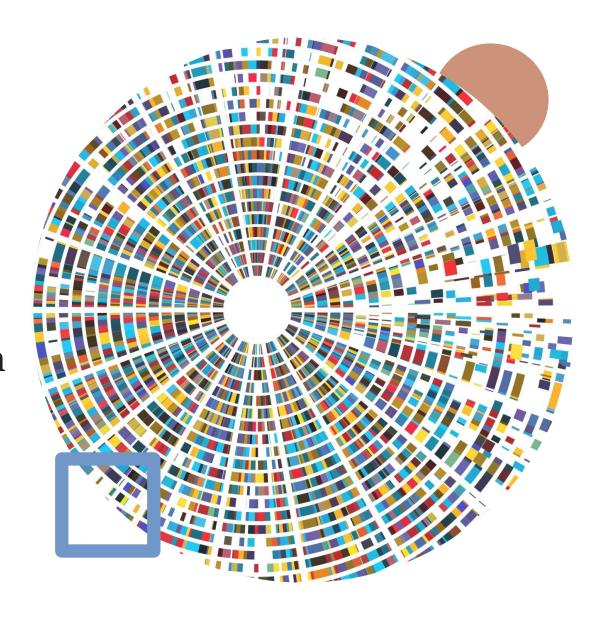
# **Sex, Love, and Relationships:**

A Functional Medicine Approach

Sara Gottfried, MD



#### Learning Objectives

At the end of this session participants will be able to:

- Define normal sexual response for men and women
- Recognize the types of male and female sexual dysfunction
- Review the evidence-based nonpharmacologic and pharmacologic treatments

#### Disclosures

Disclosure of Financial Relationships related to this CME program or products discussed

None

Off-Label Usage

Testosterone (for women)

# Are We Asking?

- 44% no formal curriculum
- 6Ps: Partners, Practices, Protection, Past History, Prevention of Pregnancy, Plus
- Most people want information from health care provider about sexual health

Lamont et al. J Obstet Gynaecol Can. 2017 Dec;39(12):e535-e541; Simon et al. Obstet Gynecol. 2017 Oct;130(4);889-905; Rubin ES, et al. *J Sex Med*. 2018;15(10):1414-1425; Warner C, et al. *J Sex Med*. 2018;15(8):1093-1102.

## Female Sexual Dysfunction

#### What's Normal?

- Rancho Bernardo, N=1303, mean age 67 (40-80)
  - 49.8% sex in past 4 weeks
  - Likelihood of sex decreased with age
  - 40% of women no sexual desire
  - Sexual desire associated with hormone use and sexual activity
- Clinic visit with N=376, mean age 73
  - 39% sexually active
  - 42% metabolic syndrome-decreased SA, desire, and low satisfaction

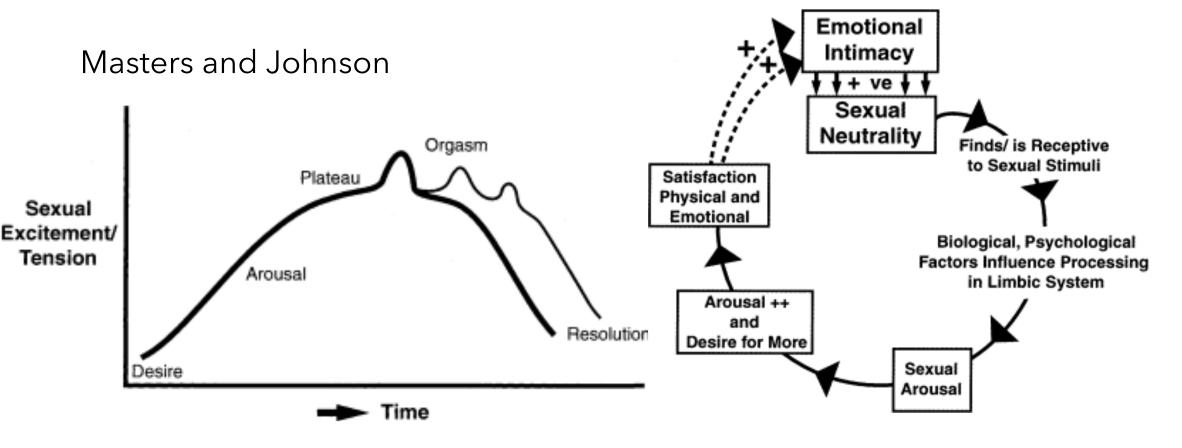


#### What's Normal?

	Mean (in mm)	Standard Deviation	Minimum (in mm)	Maximum (in mm)
Width of clitoris	4.62	2.538	1	22
Length of clitoris	6.89	4.965	0.5	34
Distance clitoris-urethra	22.63	7.661	3	65
Introitus opening	27.91	10.36	6	75
Length of perineum	21.34	8.544	3	55
Length of labia majora (right)	79.71	15.25	12	180
Length of labia majora (left)	79.99	15.44	20	180
Length of labia minora (right)	42.1	16.35	6	100
Length of labia minora (left)	42.97	16.29	5	100
Width of labia minora (right)	13.4	7.875	2	61
Width of labia minora (left)	14.15	7.643	1	42



#### Female Sexual Response



BJOG: An International Journal of Obstetrics & Gynaecology, Volume: 109, Issue: 4, Pages: 357 363, First published: 22 December 2003

## Transition from Normal to Dysfunction

- GxE: Androgen receptor... how many CAG repeats?<sup>1</sup>
- In Rancho Bernardo, 33% reported low or no sexual desire, but overall 61% were satisfied<sup>2</sup>
- Motivations complex. Does desire precede sex in women?<sup>3</sup>
- Women with a history of childhood sexual abuse show higher levels of distress in the context of good sexual functioning<sup>4</sup>
- Surgical menopause overall improves sexual function<sup>5</sup>



## PRESIDE Study

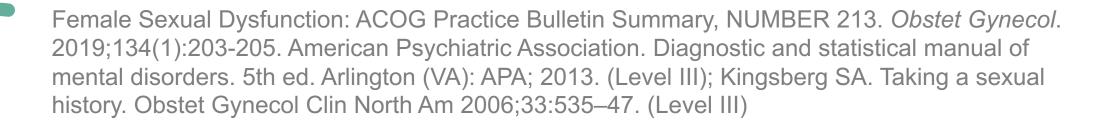
- Prevalence of Female Sexual Problems Associated with Distress and Determinants of Treatment Seeking (PRESIDE)
- N=31,581 female respondents >=18
- 43% sexual problem
- 22% sexually-related personal distress (score>=15 on Female Sexual Distress Scale), most common aged 45-64
- Correlates of sexual problems:
  - Poor self-assessed health, low education level, depression, anxiety, thyroid conditions, and urinary incontinence



## Female Sexual Dysfunction

Female sexual dysfunction encompasses various conditions that are characterized by reported personal distress in one or more of the following areas:

- Desire
- Arousal
- Orgasm
- Pain



## Androgen Receptor (AR)

- Effect of testosterone depends on exposure of + sensitivity of AR
- Cytosine-adenine-guanine (CAG) trinucleotide repeat polymorphism in the AR gene has an impact on AR function in men. However, large studies are lacking in women.
- Cross-sectional study of n=529 women 19-65 found increasing numbers of CAG repeats were correlated to increased sexual function. Women with problems achieving orgasm had a significantly lower number of CAG repeats than women that reported no problems reaching orgasm.
- No associations between CAG repeat lengths and other aspects of female sexual dysfunction, including Female Sexual Interest and Desire Disorder (formerly hypoactive sexual desire disorder).



## Common Etiologies and Risk Factors

- Anxiety disorder
- Diabetes
- Depression
- Female genital mutilation
- Genitourinary syndrome of menopause
- History of sexual abuse
- Hypertension
- Hysterectomy
- Intimate partner violence
- Medications
- Negative sexual attitudes

- Neurologic disease
- Personality traits of perfectionism and self-dislike
- Postpartum period
- Premature ovarian failure
- Psychologic sequelae of gynecologic cancer and breast cancer
- Relationship discord
- Stress-emotional or environmental
- Stress urinary incontinence
- Substance use disorder

Female Sexual Dysfunction: ACOG Practice Bulletin Summary, NUMBER 213. *Obstet Gynecol.* 2019;134(1):203-205.

## DHEA and Cortisol = Salivary Markers of HPA Axis Dysregulation in Women with Low Desire

- Study measured HPA axis function morning and evening salivary cortisol and DHEA, the cortisol awakening response (CAR), diurnal cortisol slope, and cortisol:DHEA ratio and examined their relationship with sexual functioning in N=275 women with (n=137) and without (n=138) HSDD.
- Results demonstrate multiple hormonal markers of HPA dysregulation in women diagnosed with HSDD:
  - Lower AM cortisol (HSDD mean = 8.20 nmol/L, SD=4.25 vs 9.36 nmol/L, SD=4.06), t(273)=2.31, p = .02
  - Lower AM DHEA [HSDD group (M = .86 nmol/L, SD = .52) showing lower, on average, morning DHEA levels, compared to the control group (M =1.11 nmol/L, SD = .69; t (273) = 3.38, p = .001]
  - Flat diurnal cortisol slope [steeper cortisol slope in control participants (M = 7.87 nmol/L, SD = 3.92) compared to HSDD participants (M = 6.44 nmol/L, SD = 4.41), t(273) = 2.85, p = .005]
  - Lower CAR [mean cortisol levels at 30 min post-waking were higher by 2.51 nmol/L (SE = 0.26, p < 0.001) than levels upon waking, while mean cortisol levels at 60 min post-waking were not significantly different from waking levels (higher by 0.27 nmol/L; SE = 0.26, p = 0.3). Moreover, the average CAR for the HSDD group was smaller by 0.99 nmol/L (SD =0.43, p = .02) than that of the control group, with significant differences between groups at both 30 min (p = .04) and 60 min (p = .02), but not at awakening (p = .17)]
- Overall, results indicate that persistently low sexual desire in women is associated with HPA axis dysregulation, with both cortisol
  and DHEA alterations potentially detrimental to sexual desire.

Basson R, et al. Dehydroepiandrosterone and cortisol as markers of HPA axis dysregulation in women with low sexual desire. *Psychoneuroendocrinology*. 2019;104:259-268.

DHEA and Cortisol =
Salivary Markers of
HPA Axis
Dysregulation in
Women with Low
Desire

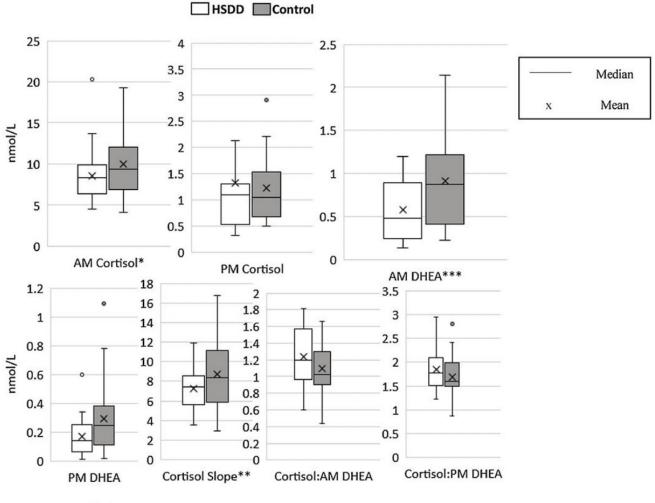


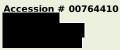
Fig. 1. Measures of HPA axis regulation compared by group. p < .05; \*\* p < .01; \*\*\* p = .001.

Basson R, et al. Dehydroepiandrosterone and cortisol as markers of HPA axis dysregulation in women with low sexual desire. *Psychoneuroendocrinology*. 2019;104:259-268.

## Case Study 1

F 46 L Androgens Cort







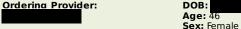
#### **Last Menstrual Period:**

2023-04-14

Collection Times: 2023-05-03 08:00AM (S)

2023-05-03 08:30AM (S) 2023-05-03 09:00AM (S) 2023-05-03 04:30PM (S) 2023-05-03 09:00PM (S) 2023-05-03 08:00AM (U) 2023-05-03 11:00AM (U) 2023-05-03 04:30PM (U)

2023-05-03 09:00PM (U)



#### **Hormone Testing Summary**



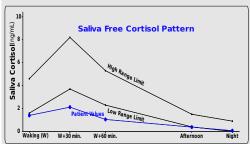






Progesterone Serum Equivalent is a calculated

#### 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.

The following videos (which can also be found on the website under the listed names along with others) may aid your understanding: <a href="DUTCH Plus Overview">DUTCH Plus Overview (quick overview)</a> <a href="Estrogen Tutorial">Estrogen Tutorial</a> <a href="Female Androgen Tutorial">Female Androgen Tutorial</a> <a href="Courtsol/CAR Tutorial">Cortisol/CAR Tutorial</a>

PLEASE BE SURE TO READ BELOW FOR ANY SPECIFIC LAB COMMENTS. More detailed comments can be found on page 7.

- The patient reports using a glucocorticoid. This may suppress adrenal function. See provider comments for more details. The Cortisol Awakening Response (CAR) was 0.72ng/mL (expected range 1.5-4.0) or 51.4% (range 50-160%). See page 5 for more details.













#### Sex Hormones and Metabolites

Ordering Provider:

DOB: **Age:** 46 Sex: Female

#### Last Menstrual Period:

2023-04-14

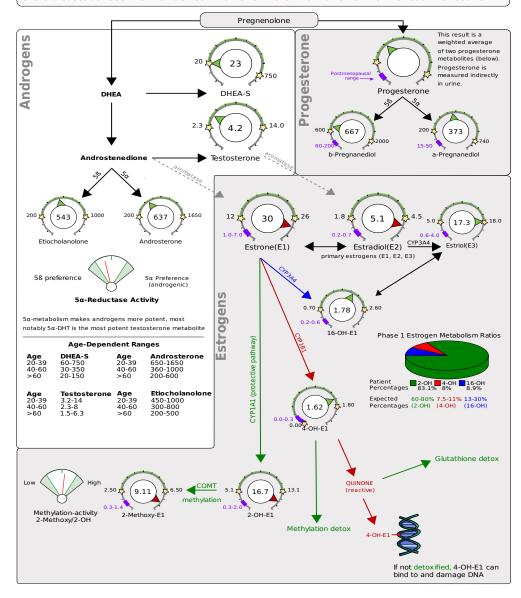
Test		Result	Units	Luteal*	Postmenopausal
Progesterone M	etabolites (Urine)			Range	Range
b-Pregnanediol	Low end of luteal range	667.0	ng/mg	600 - 2000	60-200
a-Pregnanediol	Within luteal range	373.1	ng/mg	200 - 740	15-50
Estrogens and M	letabolites (Urine)				
Estrone(E1)	Above luteal range	29.7	ng/mg	12 - 26	1.0-7.0
Estradiol(E2)	Above luteal range	5.1	ng/mg	1.8 - 4.5	0.2-0.7
Estriol(E3)	High end of luteal range	17.3	ng/mg	5 - 18	0.6-4.0
2-OH-E1	Above luteal range	16.7	ng/mg	5.1 - 13.1	0.3-2.0
4-OH-E1	High end of luteal range	1.62	ng/mg	0 - 1.8	0-0.3
16-OH-E1	Within luteal range	1.78	ng/mg	0.7 - 2.6	0.2-0.6
2-Methoxy-E1	Above luteal range	9.11	ng/mg	2.5 - 6.5	0.3-1.4
2-OH-E2	High end of luteal range	1.1	ng/mg	0 - 1.2	0-0.3
4-OH-E2	Above luteal range	1.22	ng/mg	0 - 0.5	0-0.1
Total Estrogen	Above range	83.6	ng/mg	35 - 70	4.0-15
Androgens and	Metabolites (Urine)				
DHEA-S	Low end of range	22.5	ng/mg	20 - 750	
Androsterone	Within range	637.0	ng/mg	200 - 1650	
Etiocholanolone	Within range	543.0	ng/mg	200 - 1000	
Testosterone	Low end of range	4.2	ng/mg	2.3 - 14	
5a-DHT	Above range	6.83	ng/mg	0 - 6.6	
5a-Androstanediol	Above range	39.7	ng/mg	6 - 30	
5b-Androstanediol	Above range	80.1	ng/mg	20 - 75	
Epi-Testosterone	Low end of range	3.7	ng/mg	2.3 - 14	

\*the Luteal Range is the premenopausal range. When patients are taking oral progesterone this range for progesterone metabolites is not luteal and reflects the higher levels expected when patients take oral progesterone. This test is intended to be taken in the luteal phase of the menstrual cycle (days 19-22 of a 28 day cycle) for premenopausal women. The ranges in the table below may be used when samples are taken during the first few days (follicular) of the cycle, during ovulation (days 11-14) or when patients are on oral progesterone. See the following pages for age-dependent ranges for androgen metabolites.

Additional Normal Ranges	Follicular	Ovulatory	Oral Pg (100mg)
b-Pregnanediol	100-300	100-300	2000-9000
a-Pregnanediol	25-100	25-100	580-3000
Estrone (E1)	4.0-12.0	22-68	N/A
Estradiol (E2)	1.0-2.0	4.0-12.0	N/A



Hormone metabolite results from the previous page are presented here as they are found in the steroid cascade. See the Provider Comments for more information on how to read the results.



Precision Analytical (Dawn Huo, Ph.D., Lab Director) 3138 Rivergate Street #301C McMinnville, OR 97128



Page 3 of 16 CLIA Lic. #38D2047310 DutchTest.com dutcholus COMPLETE WITH CORTISOL AWAKENING RESPONSE





#### Adrenal

Orderina Provider:

Age: 46
Sex: Female

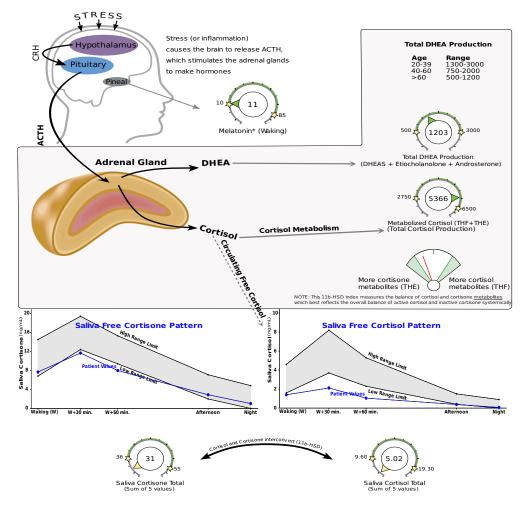
#### **Last Menstrual Period:**

2023-04-14

Collection Times: 2023-05-03 08:30AM (S) 2023-05-03 08:30AM (S) 2023-05-03 09:00AM (S) 2023-05-03 09:00PM (S) 2023-05-03 12:00PM (S) 2023-05-03 12:00PM (W) 2023-05-03 11:00AM (U) 2023-05-03 04:30PM (U) 2023-05-03 09:00PM (U)

Category	Test		Result	Units	Normal Range
Free Cortis	ol and Cortisone (Saliva)				
	Saliva Cortisol - Waking (W)	Below range	1.4	ng/mL	1.6 - 4.6
	Saliva Cortisol - W+30 min.	Below range	2.12	ng/mL	3.7 - 8.2
	Saliva Cortisol - W+60 min.	Below range	1.05	ng/mL	2.3 - 5.3
	Saliva Cortisol - Afternoon	Below range	0.38	ng/mL	0.4 - 1.5
	Saliva Cortisol - Night	Low end of range	0.07	ng/mL	0 - 0.9
	Saliva Cortisone - Waking (W)	Low end of range	7.67	ng/mL	6.8 - 14.5
	Saliva Cortisone - W+30 min.	Below range	11.67	ng/mL	12.4 - 19.4
	Saliva Cortisone - W+60 min.	Below range	7.98	ng/mL	9.4 - 15.3
	Saliva Cortisone - Afternoon	Low end of range	2.88	ng/mL	2 - 7.1
	Saliva Cortisone - Night	Within range	1.03	ng/mL	0 - 4.8
	Saliva Cortisol Total	Below range	5.02	ng/mL	9.6 - 19.3
	Saliva Cortisone Total	Below range	31.23	ng/mL	36 - 55
Creatinine	(Urine)				
	Creatinine A (Waking)	Within range	0.6	mg/ml	0.2 - 2
	Creatinine B (Morning)	Within range	1.53	mg/ml	0.2 - 2
	Creatinine C (Afternoon)	Within range	0.34	mg/ml	0.2 - 2
	Creatinine D (Night)	Within range	0.78	mg/ml	0.2 - 2
Cortisol Me	etabolites and DHEA-S (Urine)				
	a-Tetrahydrocortisol (a-THF)	Within range	232.0	ng/mg	75 - 370
	b-Tetrahydrocortisol (b-THF)	Within range	1921.0	ng/mg	1050 - 2500
	b-Tetrahydrocortisone (b-THE)	Within range	3213.0	ng/mg	1550 - 3800
	Metabolized Cortisol (THF+THE)	Within range	5366.3	ng/mg	2750 - 6500
	DHEA-S	Low end of range	23.0	ng/mg	20 - 750
Additional	Cortisol and Cortisone (Saliva)				
**	Saliva Cortisol - Extra 1	Within range	0.41	ng/mL	0 - 0.9
**	Saliva Cortisone - Extra 1	Above range	5.36	ng/mL	0 - 4.8
**	b-Tetrahydrocortisol (b-THF) b-Tetrahydrocortisone (b-THE) Metabolized Cortisol (THF+THE) DHEA-S Cortisol and Cortisone (Saliva) Saliva Cortisol - Extra 1	Within range Within range Within range Low end of range Within range	1921.0 3213.0 5366.3 23.0	ng/mg ng/mg ng/mg ng/mg	1050 - 2500 1550 - 3800 2750 - 6500 20 - 750





The Cortisol Awakening Response (CAR) is the rise in salivary cortisol between the waking sample and the sample collected 30 (as well as 60) minutes later. This "awakening response" is essentially a "mini stress test" and is a useful measurement in addition to the overall up-and-down (diurnal) pattern of free cortisol throughout the day. This patient shows a waking cortisol of 1.40 and an increase to 2.12 after 30.0 minutes. This is an increase of 0.72ng/mL or 51.4%. Expected increases differ depending on the methods used. Preliminary research shows that 50-160% or 1.54.0ng/mL increases are common with samples collected 30 minutes after waking. Generally this result is a little higher than the waking sample but is not in this case. To date, data suggests that expected results may be 0-70% higher, and this guideline is considered for research only.



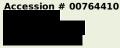


Page 5 of 16

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#### Organic Acid Tests (OATs)

Ordering Provider:

Age: 46
Sex: Female

#### Last Menstrual Period:

2023-04-14

Collection Times: 2023-05-03 08:00AM (5) 2023-05-03 08:00AM (5) 2023-05-03 09:00AM (5) 2023-05-03 04:30PM (5) 2023-05-03 04:30PM (5) 2023-05-03 03:00AM (U) 2023-05-03 03:00AM (U) 2023-05-03 04:30PM (U) 2023-05-03 09:00PM (U)

Category	Test		Result	Units	Normal Range	
Category		Nutritional Owner's As		Jilles	Normai Kange	
		Nutritional Organic Ac	ias			
Vitamin B12	Marker (may be deficient if hi	J , , ,				
	Methylmalonate (MMA)		1.92	ug/mg	0 - 2.5	
Vitamin B6 N	larkers (may be deficient if hi	gh) - (Urine)				
	Xanthurenate	High end of range	1.11	ug/mg	0.12 - 1.2	
	Kynurenate	Above range	5.03	ug/mg	0.8 - 4.5	
Glutathione I	Marker (may be deficient if lov	w or high) - (Urine)				
	Pyroglutamate	Within range	39.4	ug/mg	28 - 58	
Biotin Marke	r (may be deficient if high) - (	Urine)				
	b-Hydroxyisovalerate	Within range	6.4	ug/mg	0 - 12.5	
Gut Marker (	potential gut putrefaction or o	dysbiosis if high) - (Urine)				
	Indican	Within range	84.8	ug/mg	0 - 100	
		<b>Neuro-related Marke</b>	rs			
Dopamine M	etabolite - (Urine)					
	Homovanillate (HVA)	Low end of range	4.3	ug/mg	3 - 11	
Norepinephri	ine/Epinephrine Metabolite - (	Urine)				
	Vanilmandelate (VMA)	Within range	4.0	ug/mg	2.2 - 5.5	
Neuroinflami	mation Marker - (Urine)					
	Quinolinate	High end of range	9.5	ug/mg	0 - 9.6	
		Additional Markers	;			
Melatonin (*i	measured as 6-OH-Melatonin	-Sulfate) - (Urine)				
	Melatonin* (Waking)	Low end of range	10.6	ng/mg	10 - 85	
Oxidative Str	ress / DNA Damage, measure	ed as 8-Hydroxy-2-deoxyg	guanosine (8	B-OHdG) -	(Urine)	
	8-OHdG (Waking)	Within range	3.71	ng/mg	0 - 5.2	

05/12/2023

## Female Sexual Dysfunction

#### Common Root Causes

- Hormonal
- Neurogenic
- Psychogenic
- Vasculogenic
- Medications
- Genetic

#### Classifications

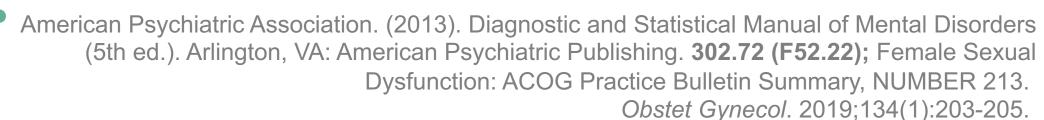
- Female Sexual Interest/Arousal Disorder
- Female Orgasmic Disorder
- Genito-Pelvic
   Pain/Penetration Disorder
- Substance/Medicationinduced Sexual Dysfunction
- Other

## Female Sexual Interest/Arousal Disorder

Lack of, or significant decrease in, sexual interest in at least 3 of the following:

- Interest in sexual activity
- Sexual or erotic thoughts
- Initiation of sexual encounters and responsiveness to a partner's initiation
- Excitement or pleasure during all or almost all sexual activity
- Interest or arousal in response to internal or external sexual or erotic cues (e.g., written, verbal, visual)
- Genital or nongenital sensations during sexual activity in almost all or all sexual encounters

Symptoms have persisted for a minimum of 6 months and cause clinically significant distress in the individual.



## Case Study 2

"763340 Peri Low Androgens Cort"

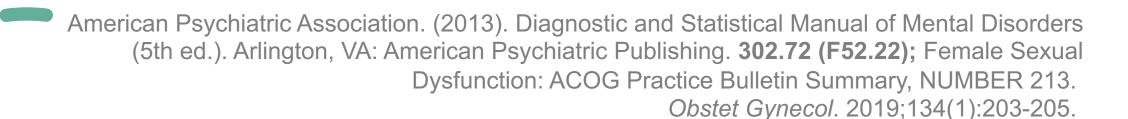
#### Jillian, 51, "I feel flat."

Lack of, or significant decrease in, sexual interest in at least 3 of the following:

TInterest in sexual activity

Sexual or erotic thoughts

- Initiation of sexual encounters and responsiveness to a partner's initiation
- Excitement or pleasure during all or almost all sexual activity
- $\uparrow$ Interest or arousal in response to internal or external sexual or erotic cues (e.g., written, verbal, visual)
- Genital or nongenital sensations during sexual activity in almost all or all sexual encounters Symptoms have persisted for a minimum of 6 months and cause clinically significant distress in the individual.



## Female Orgasmic Disorder

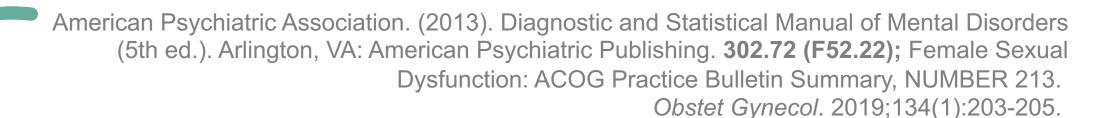
- Marked delay in, marked infrequency of, or absence of orgasm, or markedly reduced intensity of orgasmic sensations, in almost all or all occasions of sexual activity.
- Symptoms have persisted for a minimum of 6 months and cause clinically significant distress in the individual.

## Genito-Pelvic Pain/Penetration Disorder

Persistent or recurrent presence of one (or more) of the following:

- Difficulty having intercourse
- Marked vulvovaginal or pelvic pain during intercourse or penetration attempts.
- Marked fear or anxiety about vulvovaginal or pelvic pain in anticipating, during, or resulting from vaginal penetration.
- Marked tensing or tightening of the pelvic floor muscles during attempted vaginal penetration.

Symptoms have persisted for at least six months and cause clinically significant distress.



# Substance/Medication-Induced Sexual Dysfunction

- A disturbance in sexual function that has a temporal relationship with substance/medication initiation, dose increase, or substance/medication discontinuation
- Causes clinically significant distress in the individual

## Substances/Medications Associated with FSD

- Hormonal contraception
- Psychiatric medications
- Antiseizure medications
- Antihypertensives
- Cholesterol-lowering
- Sleep medications
- Pain medications

- Anticholinergics (Parkinson's)
- HIV medications
- Hormone blockers, e.g., GnRH agonists, aromatase inhibitors
- Alcohol, cannabis, narcotics

## Initial Approach

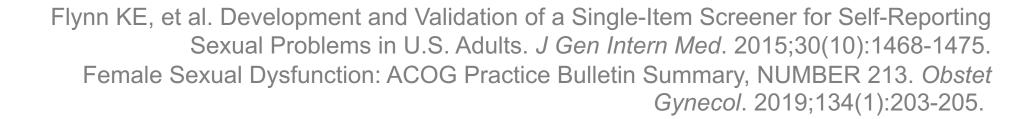
#### Screen: PROMIS® SexFS

• 8-item checklist of common sexual problems developed by Flynn et al, 2015

#### Query/normalize:

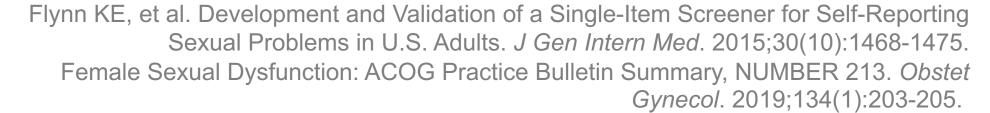
"Many women experience concerns about sex. Are you experiencing any issues? What is concerning you?"

#### Comprehensive sexual history



#### Initial Approach

- Physical examination
- Comprehensive testing
  - I recommend a combination of serum and dried urine/saliva testing
- Diagnosis if symptoms >= 6 months except meds/substances
- Psychological referral: sexual skills training, cognitivebehavioral therapy (with or without pharmacotherapy), mindfulness-based therapy, couples therapy
- Hormone therapy



#### Genitourinary Syndrome of Menopause

- Estrogen deficiency involving changes to the labia, introitus, clitoris, vagina, urethra, and bladder
- Vulvovaginal atrophy (VVA) is a component of GSM
- Highly prevalent yet unrecognized, undertreated
- Treatment: nonhormonal lubricants and moisturizers, physical therapy, low-dose vaginal estrogen therapy, vaginal dehydroepiandrosterone, and oral ospemifene



#### Hormones and FSD

- Estrogen and/or DHEA therapy
  - Local for GSM
  - Systemic
- Progesterone
- Testosterone
- SERM (Ospemifene)

Bruyniks N, et al. Systematic indirect comparison of ospemifene versus local estrogens for vulvar and vaginal atrophy. *Climacteric*. 2017;20(3):195-204. Archer DF, et al. Ospemifene for the treatment of menopausal vaginal dryness, a symptom of the genitourinary syndrome of menopause. *Expert Rev Endocrinol Metab*. 2019;14(5):301-314; Di Donato V, et al. Ospemifene for the treatment of vulvar and vaginal atrophy: A meta-analysis of randomized trials. Part II: Evaluation of tolerability and safety. *Maturitas*. 2019;121:93-100; Female Sexual Dysfunction: ACOG Practice Bulletin Summary, NUMBER 213. *Obstet Gynecol*. 2019;134(1):203-205.

# Does Serum T Predicts Clinical Outcomes in Women?

#### Muscle mass

- Handelsman DJ, et al. *Endocr Rev.* 2018;39(5):803-829
- Wright TJ, et al. *J Cachexia Sarcopenia Muscle*. 2018;9(3):482-496<sup>2</sup>
- Tapper J, et al. *Menopause*. 2019;26(12):1405-1414<sup>3</sup>

#### Libido

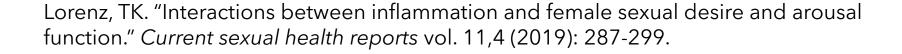
- Cappelletti M, et al. *Horm Behav*. 2016;78:178-193: "The likelihood that an androgen-only clinical treatment will meaningfully increase women's sexual desire is minimal"
- Need E2 and T: Alexander JL, et al. Menopause. 2004;11(6 Part 2 of 2):749-765
- Need E2 and supraphysiologic T: Cappelletti M, et al. *Horm Behav*. 2016;78:178-193.
- TT: Sherwin BB, et al. Psychosomatic Medicine.1987;49(4):397-409

## Lack of correlation between T levels (or E2) and desire or other sexual function

- "Sensitive assays lacking" Bachmann G, Fertil Steril. 2002;77(4):660-665<sup>4</sup>
- Dennerstein L, et al. Fertility and Sterility. 2002;77:42-48<sup>5</sup>
- Davis SR, et al. Journal of the American Medical Association. 2005;294(1):91–96°
- 1. TT (endogenous)
- 2. Exogenous TRT (100 mg testosterone enanthate)
- 3. Exogenous (3, 6.25, 12.5, or 25 mg testosterone enanthate)
- 4. "Female androgen insufficiency" defined as consisting of a pattern of clinical symptoms in the presence of decreased bioavailable T and normal estrogen status
- 5. Free T is best in women but lack of consensus
- 6. No single androgen level is predictive of low female sexual function, and the majority of women with low dehydroepiandrosterone sulfate levels did not have low sexual function.

#### Excess Inflammation and Desire

- Inflammation may interfere with female sexual desire and arousal via direct (neural) and indirect (endocrine, vascular, social/behavioral) pathways
- Clinical implications
  - Need assessment for sexual dysfunction in patients with inflammationrelated conditions
  - Consider anti-inflammatory diets to improve sexual desire and arousal function
  - Remember chronic inflammation as moderator of sexual effects of hormonal treatments
  - Although the evidence points to a role for inflammation in the development and maintenance of female sexual dysfunction, the precise nature of these associations remains unclear.



# Orgasmic Meditation: Potential Solutions or Sexual Wellness Cult?

- Orgasmic meditation is a unique meditation practice that combines mindfulness, touch, and pleasure.
- Partnered experience of stroking the clitoris for 15 minutes at 1:00, with only goal: let go and feel.
- The stroking is specific on the upper-left quadrant of the clitoris in an up-and-down motion, no firmer than you would stroke an eyelid. It's done (usually) by male partners wearing latex gloves dipped or coated in lube. There is no stroking of male genitalia.
- Newberg, Andrew B et al. "Alterations in Functional Connectivity Measured by Functional Magnetic Resonance Imaging and the Relationship With Heart Rate Variability in Subjects After Performing Orgasmic Meditation: An Exploratory Study." Frontiers in psychology vol. 12 708973. 11 Nov. 2021, doi:10.3389/fpsyg.2021.708973

**Businessweek** | Feature

# The Dark Side of the Orgasmic Meditation Company

OneTaste is pushing its sexuality wellness education toward the mainstream. Some former members say it pushed them into sexual servitude and five-figure debts.

#### Orgasmic Meditation: fMRI study

## Neurophysiological analysis of the relationship between sexual stimulation and spiritual experience

**Background:** We measured changes in resting brain functional connectivity, with blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI), associated with a creative meditation practice that is augmented by clitoral stimulation and is designed to not only achieve a spiritual experience but to help individuals manage their most intimate personal relationships. Briefly, the meditative state is attained by both the male and female participants while the male stimulates the woman's clitoris. The goal of this practice, called orgasmic meditation (OM), according to the practitioners is not sexual, but to use the focus on clitoral stimulation to facilitate a meditative state of connectedness and calm alertness between the two participants.

**Methods:** fMRI was acquired on N=20 pairs of subjects shortly following one of two states that were randomized in their order - during the OM practice or during a neutral condition. Resting BOLD image acquisition was performed at completion of the practice to assess changes in functional connectivity associated with the performance of the practice.

**Results:** The results demonstrated significant changes (p < 0.05) in functional connectivity associated with the OM compared to the neutral condition. For the entire group there was altered connectivity following the OM practice involving the left superior temporal lobe, the frontal lobe, anterior cingulate, and insula. In female subjects, there was altered connectivity involving the cerebellum, thalamus, inferior frontal lobe posterior parietal lobe, angular gyrus, amygdala and middle temporal gyrus, and prefrontal cortex. In males, functional connectivity changes involved the supramarginal gyrus, cerebellum, and orbitofrontal gyrus, cerebellum, parahippocampus, inferior temporal gyrus, and anterior cingulate.

**Conclusion:** Overall, these findings suggest a complex pattern of functional connectivity changes occurring in both members of the couple pair that result from this unique meditation practice. The changes represent a hybrid of functional connectivity findings with some similarities to meditation based practices and some with sexual stimulation and orgasm. This study has broader implications for understanding the dynamic relationship between sexuality and spirituality.



# NAMS 2022 Position Statement

"The 2022 Hormone Therapy Position Statement of The North American Menopause Society" Advisory Panel. The 2022 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2022;29(7):767-794.

doi:10.1097/GME.0000000000002028

#### **SEXUAL FUNCTION**

- Both systemic hormone therapy and low-dose vaginal ET increase lubrication, blood flow, and sensation of vaginal tissues. (Level I)
- Systemic hormone therapy generally does not improve sexual function, sexual interest, arousal, or orgasmic response independent of its effect on GSM. (Level I)
- If sexual function or libido are concerns in women with menopause symptoms, transdermal ET may be preferable over oral ET because of minimal effect on sex hormone-binding globulin and free testosterone levels. (Level II)
- Low-dose vaginal ET improves sexual function in postmenopausal women with GSM. (Level I)
- Non estrogen alternatives FDA approved for dyspareunia include ospemifene and intravaginal DHEA. (Level I)

# NAMS 2022 Position Statement

"The 2022 Hormone Therapy Position Statement of The North American Menopause Society" Advisory Panel. The 2022 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2022;29(7):767-794.

doi:10.1097/GME.0000000000002028

#### **GENITOURINARY SYMPTOMS**

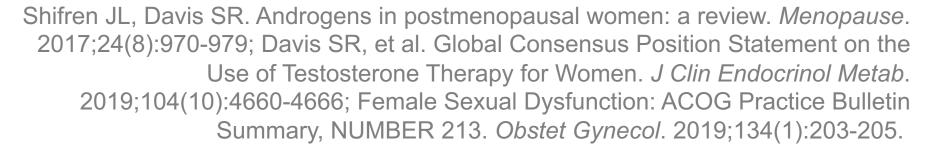
- Low-dose vaginal ET preparations are effective and generally safe for the treatment of GSM, with minimal systemic absorption, and are preferred over systemic therapies when ET is used only for genitourinary symptoms. (Level I)
- For women with breast cancer, low-dose vaginal ET should be prescribed in consultation with their oncologists. (Level III)
- Progestogen therapy is not required with low-dose vaginal estrogen, but RCT data are lacking beyond 1 year. (Level II)
- Non estrogen prescription FDA-approved therapies that improve VVA in postmenopausal women include ospemifene and intravaginal DHEA. (Level I)
- Vaginal bleeding in a postmenopausal woman requires thorough evaluation.
   (Level I)

# ACOG Vaginal Estrogen in Women with h/o Estrogen-Dependent Breast Cancer

Formulation	Composition	FDA-Approved Dosages*  The usual dosage range is 2–4 g (marked on the applicator) daily for 1 week or 2 weeks, then gradually reduced to one half of the initial dosage for a similar period. A maintenance dosage of 1 g one to three times a week may be used after restoration of the vaginal mucosa has been achieved.				
Vaginal cream	17β-estradiol					
Vaginal cream	Conjugated equine estrogen	Cyclic administration of 0.5 g intravaginally (daily for 21 days the off for 7 days) for treatment of moderate-to-severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause. Twice weekly administration of 0.5 g intravaginally (for example, Monday and Thursday) for treatment of moderate-to-severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause. <sup>‡</sup>				
Vaginal ring	17β-estradiol	2-mg ring releasing 7.5 micrograms/d for 90 days				
Vaginal tablet	Estradiol hemihydrate	10 micrograms/d for 2 weeks and then 10 micrograms/d two time a week				

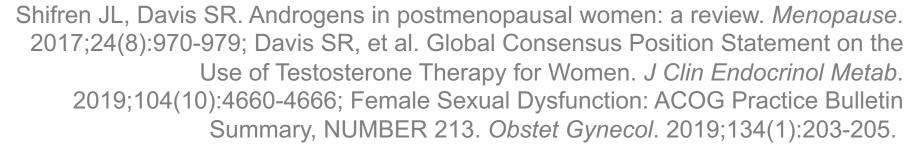
### **Testosterone**

- Off label use for Female Sexual Interest and Arousal Disorder
- FDA approved for Male Hypogonadism
- Supported by Global Consensus Position Statement (JCEM) and ACOG Clinical Management Guidelines
- Short-term use of transdermal testosterone can be considered as a treatment option for postmenopausal women (Level B) who have been appropriately counseled about the potential risks and unknown long-term effects.



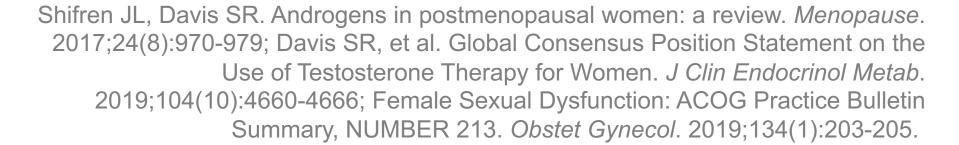
### Testosterone (Cont.)

- 3-6 month trial (Level C)
- Assess testosterone levels at baseline and after 3-6 weeks of treatment to ensure levels are within the normal range for reproductive aged women
- Discontinue at 6 months in women who do not show a response
- If ongoing therapy used, follow up clinical evaluation and testosterone measurement q6m to rule out T excess



### Other ACOG Recommendations

- Systemic DHEA is ineffective (Level A)
- Evidence insufficient for testosterone premenopausally (B)
- Sildenafil should not be used outside of clinical trials (B, FDAapproved for men with erectile dysfunction)
- Flibanserin can be considered in premenopausal women without depression



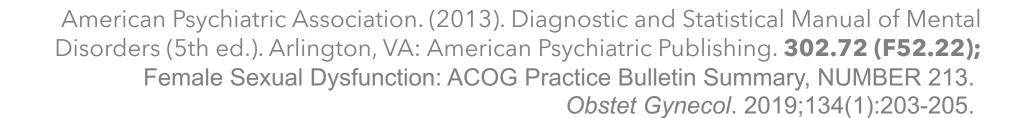
# Jillian, 51, "Life is in technicolor." Rx: Transdermal E2, oral Pg, transdermal T

Lack of, or significant decrease in, sexual interest in at least 3 of the following:

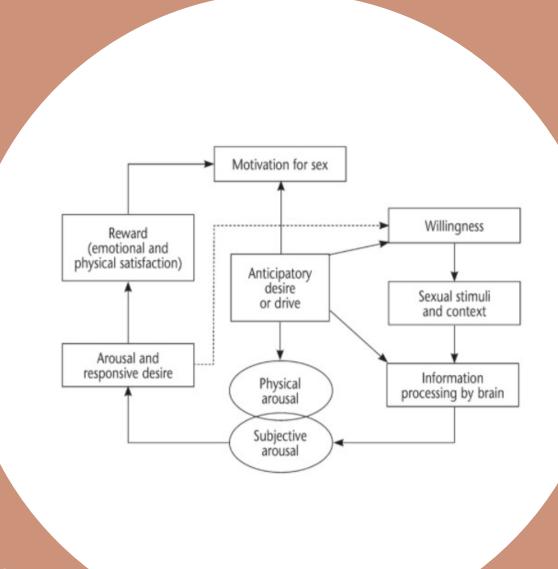
Tinterest in sexual activity

**←**Sexual or erotic thoughts

- Initiation of sexual encounters and responsiveness to a partner's initiation
- Excitement or pleasure during all or almost all sexual activity
- Interest or arousal in response to internal or external sexual or erotic cues (e.g., written, verbal, visual)
- Genital or nongenital sensations during sexual activity in almost all or all sexual encounters Symptoms have persisted for a minimum of 6 months and cause clinically significant distress in the individual.



# Circular Sexual Response Cycle



Female Sexual Dysfunction: ACOG Practice Bulletin #213. *Obstet Gynecol*. 2019;134(1):203-205.

# What Helps Both Male and Female Low Sexual Desire? Maybe Kisspeptin

- N=32 women aged 19-48 with low sexual desire, kisspeptin injections boosted brain activity in key brain parts responsible for arousal while watching erotic videos. These areas did not light up after placebo or dummy injections.
- Women who were more distressed by their low libido showed even greater improvements in brain activity after kisspeptin shots, the study showed. What's more, these women felt sexier after kisspeptin injections.
- "People have no idea why...they suddenly lose interest in sex not only with a partner, but on their own," DeLucia said. "They no longer have fantasies or find others attractive, and it often gets dismissed by providers because they feel helpless with no good treatment to offer." Kisspeptin could change all of this if further studies pan out. "Kisspeptin seems to be the first hormone to safely and comfortably enhance desire in both men and women," said DeLucia, who has no ties to the new research.
- Low sexual desire is the great divide, she said. "Relationships work when both parties feel loved, desired and appreciated," DeLucia said. "When a partner no longer feels desire, doubt and frustration and a feeling of rejection set in. These feelings are corrosive, and resentment begins."



# Case Study 3

"763340 Peri Low Androgens Cort"







Orderina Provider:





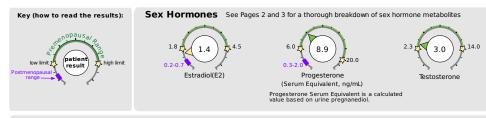
#### Last Menstrual Period:

2023-04-11

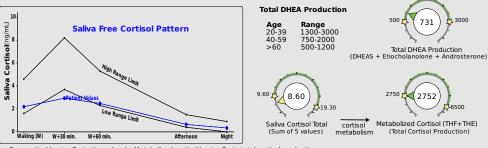
Collection Times: 2023-04-30 06:00AM (S) 2023-04-30 06:30AM (S) 2023-04-30 08:30AM (S) 2023-04-30 04:00PM (S) 2023-04-30 08:52PM (S) 2023-04-30 06:00AM (U) 2023-04-30 08:30AM (U) 2023-04-30 04:09PM (U)

2023-04-30 08:52PM (U)

#### **Hormone Testing Summary**



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.

The following videos (which can also be found on the website under the listed names along with others) may aid your understanding:

DUTCH Plus Overview (quick overview) Estrogen Tutorial Female Androgen Tutorial Cortisol/CAR Tutorial

PLEASE BE SURE TO READ BELOW FOR ANY SPECIFIC LAB COMMENTS. More detailed comments can be found on page 7.

The Cortisol Awakening Response (CAR) was 0.75ng/mL (expected range 1.5-4.0) or 34.2% (range 50-160%). See page 5 for more details.









#### Sex Hormones and Metabolites

Ordering Provider:

Precision Analytical (Dawn Huo, Ph.D., Lab Director)

3138 Rivergate Street #301C

McMinnville, OR 97128

DOB: Age: 51 Sex: Female

#### **Last Menstrual Period:**

2023-04-11

2023-04-30 06:00AM (S) 2023-04-30 06:30AM (S) 2023-04-30 08:30AM (S) 2023-04-30 04:00PM (S) 2023-04-30 08:52PM (S) 2023-04-30 06:00AM (U) 2023-04-30 08:30AM (II) 2023-04-30 04:09PM (U) 2023-04-30 08:52PM (U)

Collection Times:

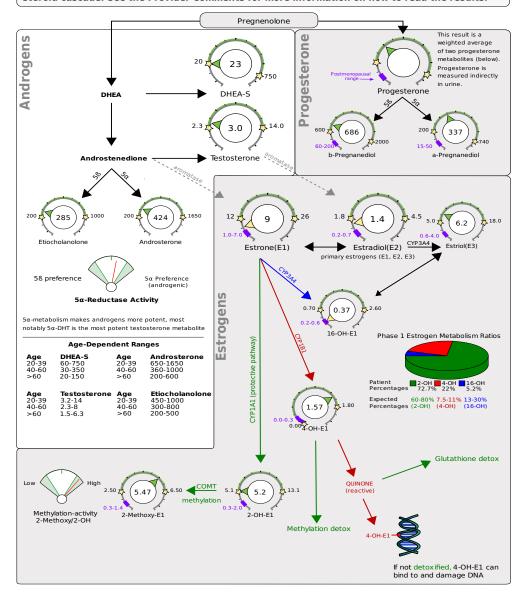
Test		Result	Units	Luteal*	Postmenopausal
Progesterone Metabolites (Urine)				Range	Range
b-Pregnanediol	Low end of luteal range	686.0	ng/mg	600 - 2000	60-200
a-Pregnanediol	Within luteal range	337.0	ng/mg	200 - 740	15-50
Estrogens and M					
Estrone(E1)	Below luteal range	8.6	ng/mg	12 - 26	1.0-7.0
Estradiol(E2)	Below luteal range	1.4	ng/mg	1.8 - 4.5	0.2-0.7
Estriol(E3)	Low end of luteal range	6.2	ng/mg	5 - 18	0.6-4.0
2-OH-E1	Low end of luteal range	5.2	ng/mg	5.1 - 13.1	0.3-2.0
4-OH-E1	High end of luteal range	1.57	ng/mg	0 - 1.8	0-0.3
16-OH-E1	Below luteal range	0.37	ng/mg	0.7 - 2.6	0.2-0.6
2-Methoxy-E1	Within luteal range	5.47	ng/mg	2.5 - 6.5	0.3-1.4
2-OH-E2	Within luteal range	0.39	ng/mg	0 - 1.2	0-0.3
4-OH-E2	Above luteal range	0.52	ng/mg	0 - 0.5	0-0.1
Total Estrogen	Below range	29.6	ng/mg	35 - 70	4.0-15
Androgens and Metabolites (Urine)					
DHEA-S	Low end of range	22.7	ng/mg	20 - 750	
Androsterone	Low end of range	424.0	ng/mg	200 - 1650	
Etiocholanolone	Low end of range	285.0	ng/mg	200 - 1000	
Testosterone	Low end of range	3.0	ng/mg	2.3 - 14	
5a-DHT	Within range	1.32	ng/mg	0 - 6.6	
5a-Androstanediol	Within range	19.7	ng/mg	6 - 30	
5b-Androstanediol	Low end of range	30.0	ng/mg	20 - 75	
Epi-Testosterone	Below range	1.8	ng/mg	2.3 - 14	

\*the Luteal Range is the premenopausal range. When patients are taking oral progesterone this range for progesterone metabolites is not luteal and reflects the higher levels expected when patients take oral progesterone. This test is intended to be taken in the luteal phase of the menstrual cycle (days 19-22 of a 28 day cycle) for premenopausal women. The ranges in the table below may be used when samples are taken during the first few days (follicular) of the cycle, during ovulation (days 11-14) or when patients are on oral progesterone. See the following pages for age-dependent ranges for androgen metabolites.

Additional Normal Ranges	Follicular	Ovulatory	Oral Pg (100mg)
b-Pregnanediol	100-300	100-300	2000-9000
a-Pregnanediol	25-100	25-100	580-3000
Estrone (E1)	4.0-12.0	22-68	N/A
Estradiol (E2)	1.0-2.0	4.0-12.0	N/A



Hormone metabolite results from the previous page are presented here as they are found in the steroid cascade. See the Provider Comments for more information on how to read the results.









#### Adrenal

Orderina Provider:

Age: 51
Sex: Female

#### **Last Menstrual Period:**

2023-04-11

Collection Times: 2023-04-30 06:00AM (S) 2023-04-30 06:30AM (S) 2023-04-30 08:30AM (S) 2023-04-30 04:00PM (S) 2023-04-30 08:52PM (S) 2023-04-30 06:00AM (U)

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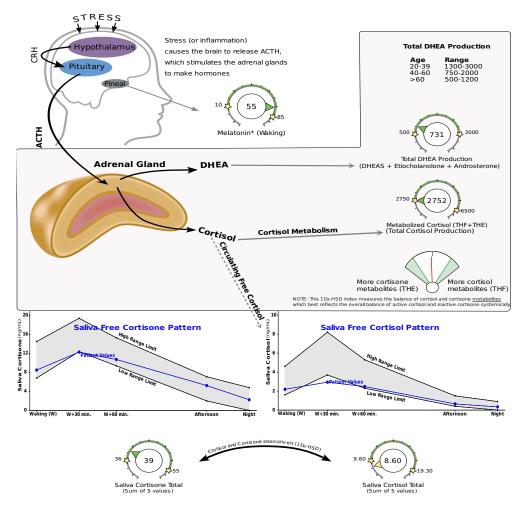
Category	Test		Result	Units	Normal Range
Free Cortisol and Cortisone (Saliva)					
	Saliva Cortisol - Waking (W)	Low end of range	2.19	ng/mL	1.6 - 4.6
	Saliva Cortisol - W+30 min.	Below range	2.94	ng/mL	3.7 - 8.2
	Saliva Cortisol - W+60 min.	Low end of range	2.48	ng/mL	2.3 - 5.3
	Saliva Cortisol - Afternoon	Within range	0.65	ng/mL	0.4 - 1.5
	Saliva Cortisol - Night	Within range	0.34	ng/mL	0 - 0.9
	Saliva Cortisone - Waking (W)	Within range	8.5	ng/mL	6.8 - 14.5
	Saliva Cortisone - W+30 min.	Below range	12.28	ng/mL	12.4 - 19.4
	Saliva Cortisone - W+60 min.	Within range	10.73	ng/mL	9.4 - 15.3
	Saliva Cortisone - Afternoon	Within range	5.24	ng/mL	2 - 7.1
	Saliva Cortisone - Night	Within range	2.25	ng/mL	0 - 4.8
	Saliva Cortisol Total	Below range	8.60	ng/mL	9.6 - 19.3
	Saliva Cortisone Total	Low end of range	39.00	ng/mL	36 - 55
Creatinine	(Urine)				
	Creatinine A (Waking)	Within range	0.72	mg/ml	0.2 - 2
	Creatinine B (Morning)	Within range	1.37	mg/ml	0.2 - 2
	Creatinine C (Afternoon)	Within range	0.31	mg/ml	0.2 - 2
	Creatinine D (Night)	Within range	1.08	mg/ml	0.2 - 2
<b>Cortisol M</b>	etabolites and DHEA-S (Urine)				
	a-Tetrahydrocortisol (a-THF)	Within range	168.0	ng/mg	75 - 370
	b-Tetrahydrocortisol (b-THF)	Below range	1021.0	ng/mg	1050 - 2500
	b-Tetrahydrocortisone (b-THE)	Low end of range	1563.0	ng/mg	1550 - 3800
	Metabolized Cortisol (THF+THE)	Low end of range	2751.5	ng/mg	2750 - 6500
	DHEA-S	Low end of range	23.0	ng/mg	20 - 750



Page 3 of 16

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The Cortisol Awakening Response (CAR) is the rise in salivary cortisol between the waking sample and the sample collected 30 (as well as 60) minutes later. This "awakening response" is essentially a "mini stress test" and is a useful measurement in addition to the overall up-and-down (diurnal) pattern of free cortisol throughout the day. This pattent shows a waking cortisol of 2.19 and an increase to 2.94 after 30.0 minutes. This is an increase of 0.75ng/mL or 34.2%. Expected increases differ depending on the methods used. Preliminary research shows that 50-160% or 1.5-4.0ng/mL increases are common with samples collected 30 minutes after waking shees guidelines are considered research only.

This patient shows a salivary cortisol of 2.48 measured 60 minutes after waking. This is an increase of 0.29ng/mL or 13.2% compared to the waking sample. To date, data suggests that expected results may be 0.70%, and this gleiline is considered for research only.











#### Organic Acid Tests (OATs)

Ordering Provider:

Age: 51
Sex: Female

#### **Last Menstrual Period:**

2023-04-11

Collection Times: 2023-04-30 06:00AM (S) 2023-04-30 06:30AM (S) 2023-04-30 08:30AM (S) 2023-04-30 04:00PM (S)

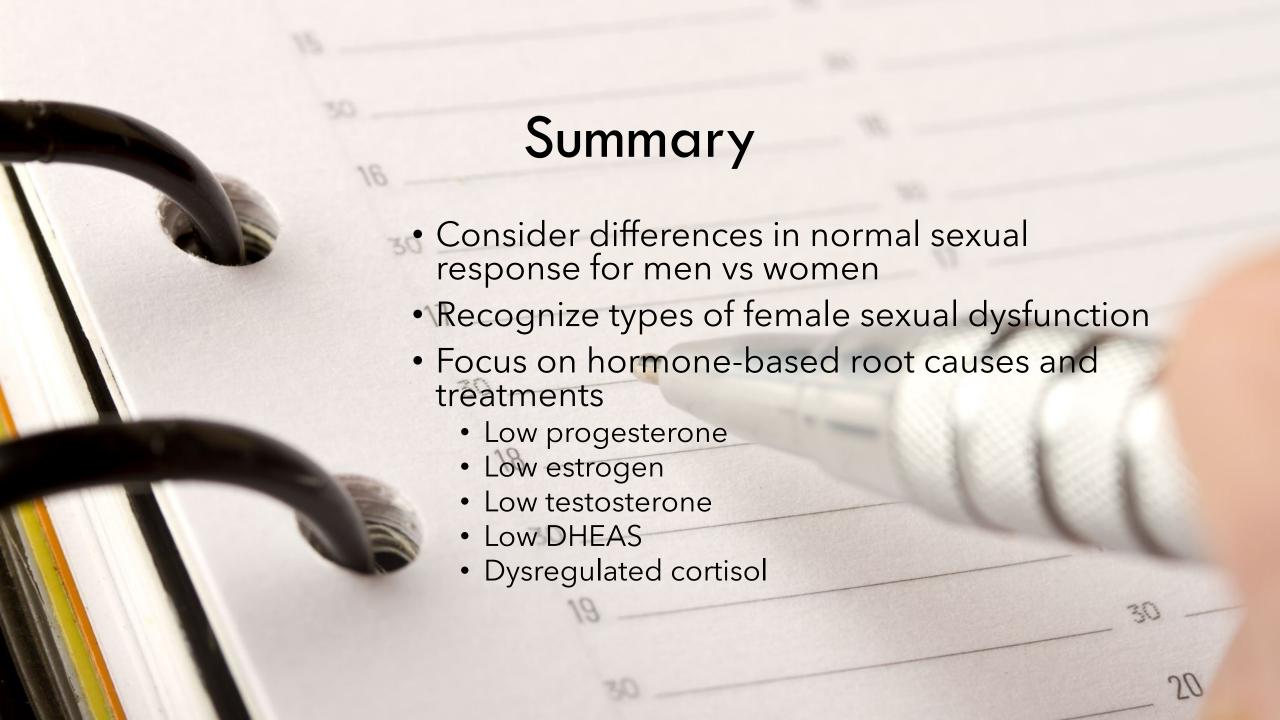
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Category	Test		Result	Units	Normal Range		
	N	utritional Organic Aci	ids				
Vitamin B12	Marker (may be deficient if hig	h) - (Urine)					
	Methylmalonate (MMA)	Within range	1.1	ug/mg	0 - 2.5		
Vitamin B6 M	larkers (may be deficient if high	h) - (Urine)					
	Xanthurenate	Within range	0.16	ug/mg	0.12 - 1.2		
	Kynurenate	Below range	0.67	ug/mg	0.8 - 4.5		
Glutathione I	Glutathione Marker (may be deficient if low or high) - (Urine)						
	Pyroglutamate	Low end of range	28.5	ug/mg	28 - 58		
Biotin Marker	Biotin Marker (may be deficient if high) - (Urine)						
	b-Hydroxyisovalerate	Within range	3.8	ug/mg	0 - 12.5		
Gut Marker (	Gut Marker (potential gut putrefaction or dysbiosis if high) - (Urine)						
	Indican	Within range	27.8	ug/mg	0 - 100		
		Neuro-related Marker	rs				
Dopamine M	etabolite - (Urine)						
	Homovanillate (HVA)	Below range	2.0	ug/mg	3 - 11		
Norepinephri	Norepinephrine/Epinephrine Metabolite - (Urine)						
	Vanilmandelate (VMA)	Below range	1.2	ug/mg	2.2 - 5.5		
Neuroinflammation Marker - (Urine)							
	Quinolinate	Within range	2.4	ug/mg	0 - 9.6		
Additional Markers							
Melatonin (*measured as 6-OH-Melatonin-Sulfate) - (Urine)							
	Melatonin* (Waking)	Within range	55.0	ng/mg	10 - 85		
Oxidative Str	Oxidative Stress / DNA Damage, measured as 8-Hydroxy-2-deoxyguanosine (8-OHdG) - (Urine)						
	8-OHdG (Waking)	Within range	1.51	ng/mg	0 - 5.2		

 Precision Analytical (Dawn Huo, Ph.D., Lab Director)
 FINAL REPORT

 3138 Rivergate Street #301C
 FINAL REPORT

 McMinnville, 0R 97128
 05/09/2023





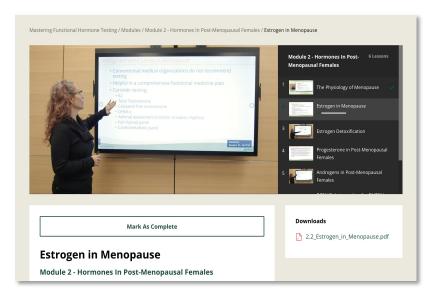
### Thank You!

#### **Exclusive Hormone Education for DUTCH Providers**

#### **DUTCH Interpretive Guide**



## Mastering Functional Hormone Testing Course



#### **Group Mentorship Sessions**



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