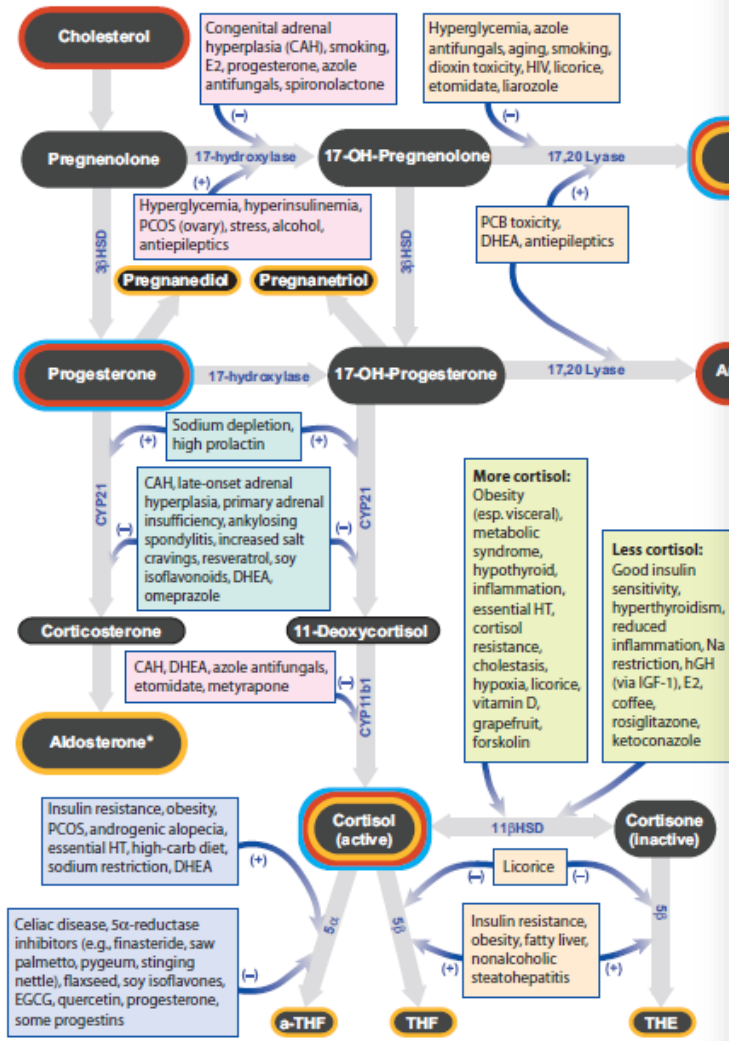
Androgens

- Insulin resistance
- Antifungals
- Smoking
- Licorice
- Alcohol
- Flax
- Phytoestrogens
- PCBs
- Inflammation
- Progestins
- HPA axis dysfunction
- Metformin

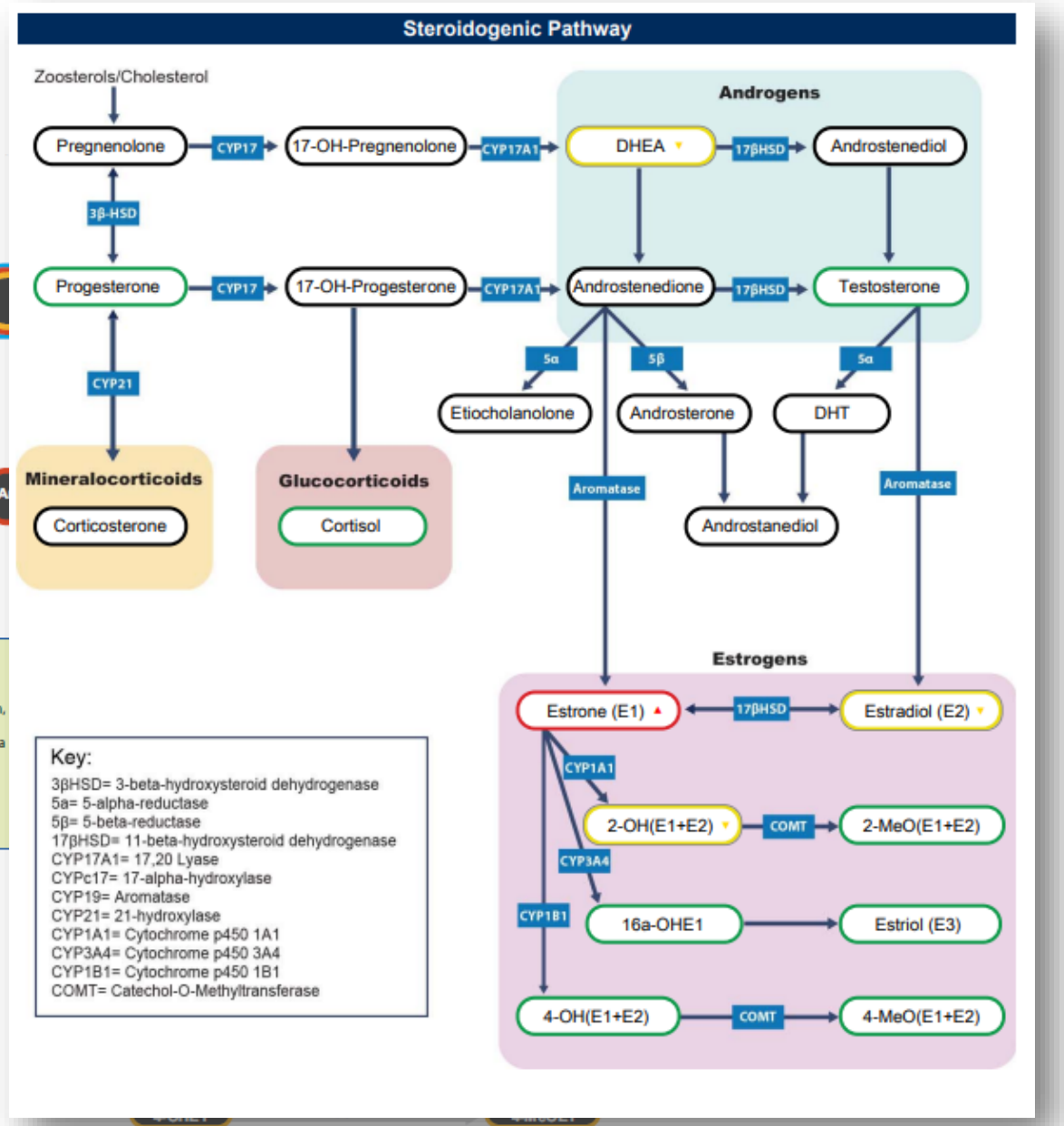
Estrogens

- Insulin resistance
- Antifungals
- Smoking
- Licorice
- Alcohol
- Flax
- Phytoestrogens
- PCBs
- Inflammation
- Caffeine
- Exercise
- Polycyclic aromatic hydrocarbons

Complex Systems



Hormones measurable by Genova Diagnostics



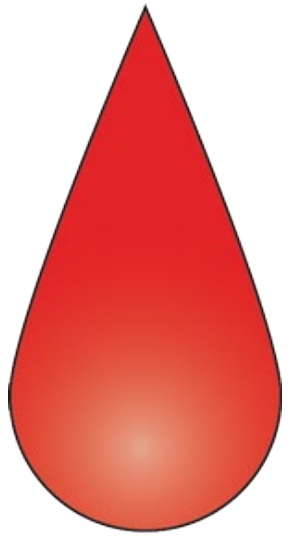
Clinical Considerations & Sample Types

- Serum
- Saliva
- Urine
- Dried Blood Spot
- Anything ChatGPT Comes Up With?

Serum Testing

Serum Testing

- Reflects circulating hormones, including bound (reserve) and un-bound (active)
- Has the most amount of literature compared to other matrices
- Important to assess binding capacity
  - Progesterone: Primarily bound by corticosteroid-binding globulin (CBG)
  - Androgens: Primarily bound by SHBG
  - Estrogens: Primarily bound by SHBG
- Albumin can bind steroids
  - However, it has low affinity for them and generally buffers major fluctuations



Hammond GL. J Endocrinol. 2016 Jul;230(1):R13-25. PMID: 27113851; PMCID: PMC5064763.

Menopause: The Journal of The North American Menopause Society
Vol. 20, No. 11, pp. 1169-1175
DOI: 10.1097/gme.0b013e31828d39a2

Percutaneous progesterone delivery via cream or gel application in postmenopausal women: a randomized cross-over study of progesterone levels in serum, whole blood, saliva, and capillary blood

Reliance on serum levels of progesterone for monitoring topical dose could lead to underestimation of tissue levels…

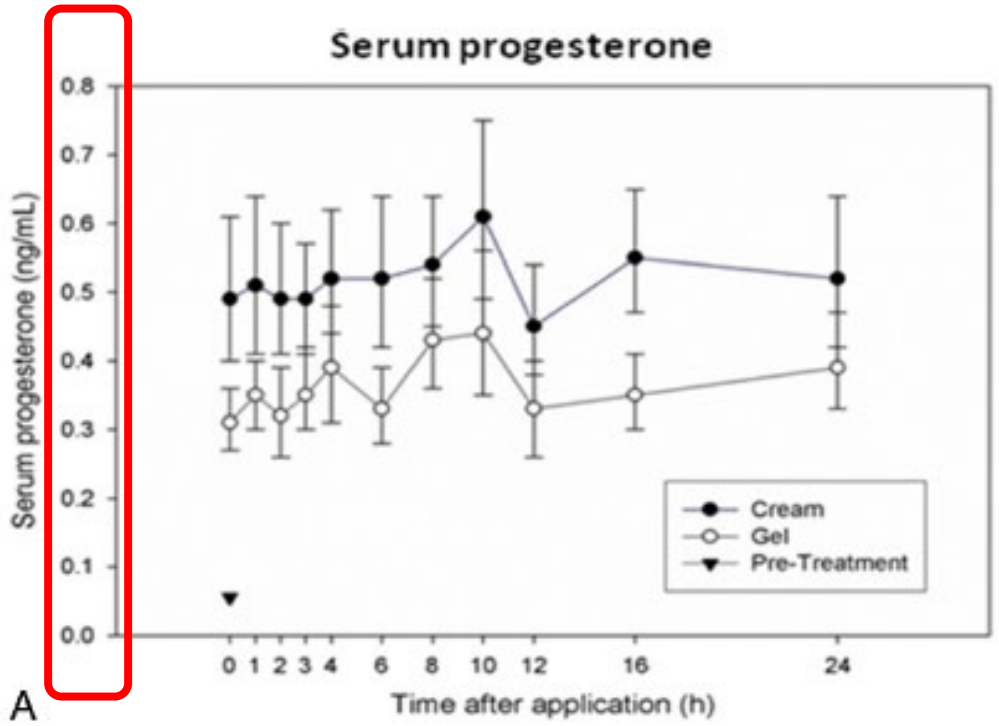
gesterone showed a peak at 1 and 6 hours after cream and gel application, respectively, and C_{max} was comparable with cream and gel. Saliva $AUC_{0\text{-}24\ h}$ was substantially higher than the corresponding area under the curve for serum or whole blood but did not differ significantly by delivery method (39.02 and 58.37 ng h mL^{-1}, $P = 0.69$). In capillary blood, C_{max} was reached at the same time (8 h) and was similar with both formulations; $AUC_{0\text{-}24\ h}$ was also similar with both formulations (1,056 ng h mL^{-1} for cream and 999 ng h mL^{-1} for gel) but was dramatically higher than the corresponding areas under the curve for venous serum and whole blood.

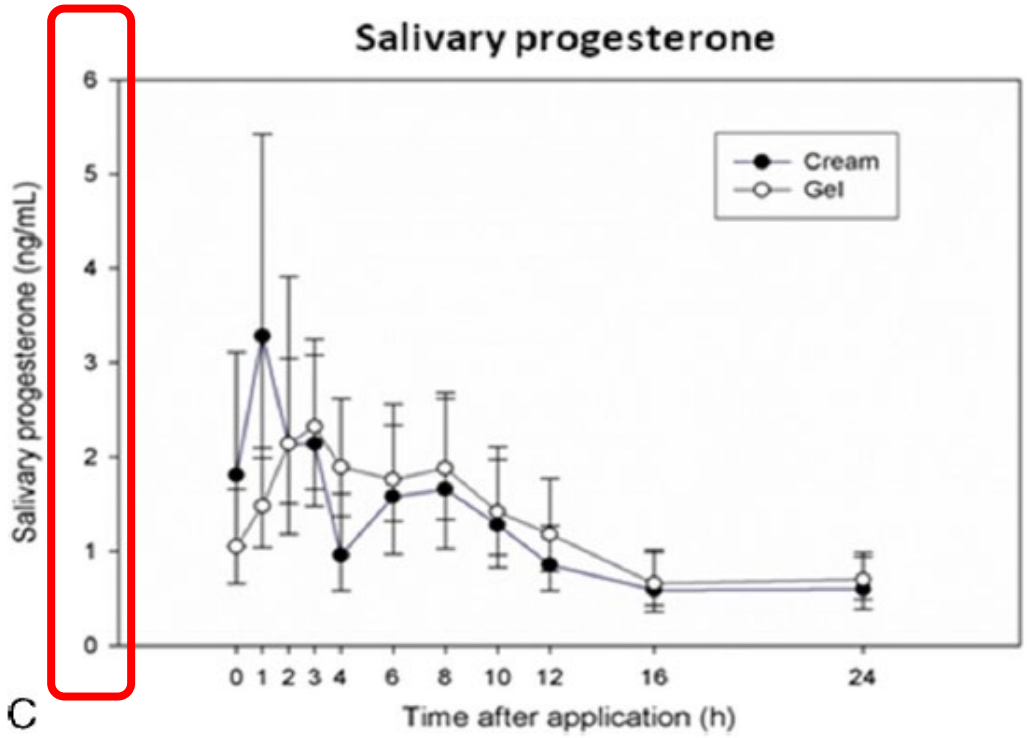
Conclusions: After application of topical progesterone, saliva and capillary blood levels are approximately 10-fold and 100-fold greater, respectively, than those seen in serum or whole blood. High capillary blood and saliva levels indicate high absorption and transport of progesterone to tissues. Reliance on serum levels of progesterone for monitoring topical dose could lead to underestimation of tissue levels and consequent overdose.

Du JY, et al. *Menopause.* 2013;20(11):1169-75.

Serum Testing and BHRT

- Historically thought to not reflect any forms of BHRT very well (under-represented)
- Topical Progesterone:





Single-Dose Limitations

- The raw concentrations of ANY measurable analyte must be interpreted in the context of the matrix
  - It doesn't imply that you must only measure analytes in the highest circulating pool
    - Only 1-2% of serotonin production occurs in the brain
  - Changes in concentration must be viewed through the lens of homeostasis
    - Serum magnesium and potassium have very small windows of allowable alteration
    - RBC magnesium and potassium have much larger windows of alteration

Single-Dose Limitations

- Bottom line:
  - Don’t think in terms of best and worst
  - Think in terms of what each measurement is telling you

Does Topical Progesterone Show Up in Serum?

British Journal of Obstetrics and Gynaecology
June 2000, Vol 107, pp. 722–726

A study to evaluate serum and urinary hormone levels following short and long term administration of two regimens of progesterone cream in postmenopausal women

Table 3. Maximum progesterone concentrations from 0–24 hours (C_{max}), area under the progesterone curve from 0–24 hours ($AUC_{0\text{-}24}$) and pregnanedial-3-glucuromide (P3G) by day. Values are given as mean (95% CI).

	Day 1	Day 42
C_{max} (nmol/L)		
20 mg twice daily	0·7 (0·1, 1·2)	5·8 (4·1, 7·4)
40 mg daily	0·8 (0·3, 1·3)	4·7 (2·2, 7·3)
TOTAL	0·7 (0·4, 1·1)	5·3 (3·9, 6·6)
$AUC_{0\text{-}24}$ (nmol×h/L)		
20 mg twice daily	3·1 (0·5, 5·6)	55·5 (33·5, 77·6)
40 mg daily	6·4 (1·6, 11·2)	48·5 (26·5, 70·5)
TOTAL	4·7 (2·2, 7·2)	52·2 (38·1, 66·3)

Conclusions Transdermal progesterone (40 mg) per day for 42 days causes a small increase in serum progesterone concentration, although there is wide variation. Whether such levels are of clinical benefit remains to be seen.

CONCLUSION

Very little progesterone could be detected in the serum following a single application of cream, but progesterone concentrations following 42 days' administration had increased, demonstrating that systemic absorption of the progesterone had occurred, the mean maximum progesterone concentration being 5·3 nmol/L.

Does Topical Progesterone Show Up in Serum?

J Pharm Pharmaceut Sci (www.cspsCanada.org) 13(4) 626 - 636, 2010

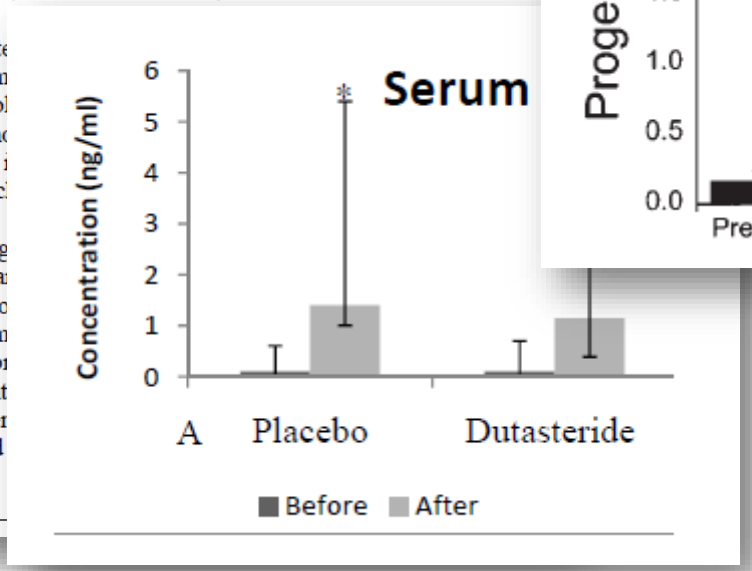
Transdermal Delivery of Bioidentical Progesterone Using Dutasteride (A 5α-Reductase Inhibitor): A Pilot Study

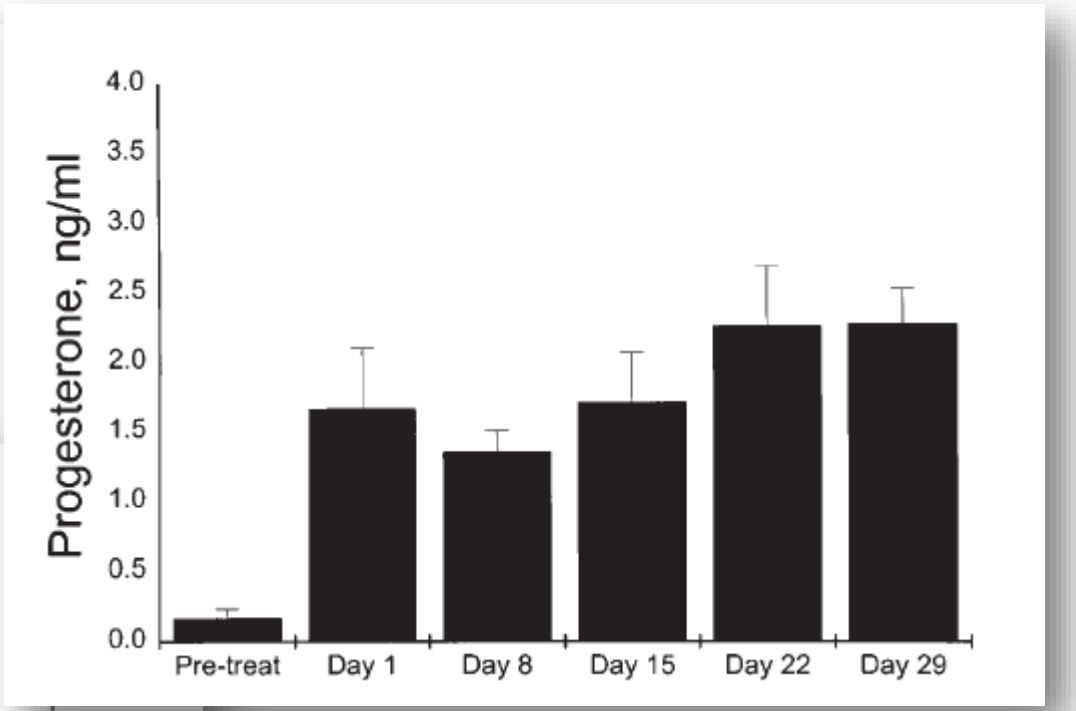
Sara Zargar-Shoshtari[a], Hannaneh Wahhabaghei[b], Abdolrasoul Mehrsai[b], Jingyuan Wen[a], Raid Alany[a,c]

[a] Drug Delivery Research Unit (2DRU), School of Pharmacy, University of Auckland, Auckland, New Zealand.
[b] Urology Research Centre, Sina Hospital, School of Medical Sciences, University of Tehran, Tehran, Iran.
[c] Current Affiliation: School of Pharmacy and Chemistry, Kingston University London, Surrey, United Kingdom.

Received, August 26, 2010; Revised, October 1, 2010; Accepted December 29, 2010; Published December 29, 2010.

ABSTRACT – Purpose. The bioavailability of transdermal progeste
can be attributed to transdermal metabolism by 5α-reductase enzym
evaluate the effect of dutasteride, an inhibitor of these metabol
transdermally delivered progesterone. **Method.** Twenty postmen
Hormone levels greater than 40IU/L were recruited to take part
allocated to either dutasteride (n=10) or placebo (n=10) groups. Eac
cream or dutasteride cream (2 mg/g) to the right arm for 15 days.
progesterone (80 mg/g) or progesterone dutasteride cream (80 mg/g
30, blood and saliva samples were collected over a 12-hour period a
Results. The baseline serum progesterone concentration on day zero
progesterone levels increased significantly ($p < 0.05$) to 1.40 ng/m
dutasteride groups, respectively. Salivary progesterone concentratio
ng/ml to 2.9 ng/ml. On average, salivary progesterone concent
Conclusion. The average serum and salivary progesterone concer
higher in the dutasteride group, but no significant difference could
enzyme is unlikely to affect the bioavailability of progesterone.





Serum Tests and Tissue Levels

- Serum progesterone does not increase to premenopausal luteal levels with topicals
  - Rarely gets over 4ng/mL, whereas luteal levels can be between 10-20ng/mL
  - However, this same dosing (or even lower) of progesterone shows antiproliferative endometrial effects in studies
    - No serum levels were given in these studies
    - Oral progesterone does correlate well with saliva
- Another counterpoint:
  - Levels of progesterone found in saliva appear to increase rapidly following application and return to baseline in 12-24 hours
  - These levels do come closer to what is seen during regular luteal cycles

Androgens

- Overall, tend to be more lipophilic than estrogens
  - This affects how they travel and are distributed in the body
  - Bind tightly to sex-hormone binding globulin (SHBG) and less so to albumin
- Testosterone
  - <5% of testosterone in the serum is unbound, or “free testosterone”
  - Levels decrease with age
  - When there are consistent levels of binding proteins, the total testosterone is relatively reliable
- Topical Testosterone and Serum Measurements
  - Likely best to test within 8 hours of most recent dose

Oral Androgen HRT and Serum

- Serum levels correlate very strongly with saliva both intraday and longitudinally
  - The biggest variability occurred at peak levels in saliva
- DHEA and DHEAS correlate well in serum

Estrogens (E1, E2, E3) and Serum

CLIMACTERIC 2005;8(Suppl 1):3–63

Pharmacology of estrogens and progestogens: influence of different routes of administratio

H. Kuhl

Department of Obstetrics and Gynecology, J. W. Goethe

Table 6 Ratio between the serum concentrations of estrone and estradiol in premenopausal and postmenopausal women as well as in postmenopausal patients treated with estradiol, depending on the route of administration. The values do not reflect the efficacy

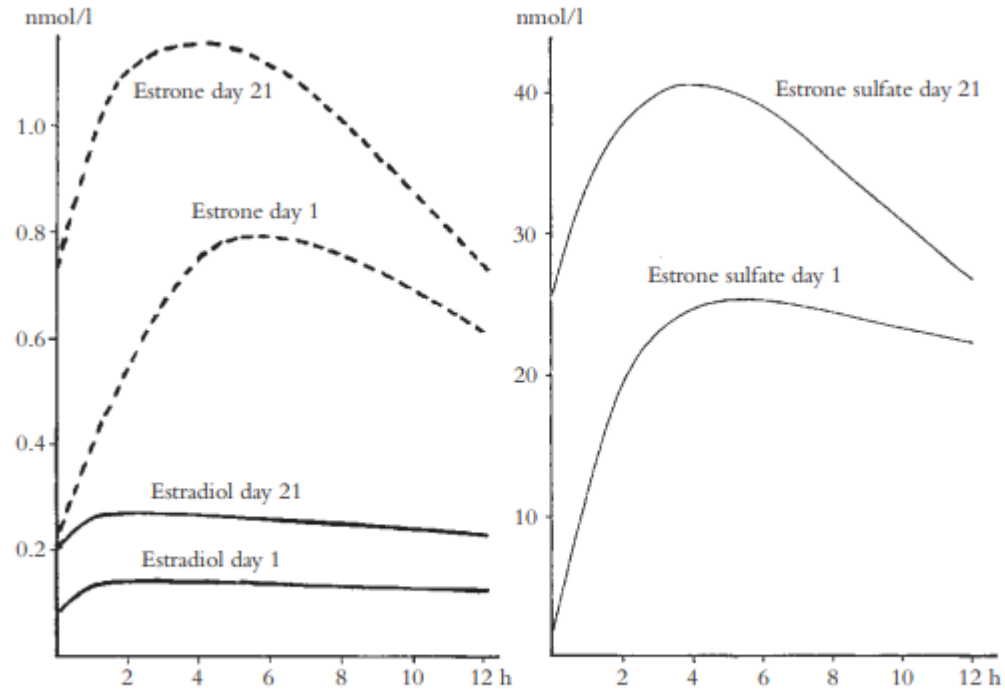
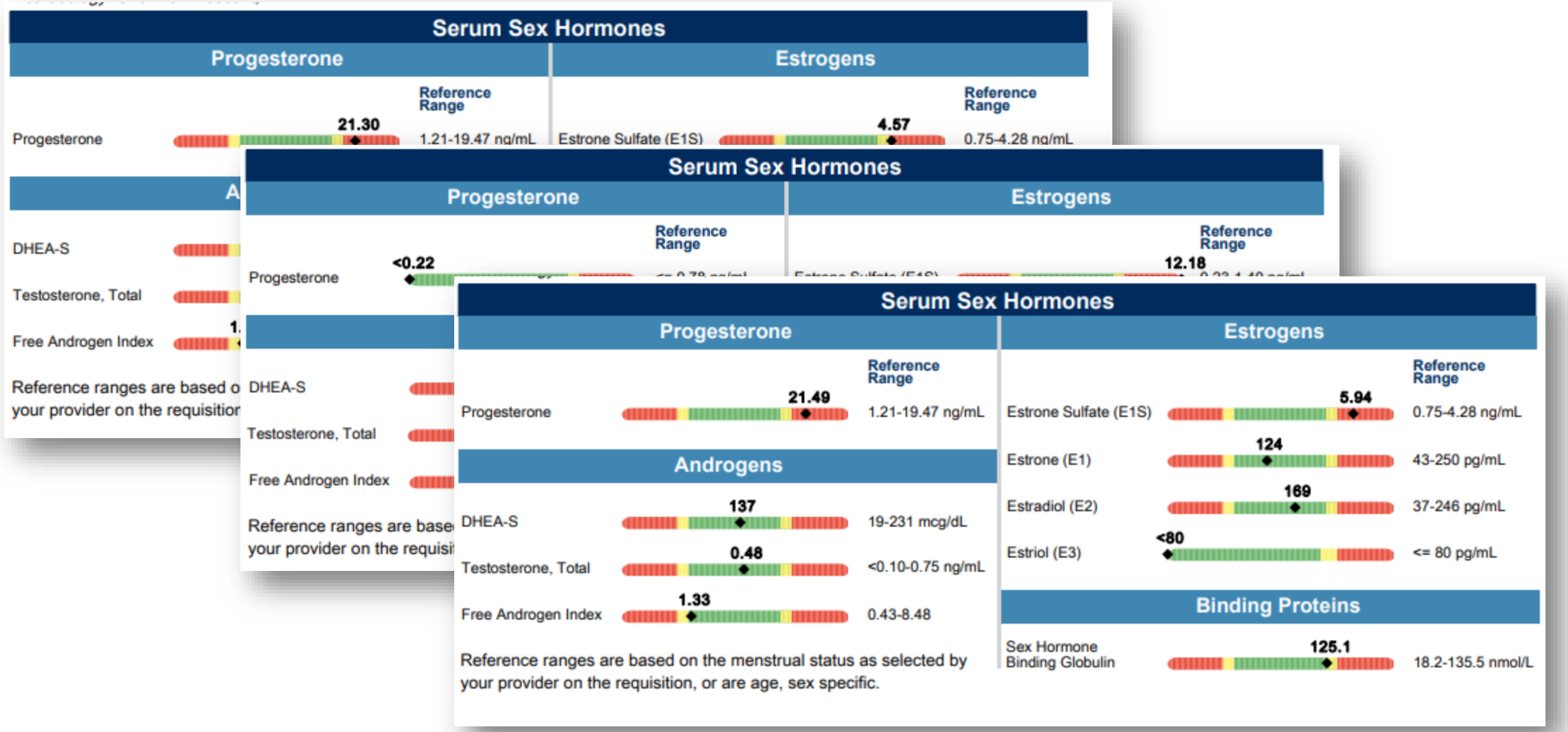


Figure 5 Serum concentrations of estradiol-17β, estrone and estrone sulfate on days 1 and 21 of treatment with 2 mg estradiol valerate (after Aedo *et al.*, 1990[30])

Serum Results of Patients on BHRT

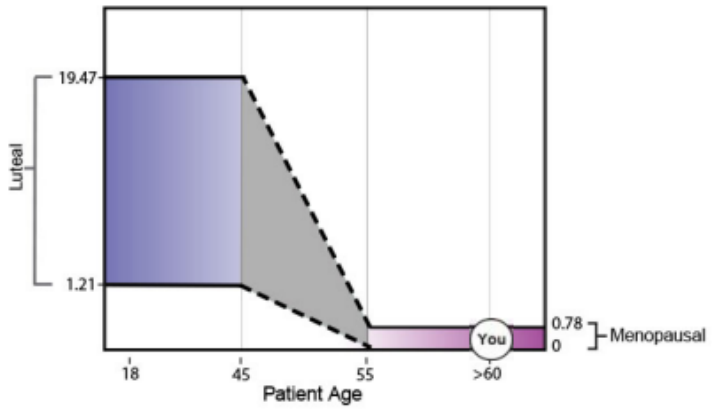


Example of Serum Hormones Across Age

Serum Sex Hormones

Progesterone

Progesterone



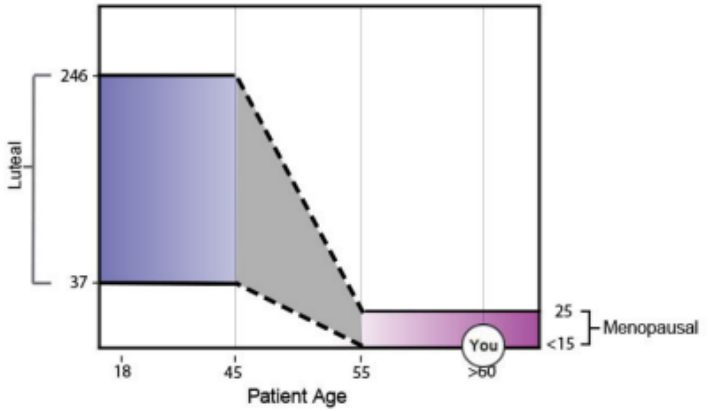
		Reference Range
Progesterone	0.32	See Chart Below

Androgens

DHEA-S	95	12-133 mcg/dL
Testosterone, Total	0.22	<0.10-0.75 ng/mL
Free Androgen Index	1.77	0.32-6.73

Estrogens

Estradiol (E2)



		Reference Range
Estradiol (E2)	<15	See Chart Below
Estrone (E1)	91	18-63 pg/mL
Estriol (E3)	<80	<= 80 pg/mL

Binding Proteins

Sex Hormone Binding Globulin	43.2	16.8-125.2 nmol/L

Need For Sex Hormone Support

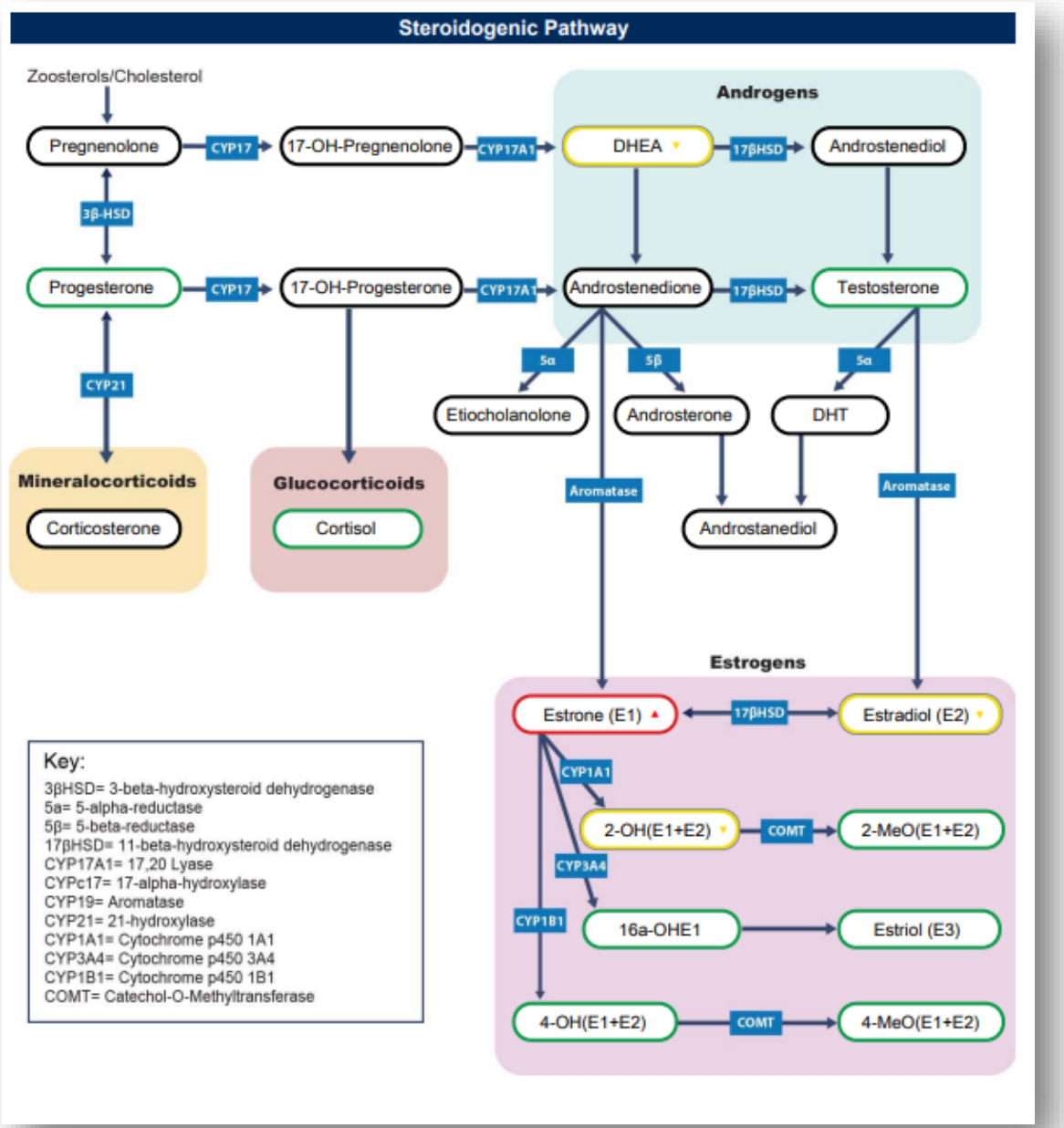
SEX HORMONES

4

- Estrone ▲
- Estradiol ▽
- Progesterone ●
- Testosterone ●

- Address Thyroid Imbalance
- Address HPA Axis
- Phytoestrogens (for estrogen support)
- Phytoandrogens (for testosterone support)
- Consider Glandulars
- Consider Hormone Precursors
- Consider BHRT

Look at the Whole Picture of the Hormone Cascade



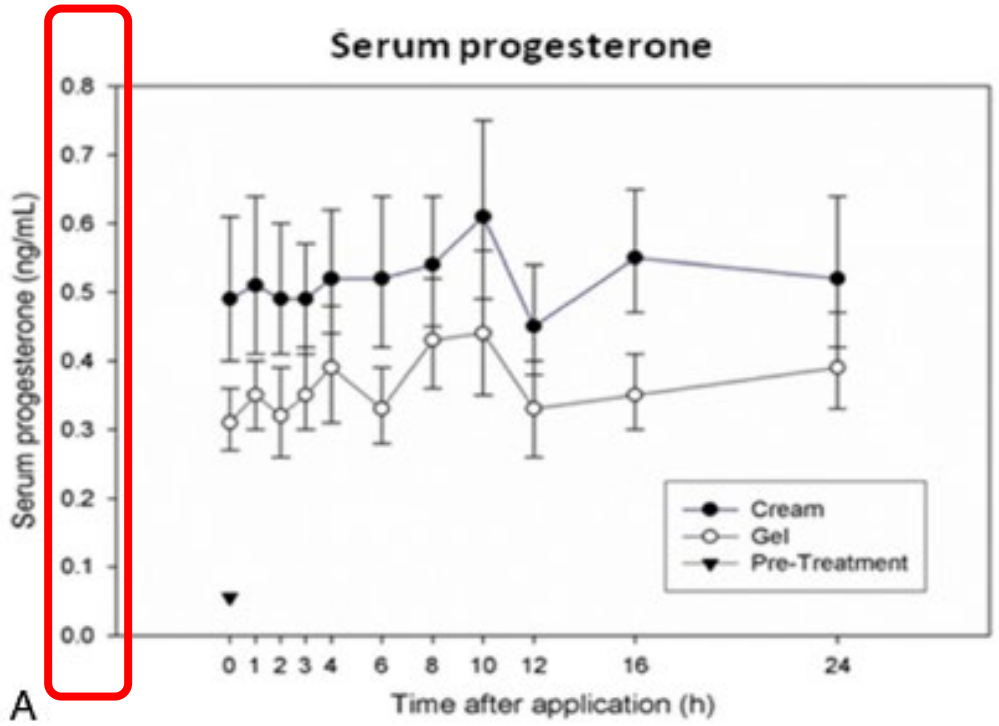
Salivary Testing

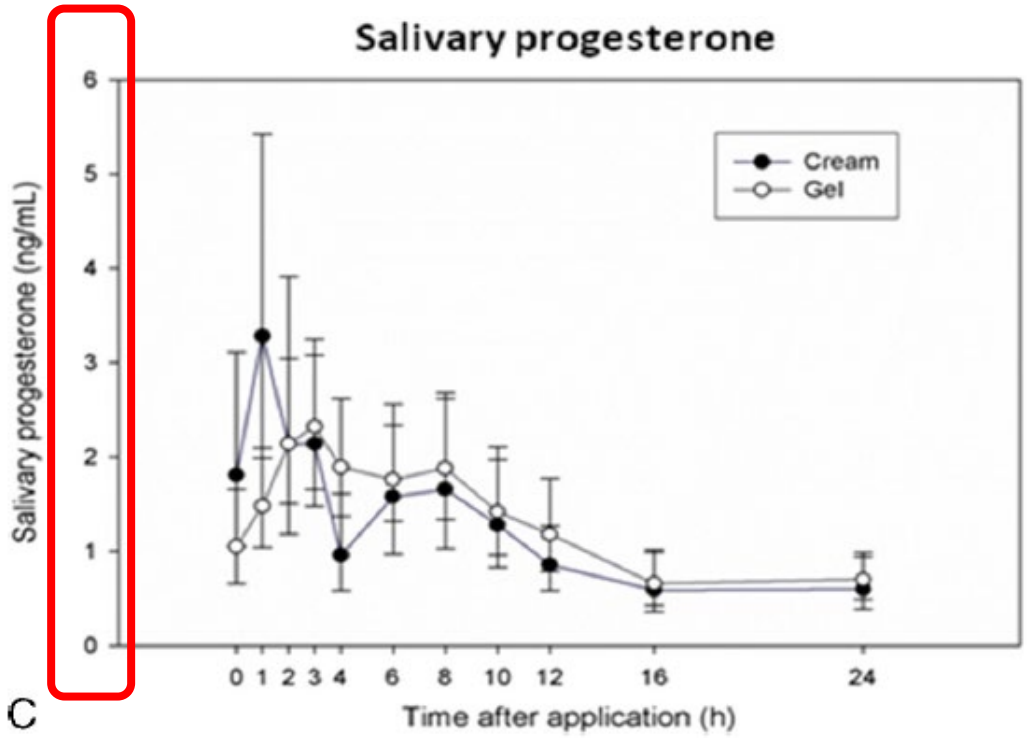
When is Salivary Testing More Useful?

- Unbound (bioavailable) fraction of the hormone
- Single or sequential samples collected over the day or month
- Assess diurnal patterns of hormones
  - Melatonin and cortisol
- Can be used to establish baseline levels pre-BHRT
- Monitor BHRT? (next slide)
- Special Precautions
  - Gingivitis (bleeding gums) can produce elevated hormone levels
  - Should not be used in conjunction with sublingual hormone treatments
  - Transdermal HRT can sometimes produce abnormally high levels

Salivary Testing and BHRT

- Assumption: Since salivary values tend to reflect those during menstrual phases, this means that the sample type is more “accurate”





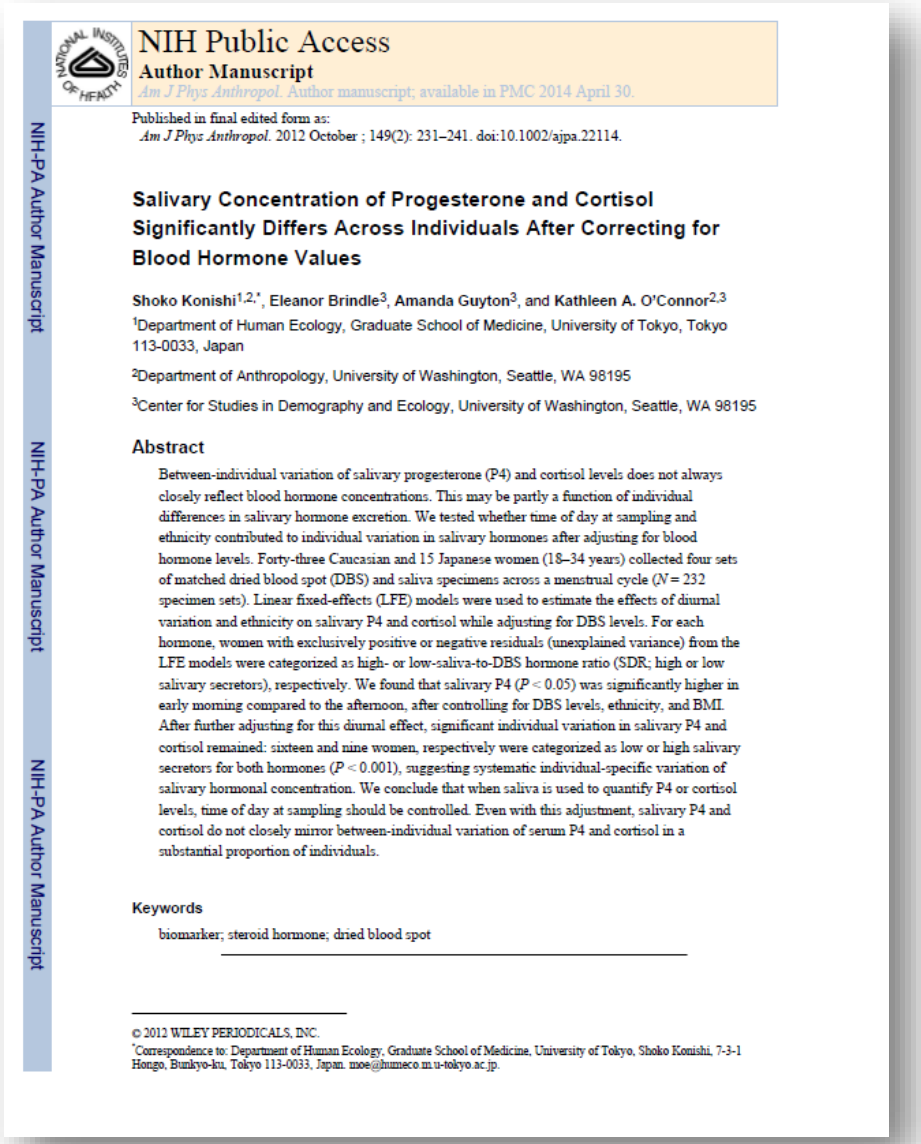
Controlling the Variables

- Time since last dose has a very large impact on the interpretation of findings
  - This is because of the dramatic fluctuation following the last dose
  - Must control for this by limiting recent exposure to the hormone
- Location of application: Thigh, Arm, Axillae
- Contamination
  - Most research articles control for this by having the participants apply topical hormones with nitrile gloves
- Individual differences in secretion of hormones into saliva!

Saliva-to-Blood Secretor Differences

- This study demonstrates that when you control for dried blood spot levels, there is tremendous variability in how much hormone a person secretes into their saliva!
  - Is it because DBS doesn't reflect hormone status?
  - Not likely! These participants are not supplementing with BHRT!

- This suggestion of "high-secretors" must be considered when results don't match the clinical picture



Published in final edited form as:
Am J Phys Anthropol. 2012 October ; 149(2): 231–241. doi:10.1002/ajpa.22114.

Salivary Concentration of Progesterone and Cortisol Significantly Differs Across Individuals After Correcting for Blood Hormone Values

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Abstract

Between-individual variation of salivary progesterone (P4) and cortisol levels does not always closely reflect blood hormone concentrations. This may be partly a function of individual differences in salivary hormone excretion. We tested whether time of day at sampling and ethnicity contributed to individual variation in salivary hormones after adjusting for blood hormone levels. Forty-three Caucasian and 15 Japanese women (18–34 years) collected four sets of matched dried blood spot (DBS) and saliva specimens across a menstrual cycle ($N = 232$ specimen sets). Linear fixed-effects (LFE) models were used to estimate the effects of diurnal variation and ethnicity on salivary P4 and cortisol while adjusting for DBS levels. For each hormone, women with exclusively positive or negative residuals (unexplained variance) from the LFE models were categorized as high- or low-saliva-to-DBS hormone ratio (SDR; high or low salivary secretors), respectively. We found that salivary P4 ($P < 0.05$) was significantly higher in early morning compared to the afternoon, after controlling for DBS levels, ethnicity, and BMI. After further adjusting for this diurnal effect, significant individual variation in salivary P4 and cortisol remained: sixteen and nine women, respectively were categorized as low or high salivary secretors for both hormones ($P < 0.001$), suggesting systematic individual-specific variation of salivary hormonal concentration. We conclude that when saliva is used to quantify P4 or cortisol levels, time of day at sampling should be controlled. Even with this adjustment, salivary P4 and cortisol do not closely mirror between-individual variation of serum P4 and cortisol in a substantial proportion of individuals.

Keywords

biomarker; steroid hormone; dried blood spot

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The Good News!

- Participants showed tremendous consistency in how much hormone they secreted into saliva
  - This means you should be able to track them over time fairly easily
  - Control for time of day and application method

- If a patient has very high salivary levels, they might not be a good candidate for salivary hormone BHRT monitoring
  - This goes potentially for topical and oral
  - We tend to see it more commonly with topical hormone users

Saliva and Tissue Levels

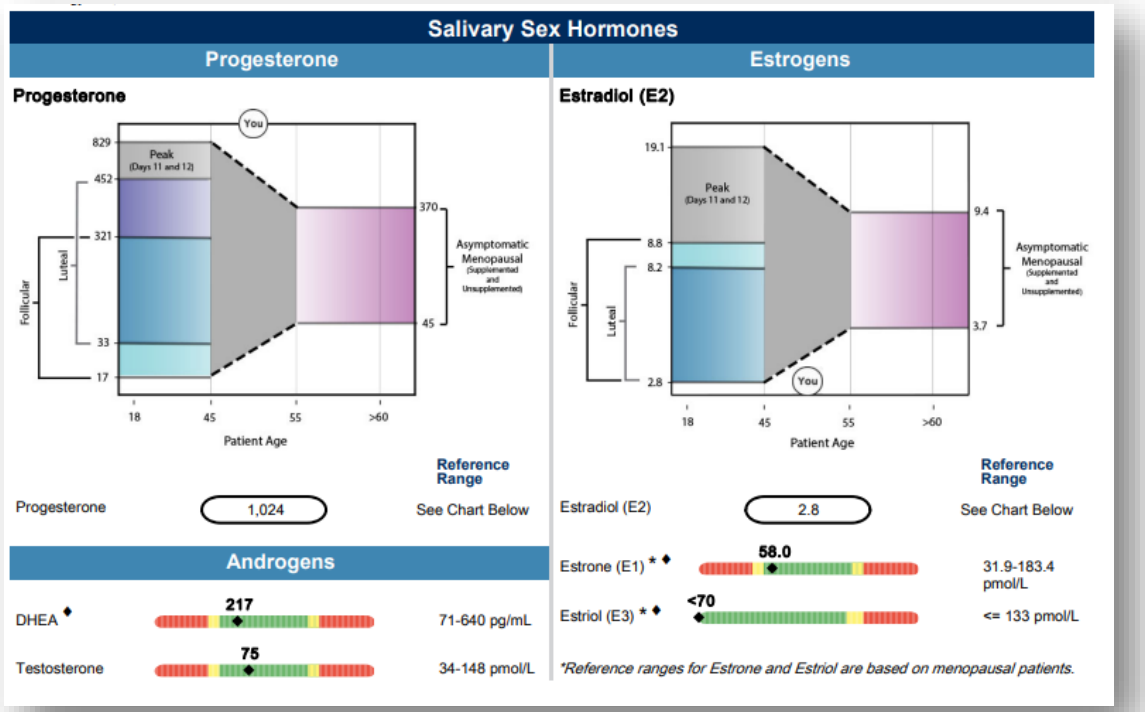
- The logic follows:
  - Physiologic doses result in symptomatic improvement and histological changes in tissues
    - From tissue biopsies
  - Physiologic doses *can* lead to salivary results that approach follicular and luteal levels
  - Therefore, salivary results = tissue levels

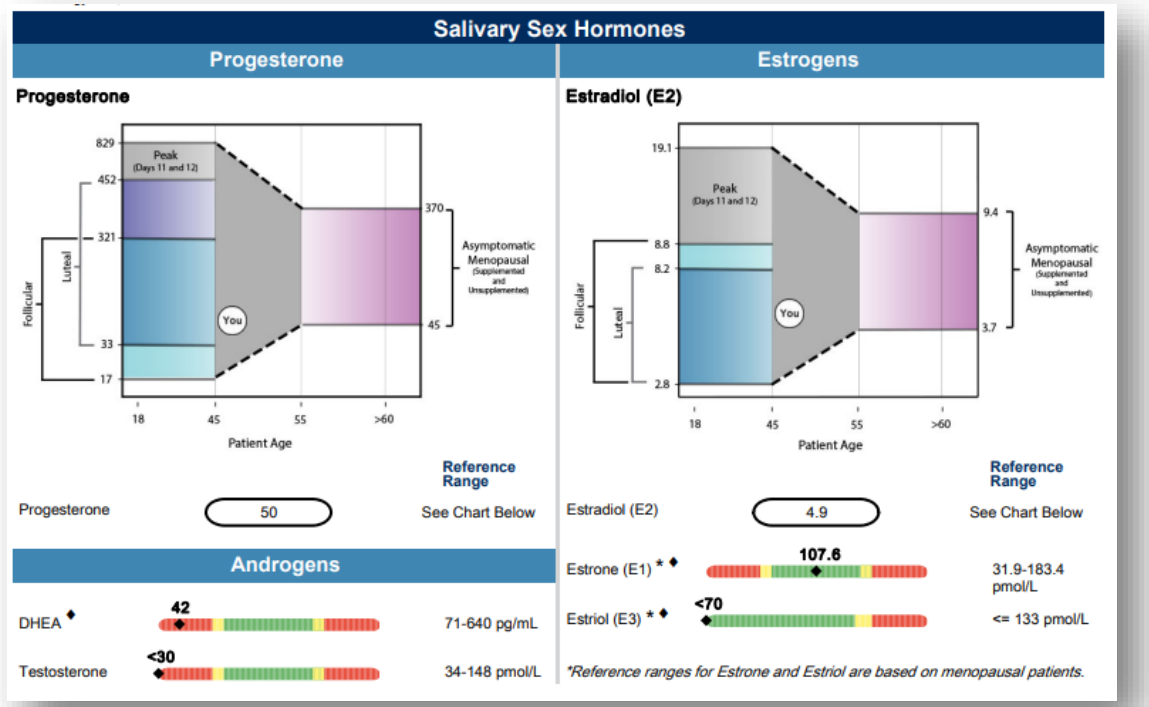
- Is this always true?
  - Differences in secretor status
  - Differences in tissue distribution/preference
  - Differences in BHRT delivery (vaginal, topical, oral)
  - Differences in solubility of each hormone (more or less lipophilic)

- *We have to always be careful about the assumptions we are making!*

Hormone Testing During Perimenopause

- Hormones rapidly fluctuate day-to-day





What Cohorts Should Be Used For Ranges?

- Population-Based Cohorts
- Questionnaire Qualified “Healthy” (asymptomatic) Patients
- Supplemented? Un-supplemented? Both

Urine Testing

Can you use Urine Testing to Monitor BHRT?

- This is currently a hotly debated topic!
- NOTE: Urine is a reflection of blood (because it is a filtrate of blood)
- Therefore, if you find blood to be unreliable when it comes to BHRT…
  - Urine must also be unreliable to track dosage, if not worse?

Table 3. Maximum progesterone concentrations from 0–24 hours (C_{max}), area under the progesterone curve from 0–24 hours (AUC_{0-24}) and pregnanedial-3-glucuromide (P3G) by day. Values are given as mean (95% CI).

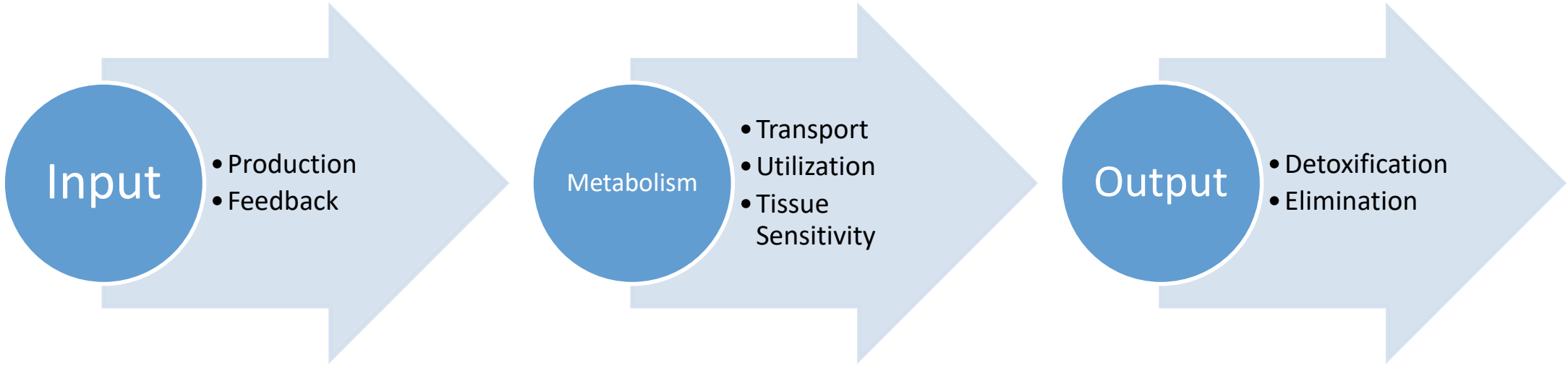
	Day 1	Day 42
C_{max} (nmol/L)		
20 mg twice daily	0·7 (0·1, 1·2)	5·8 (4·1, 7·4)
40 mg daily	0·8 (0·3, 1·3)	4·7 (2·2, 7·3)
TOTAL	0·7 (0·4, 1·1)	5·3 (3·9, 6·6)
AUC_{0-24} (nmol×h/L)		
20 mg twice daily	3·1 (0·5, 5·6)	55·5 (33·5, 77·6)
40 mg daily	6·4 (1·6, 11·2)	48·5 (26·5, 70·5)
TOTAL	4·7 (2·2, 7·2)	52·2 (38·1, 66·3)
P3G (μmol/L)		
20 mg twice daily	0·3 (0·1, 0·5)	0·7 (0·4, 1·0)
40 mg daily	0·3 (0·1, 0·5)	0·8 (0·1, 1·6)
TOTAL	0·3 (0·2, 0·4)	0·8 (0·4, 1·1)

Two sample *t* tests were used to compare the day 42 values between each dose groups for C_{max}, AUC_{0-24} and urinary pregnanediol-3-glucuronide concentration and no significant difference was observed.

Parents or Children?

- Urine Testing tells you how much of the parent hormone has been *metabolized*
  - Progesterone -> Pregnanediol
  - Androgens -> Ketosteroids
  - Estrogens -> Estrogen metabolites

- This is because very little of the parent hormones are excreted in the urine intact



Urine Testing and Topical BHRT

- Urine hormone levels represent excreted levels
- Therefore, if the urine levels are robust, there is a concern around tissue saturation
- If the levels are moderate or low, interpretation may be more difficult
  - We don't know whether this is because of dose or because sluggish detoxification and elimination

- Method of Testing
  - 24-Hour: always the best method as it captures total daily output
  - First-morning void or spot-urine: always assuming

What are the Pro's of Urine Testing?

- Urine testing gives you insight into how hormones are being detoxified

- Lots of valuable clinical insight with your BHRT patients
  - Estrogen detoxification and risk assessment
  - Potential dihydrotestosterone (DHT) production
  - Total androgen vs corticosteroid balance (anabolic/catabolic balance)

A Common Finding on BHRT Urine Results

Estrogen Metabolism

Urine Estrogens

		Reference Range
Estrone (E1) ◆	31.4	2.0-26.2 mcg/g Creat.
Estradiol (E2)	19.0	0.6-11.2 mcg/g Creat.
Estriol (E3) ◆	16.3	0.6-19.9 mcg/g Creat.

Enzyme Activity

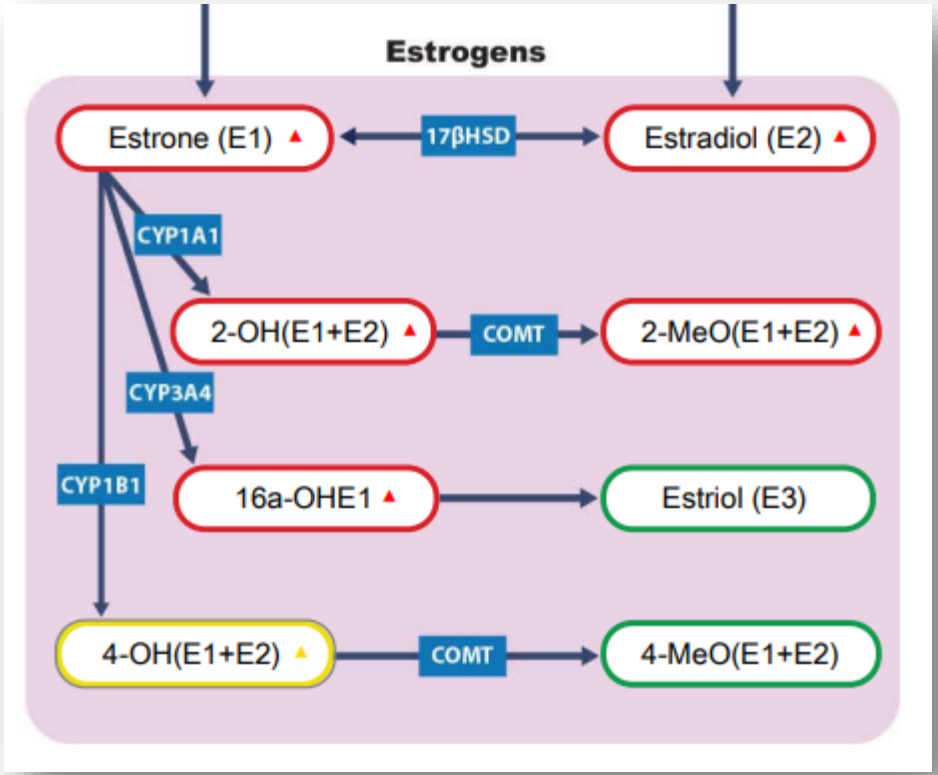
2-OH(E1+E2)/ 16α-OHE1 Ratio	4.1	0.3-13.7
Methylation Activity ◆ 2-OH/2-MeO Ratio	4.4	1.6-10.7

Phase 1 Estrogen Metabolites

		Reference Range
2-Hydroxyestrone+ 2-Hydroxyestradiol 2-OH(E1+E2)	53.5	1.3-36.3 mcg/g Creat.
16α-Hydroxyestrone 16a-OHE1	13.1	0.5-8.9 mcg/g Creat.
4-Hydroxyestrone+ ◆ 4-Hydroxyestradiol 4-OH(E1+E2)	5.6	<= 5.9 mcg/g Creat.

Phase 2 Estrogen Metabolites

2-Methoxyestrone+ ◆ 2-Methoxyestradiol 2-MeO(E1+E2)	12.2	0.2-8.6 mcg/g Creat.
4-Methoxyestrone+ ◆ 4-Methoxyestradiol 4-MeO(E1+E2)	<dl	<= 1.0 mcg/g Creat.



Phase 1 Estrogen Metabolites

- **2-OH (E1+E2**)- Little estrogen receptor binding, blocks action of potentially carcinogenic estrogens, seen as the safe metabolite, but must be methylated
- **16-OH (E1) -** Has full estrogenic activity, stimulates estrogen receptors, and is associated with an increased risk of breast cancer
- **4-OH (E1+E2) -**This metabolite can be oxidized rather than phase II conjugated; oxidation leads to the production of the 3,4 quinone metabolite that can create DNA adducts (damage), increasing the risk of breast cancer
  - Glutathione conjugation is known to reduce the damage to DNA

Always Compare the Good, Bad, and Ugly

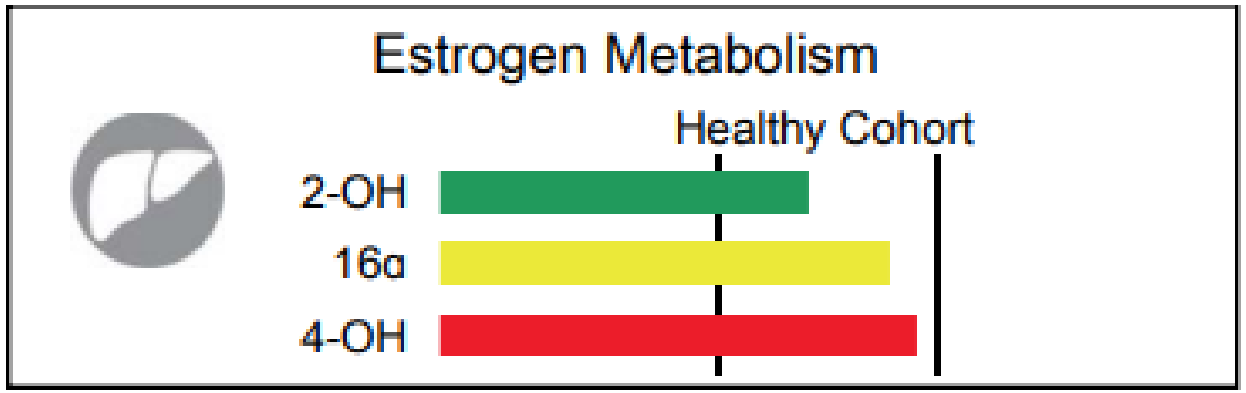
Need For Detoxification Support

ESTROGEN METABOLISM

7

2-OH-E1/E2	▲
4-OH-E1/E2	△
2/16 Ratio	●
Methylation Activity	●

- Methylation Support: B-Vitamins, Mg, Betaine
- Cruciferous vegetables, berries, rosemary
- Soy isoflavones, DIM, I3C
- Bioflavanoids, Glutathione
- Reduce sugar, stress, environmental toxicity
- Reduce adiposity
- Physical activity



Urine Hormones Summary

Urine hormone testing is a useful diagnostic tool for:

- Assessing risk for estrogen metabolism and providing useful data in designing a protocol for nutritional intervention
- Providing specific data regarding methylation activity
- Examining the role of stress on hormone metabolism
- Focusing on the parent estrogen's phase I and II metabolites

- Method of collection must be considered:
  - Hormone excretion is not linear

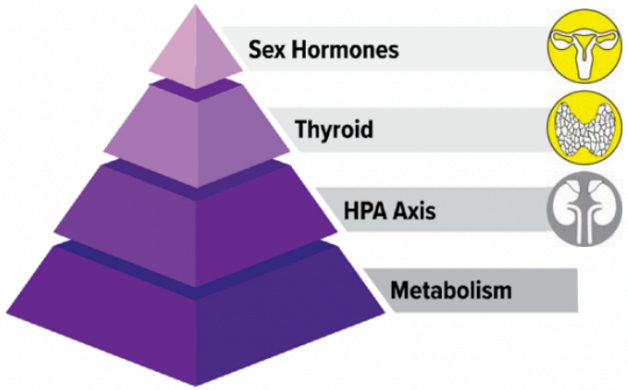
So….wait? What do I do?

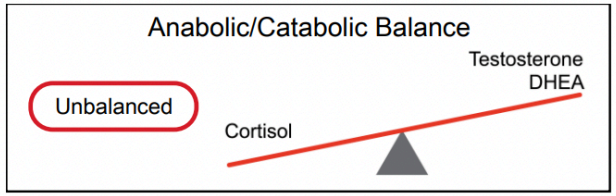
- There is no perfect hormone evaluation; no single test for all circumstances

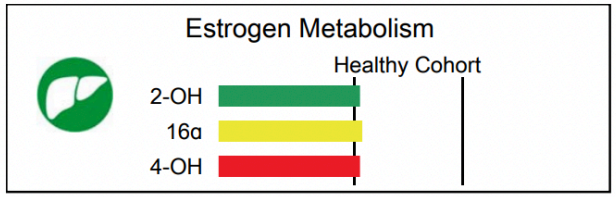
- It’s important to always think about…what do I want to know?
  - Is my patient suffering from andropause or menopausal symptoms?
  - Is my BHRT therapy being metabolized in a healthy way?
  - Do I need to alter my patient’s topical hormone dose?

- These are all different questions that require different approaches

Results Overview







Functional Imbalance Scores

Key (<2) : Low Need for Support (2-3) : Optional Need for Support (4-6) : Moderate Need for Support (7-10) : High Need for Support

	Need For HPA Axis Support	Need For Thyroid Support	Need For Sex Hormone Support	Need For Detoxification Support
	ADRENOCORTEX	THYROID	SEX HORMONES	ESTROGEN METABOLISM
	2	4	4	1
Biomarkers	Cortisol Curve ▼ Morning Cortisol ● DHEA ● DHEA:Cortisol ●	TSH △ rT3 △ FT3 ● Thyroid Antibodies ●	Estradiol ▲ Testosterone ▼ Progesterone ● Estrone ●	2-OH-E1/E2 ▽ Methylation Activity ▽ 4-OH-E1/E2 ● 2/16 Ratio ●
Therapeutic Support Options	• Stress Reduction • Mindfulness Training • HRV Biofeedback • Breathwork Training • Exercise/Yoga/Tai Chi • Herbal Adaptogens • Lower Blood Sugar • B-Vitamins • Phosphoserine • Glandulars	• Minerals: Se, Zn, Iron • Tyrosine • Adequate Iodine • Stress Reduction • Reduce Environmental Exposures • Antioxidant Support • Assess Medications • Smoking Cessation • Consider Thyroid HRT	• Address Thyroid Imbalance • Address HPA Axis • Phytoestrogens (for estrogen support) • Phytoandrogens (for testosterone support) • Consider Glandulars • Consider Hormone Precursors • Consider BHRT	• Methylation Support: B-Vitamins, Mg, Betaine • Cruciferous vegetables, berries, rosemary • Soy isoflavones, DIM, I3C • Bioflavanoids, Glutathione • Reduce sugar, stress, environmental toxicity • Reduce adiposity • Physical activity

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The Lab Report

www.tenetsofhealth.com

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Thank You!!!