

DUTCH Test®

# Treatment Guide



**PRECISION**  
**ANALYTICAL INC.**  
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For Healthcare Providers

This Treatment Consideration Guide has been created to assist you in your evaluation of treatment options for patients based on comprehensive hormone analysis like the DUTCH Test®. This document has separate guides for families of hormones – cortisol, progesterone/estrogen and testosterone (T). Separate guides are offered for male and female T as well as for premenopausal and postmenopausal women regarding progesterone (Pg) and estrogen.

This treatment guide will help you work through the questions below for each family of hormones.

**1. What symptoms of hormone dysfunction does your patient have?**

Example – A premenopausal woman, we'll call Jane, is suffering from depression and insomnia, both symptoms of high cortisol (see page 4).

**2. What else might cause these symptoms?**

Example – The depression and insomnia Jane is experiencing could be caused by high cortisol but both could also be a result of thyroid issues, blood sugar dysregulation or low progesterone (see page 4).

**3. Are your patient's lab levels abnormal?**

Example – In Jane's case, the DUTCH Complete™ or DUTCH Plus® will help in assessing if her HPA axis is in overdrive, characterized by "High Cortisol." (see page 5). For questions #4 and #5 below, we will assume her cortisol labs were characterized as "High Cortisol."

**4. What root causes might influence your patient's abnormal lab levels?**

Example – Before considering treatments like adaptogens, root causes of high cortisol like acute inflammation, pain, hyperthyroidism or acute infection should be ruled out. (see page 6).

**5. What treatments may be considered for your patient's hormonal dysfunction?**

Example – After ruling out root causes of high cortisol, the provider may want to consider lifestyle changes, meditation/prayer, supplements, adaptogens and/or calming support. (see page 7).

**6. What specific products might be considered based on the answers above?**

Precision Analytical has created supplement guides to match the answers of question #5, with specific products from best-in-class functional medicine supplement brands. The letters in the bottom right corners (see pages 7, 11, 12, 17, 21) refer to supplement product guides. Please contact Precision Analytical at [marketing@dutchtest.com](mailto:marketing@dutchtest.com) if you are interested in these company-specific guides or go to <https://dutchtest.com/supplement-guides/>.

## Table of Contents

Hormone	Page(s)
Cortisol .....	4 - 7
Progesterone/Estrogen .....	8 - 12
HRT Guide - Female .....	13
Testosterone - Female .....	14 - 17
Testosterone - Male .....	18 - 21
HRT Guide - Male .....	22

### Disclaimer:

*Practitioners should strongly consider foundational work with every patient, including diet and lifestyle evaluation, environmental exposure minimization, hydration, exercise, proper sleep, and stress reduction. If these areas are not also addressed, any treatment may be considerably less effective. In most cases other lab tests (thyroid hormones, CBC, CMP, vitamin D, etc.) will also be incorporated into the evaluation.*

*This guide contains general information about testing, conditions, and treatment considerations. It is provided as an information resource only and should not be used or relied on for any diagnostic or treatment purposes. This medical information is for medical practitioners only and is not intended for patient education.*

*Please keep in mind this is not a protocol-driven guide. Functional medicine is about evaluating each patient individually, and tailoring a program based on their history, symptoms, causation, lifestyle, testing results, and needs.*

*Moreover, research is dynamic. Some of the treatment considerations have a great deal of data behind them, while others are limited to a study or two. As a result, practitioners should do their own due diligence and research appropriately for their patients.*

# Cortisol: Symptoms

Physiology - Female or Male	
Cortisol is a hormone released by the adrenal glands in small amounts in a circadian rhythm and in larger amounts during times of stress. Cortisol can help control blood sugar levels, regulate metabolism, help reduce inflammation and assist with memory formulation.	
Low Cortisol	
Symptoms	<u>What are other causes of these symptoms (other than low cortisol)?</u>
Fatigue/Burnout	Low T, sleep dysregulation, lifestyle/diet choices, infection, autoimmunity, blood sugar dysregulation, nutrient deficiency, neurotransmitter issues, thyroid issues, electrolyte imbalance, high histamine
Low Mood/Low Motivation	Neurotransmitter issues, thyroid issues, nutrient deficiency, low or high estrogen, low testosterone, low DHEA
Low Libido	Low T, low DHEA, low estrogen, sleep dysregulation, neurotransmitter issues, thyroid issues
Sleep Apnea	Overweight, head/neck anatomy, infection (especially sinus), high histamine
Orthostatic Hypotension	Dehydration, nutrient deficiency, electrolyte imbalance, POTS, blood sugar dysregulation
Feeling Dizzy/Weak Fainting	Dehydration, nutrient deficiency, electrolyte imbalance, infection, sleep dysregulation, blood sugar dysregulation
High Cortisol	
Symptoms	<u>What are other causes of these symptoms (other than high cortisol)?</u>
Anxiety/Depression/Panic Attacks	High estrogen, low Pg, neurotransmitter issues, thyroid issues, sleep dysregulation, blood sugar dysregulation, nutrient deficiency
Insomnia	Blood sugar dysregulation, nighttime blue light exposure, caffeine or alcohol before bed, thyroid issues, gut dysbiosis, low Pg, low melatonin
Weight Gain (belly fat)	Lifestyle/diet choices, low T, low DHEA, high estrogen, hypothyroidism, blood sugar dysregulation, sleep dysregulation
Brain Fog	Low estrogen, nutrient deficiency, neurotransmitter issues, thyroid issues, blood sugar dysregulation
Inflammation or Pain	Autoimmunity, low estrogen, infection, thyroid issues, high histamine, lifestyle/diet choices
Insulin/Blood Sugar Dysregulation	Lifestyle/diet choices, lack of exercise, nutrient deficiency
High Blood Pressure	Kidney disease, nutrient deficiency, cardiovascular issues, age, tobacco use, diabetes, overweight/obesity, lifestyle/diet changes
Hair Loss	Thyroid issues, iron deficiency, endocrine disruptors, nutrient deficiency, high androgens (T or DHT)

# Cortisol: Lab Assessments

Lab assessment for cortisol (and to some degree DHEA) is intended to differentiate optimal HPA axis function (expected CAR and up-and-down free cortisol pattern) from varying degrees of hyper and hypocortisol states. While the following spectrum is only conceptual, it may be helpful in identifying the probable HPA axis function of your patient before moving on to root cause analysis and treatment options on the following page.



The information below may be helpful in characterizing an individual's potential HPA axis dysfunction as described in the above.

**Low Cortisol:** *Insufficient cortisol release was once considered Phase 3 Adrenal Fatigue but is now better understood as HPA axis dysfunction. Low cortisol is rarely the result of a "fatigued" adrenal gland incapable of producing cortisol.*

- Low free cortisol in more than 1 point
- Low for the 5-sample total of free cortisol
- Low free cortisol at 1 point with low metabolized cortisol
- Flat CAR (Cortisol Awakening Response)

**Adaptive Cortisol:** *Once described as Phase 2 Adrenal Fatigue. Patients may present with a dysfunctional HPA axis and cortisol output, but not strictly "high" or "low." Some results may be low and some may be high, or the patient may show an abnormal diurnal cortisol pattern.*

- Low or high free cortisol in at least 1 point
- Normal free cortisol with abnormal (high or low) DHEA
- Abnormal diurnal up-and-down pattern of free cortisol
- Symptoms of HPA axis dysfunction with normal labs

**High Cortisol:** *Characterized by an excited HPA axis and once described as Phase 1 Adrenal Fatigue. The characteristic of this state is elevated cortisol, which may present on the DUTCH test in different patterns.*

- High free cortisol total or high for more than 1 point
- High free cortisol at 1 point with high metabolized cortisol
- Exaggerated CAR
- Normal free cortisol with elevated free cortisone pattern (rare)

Disease States	Further testing required for diagnosis.
Addison's Disease (rare)	<ul style="list-style-type: none"><li>• Very low (approaching zero) free cortisol. Confirmed by low free cortisone, and metabolized cortisol &lt;1000ng/mg</li><li><i>Addison's disease is rare. Similar results are seen when adrenal hormone production is suppressed by medications (glucocorticoids, opioids, etc.). Rule out pharmacological suppression first.</i></li></ul>
Cushing's Disease (rare)	<ul style="list-style-type: none"><li>• Free cortisol (and cortisone) high throughout the day without expected diurnal pattern</li><li>• Bedtime cortisol well outside of reference range (&gt;4 times upper range limit). Metabolized cortisol is typically very elevated as well</li></ul>

# Cortisol: Potential Root Causes of Abnormal Lab Levels

Low Cortisol	Low DHEA	High Cortisol	High DHEA
<ul style="list-style-type: none"><li>Medications (glucocorticosteroids, opioids, accutane)</li><li>Long-term stress</li><li>Pituitary or hypothalamic dysfunction/lesion</li><li>Head trauma/TBI affecting pituitary/hypothalamus</li><li>Hypothyroidism: may be associated with low metabolized cortisol, high free cortisol, and high free cortisone with a preference for more cortisol (THF) metabolites.</li><li>Non-classical congenital adrenal hyperplasia</li><li>Sleep dysregulation</li><li>Surgical removal of adrenal gland</li><li>Addison's disease</li></ul>	<ul style="list-style-type: none"><li>Age – naturally declines with aging</li><li>HPA axis dysfunction</li><li>Inflammation (inflammation lowers sulfation so DHEA higher but DHEA-S lower)</li><li>SULT2A1 problems (higher DHEA but lower DHEA-S)</li><li>Medications (glucocorticosteroids, opioids, Pulmicort inhaler, Metformin/Glucophage)</li></ul>	<ul style="list-style-type: none"><li>Cortisol supplementation</li><li>Stress</li><li>Acute inflammation</li><li>Acute pain</li><li>Blood sugar/insulin dysregulation</li><li>Caffeine use</li><li>Hyperthyroidism: may be associated with high metabolized cortisol, low free cortisol, and low free cortisone with a preference for more cortisone (THE) metabolites.</li><li>Acute infection</li><li>Cushing's syndrome or disease</li></ul>	<ul style="list-style-type: none"><li>DHEA supplementation</li><li>Medications (Alprazolam, Anastrozole, Methylphenidate, Amlodipine, Diltiazem and Bupropion)</li><li>Alcohol</li><li>Nicotine</li><li>Elevated cortisol</li><li>STS enzyme increased activity (higher DHEA but lower DHEA-S)</li><li>Non-classical congenital adrenal hyperplasia</li><li>Adrenal tumor</li><li>High prolactin</li></ul> <p><i>On the DUTCH test®, see Total DHEA Production (DHEA + Etiocholanolone + Androsterone)</i></p>

# Cortisol: Potential Treatments for Consideration

	Low Cortisol or Low Adaptive Cortisol	High Cortisol or High Adaptive Cortisol
General	<p>For patients with low cortisol production, consider root causes first. Patients may also benefit from the following treatment options:</p> <ul style="list-style-type: none"> <li>Adaptogenic support: Includes combinations of siberian ginseng (<i>eleutherococcus</i>), rhodiola, schisandra, licorice root, and maca.</li> <li>Adrenal glandular: There is limited clinical research available regarding their clinical impact.</li> <li>*Circadian training: Encourage full spectrum light exposure (especially on waking) and appropriate sleep hygiene and darkness before bed.</li> <li>Cortisol therapy: Corticosteroid medications should be considered only when appropriate and with great care.</li> </ul> <p style="text-align: right;">A</p>	<p>For patients with high cortisol production, lifestyle (stress) changes play a central role. The following treatment options may be beneficial as well:</p> <ul style="list-style-type: none"> <li>Reduce inflammation, stress, and/or infection</li> <li>Meditation/prayer</li> <li>Calming support: Includes combinations of GABA support (<i>pregnenolone</i>), L-taurine, 5-HTP, L-theanine, magnolia, jujube, chamomile, milky oat seed, passionflower, skullcap, phosphatidylserine, and maca.</li> <li>Adaptogenic support: Includes combinations of ashwagandha, siberian ginseng, rhodiola, holy basil, cordyceps, schisandra berries, and bacopa.</li> </ul> <p style="text-align: right;">B</p>
Considerations if Low CAR	With low cortisol production and a flat or low CAR, focus on full spectrum light exposure and products listed above within 30 minutes of waking.	<p style="text-align: right;">C</p> <p>Patients with higher cortisol production rarely exhibit a low CAR. If they do, their diurnal pattern is likely highly dysfunctional and *circadian training should be considered.</p> <p style="text-align: right;">D</p>
Considerations if High CAR	Patients with lower cortisol production rarely exhibit a high CAR.	<p style="text-align: right;">E</p> <p>With high cortisol and an exaggerated CAR, address the cause (anticipatory stress, inflammation, blood sugar, etc). Focus on calming support, meditation, breath work, and vagus nerve stimulation (humming, gargling, singing loudly), especially within 30 minutes of waking.</p> <p style="text-align: right;">F</p>
Considerations if High Bedtime Cortisol	Focus on *circadian training and taking any products intended to lower cortisol, like phosphatidylserine; best taken in the evening.	<p style="text-align: right;">G</p> <p>Address the root cause such as inflammation, blood sugar, or stress. Focus on *circadian training. Consider taking phosphatidylserine and other calming support at night.</p> <p style="text-align: right;">H</p>
Considerations if DHEA is Lower  (See "Total DHEA Production" on DUTCH report)	If DHEA and cortisol levels are low, improving HPA axis function is critical. Providers may additionally consider DHEA supplementation (typically 5-10mg for female, 10-50mg for male patients. Commonly taken orally or sublingually).	<p style="text-align: right;">I</p> <p>The HPA axis is functional (cortisol is elevated), but DHEA is not being adequately produced. DHEA supplementation may be considered (typically 5-10mg for female, 10-50mg for male patients. Commonly taken orally or sublingually).</p> <p style="text-align: right;">J</p>
Considerations if DHEA is Higher	Alcohol, nicotine, certain medications (alprazolam, anastrozole, calcium channel blockers and bupropion), and poor blood sugar/insulin commonly results in higher levels of DHEA when cortisol is low. Balance blood sugar/insulin with diet/lifestyle, inositol, berberine, magnesium, a-lipoic acid, fiber, etc. Use lab testing (HbA1c, insulin, etc) as needed.	<p style="text-align: right;">K</p> <p>See comments to the left, but also consider that if cortisol is made in high amounts, general HPA axis excitation (stress response) may also be responsible for creating higher levels of DHEA (an adrenal hormone).</p> <p style="text-align: right;">L</p>
Considerations if Metabolized Cortisol is Lower  Metabolized cortisol is the best marker for total glandular output.	<p>Because free cortisol levels are low, the lower levels of metabolites simply confirm the low output of cortisol.</p> <p>If free cortisol is normal in some samples and low for others, the low metabolized cortisol may imply that overall production is truly low.</p>	<p>If metabolite levels are generally lower than free cortisol, the patient may have sluggish cortisol clearance. This pattern (higher free, lower metabolites of cortisol) is common in patients with hypothyroidism and has also been observed with poor liver function and anorexia.</p>
Considerations if Metabolized Cortisol is Higher	Even though free cortisol is low, cortisol metabolites are high. This pattern of rapid cortisol clearance/metabolism may be seen in obesity or extreme hyperthyroidism patients and possibly with long-term stress. Support the HPA axis without promoting more cortisol production.	Because free cortisol levels are elevated, the higher levels of metabolites simply confirm the high output of cortisol.

# Progesterone | Estrogen: Symptoms

## Physiology - Female

Progesterone (Pg) is a hormone secreted after ovulation by the ovaries (it can be made in the placenta and adrenal glands as well). It primarily regulates the condition of the inner lining (endometrium) of the uterus however like estrogen, its systemic effects are numerous. Estrogen regulates the growth, development and physiology of the human reproductive system. Estrogen is an important sex hormone produced primarily by the ovaries in premenopausal women and from circulating adrenal androgens in postmenopausal women. The biological actions of estrogen are mediated by binding to the estrogen receptors in target organs.

## Low Progesterone

### Symptoms

	<b>What are other causes of these symptoms (other than low progesterone)?</b>
Anxiety	High estrogen, high DHEA, neurotransmitter issues, hyperthyroidism, high cortisol
Infertility	Thyroid issues, autoimmunity, nutrient deficiency, PCOS, adenomyosis, anatomical issues, endocrine disruptors
Insomnia	Blood sugar dysregulation, blue light exposure at night, stress, caffeine or alcohol before bed, thyroid issues, gut dysbiosis, low melatonin
Irritability	High estrogen, high T/DHEA, sleep dysregulation, stress, neurotransmitter issues, low melatonin
Menorrhagia	High estrogen, endocrine disruptors, adenomyosis, polyps, fibroids, hypothyroidism, iron deficiency
PMS/PMDD	High estrogen, endocrine disruptors, neurotransmitter issues, blood sugar dysregulation, stress, nutrient deficiency, high histamine

## Low Estrogen

### Symptoms

	<b>What are other causes of these symptoms (other than low estrogen)?</b>
Bone Loss	Thyroid issues, sleep dysregulation, medications
Hot Flashes	Low Pg, SNS excitaton/stress/cortisol, sleep dysregulation
Insomnia	Low Pg, SNS excitaton/stress/cortisol, serotonin/GABA/dopamine issues, blood sugar dysregulation, sleep dysregulation
Joint Pain/Skin Issues	Thyroid issues, sleep dysregulation, SNS excitaton/stress/cortisol, blood sugar dysregulation
Low Sex Drive	SNS excitaton/stress/cortisol, low androgens, thyroid issues, serotonin/GABA/dopamine issues, sleep dysregulation
Mood Issues/Brain Fog	Low Pg, low androgens, thyroid issues, serotonin/GABA/dopamine issues, blood sugar dysregulation, sleep dysregulation
Night Sweats	Low Pg, SNS excitaton/stress/cortisol, sleep dysregulation, hyperthyroidism
Vaginal Dryness	Low DHEA, Sjogren's Syndrome, vaginal infection, breastfeeding
Weight Gain	SNS excitaton/stress/cortisol, low androgens, thyroid issues, blood sugar dysregulation, sleep dysregulation, scleroderma

## High Estrogen

### Symptoms

	<b>What are other causes of these symptoms (other than high estrogen)?</b>
Acne	Endocrine disruptors, elevated 5a reductase/DHT
Dysmenorrhea	Iron deficiency, fibroids/polyps/adenomyosis, endometriosis
Menorrhagia	Thyroid issues, iron deficiency, fibroids/polyps/adenomyosis, slow/suboptimal estrogen metabolism
Mood Issues	SNS excitaton/stress/cortisol, thyroid issues, serotonin/GABA/dopamine issues, elevated 5a-reductase, blood sugar dysregulation
Swelling	Aldosterone issues
Tender Breasts	Slow/suboptimal estrogen metabolism
Weight Gain	SNS excitaton/stress/cortisol, thyroid issues, blood sugar dysregulation

# Progesterone | Estrogen: Lab Assessments

## Assessing Estrogen Status

Estrogen status (low, normal, or high) is primarily based on the hormone estradiol (E2). Postmenopausal women make about 10 times less estrogen, mostly of adrenal origin. While E2 is the strongest estrogen, estrone (E1) and 16-OH-E1 are also significantly estrogenic. Carefully consider all estrogen metabolites, but give more weight to the levels of E2.

"Optimal" levels may depend on many factors, including the corresponding Pg values and patient history and symptoms. This guide may not be appropriate for women on HRT and the categorizations are made assuming women are NOT on HRT.

## Assessing Estrogen Metabolites

Estrogen metabolites must also be considered. E1 and E2 are both metabolized by three competing (2, 4, and 16-OH) pathways. Generally, metabolism that heavily favors 4-OH is considered a potential risk factor for estrogen-related cancers (although this is a complicated issue). Conversely, 2-OH metabolites (particularly 2-methoxy estrogens) are considered more protective.

"Poor Phase 1 Metabolism" on page 11 and 12 generally refers to a pattern that favors 4-OH or 16-OH estrogens over the more protective 2-OH estrogens. "Poor Methylation" refers to a patient who is not readily converting "hydroxy estrogens" (like 2-OH-E1) to "methylated estrogens" (2-methoxy-E1). Both of these patterns can be assessed on the estrogen metabolism page of the DUTCH test.

*Some scenarios on this guide may suggest Hormone Replacement Therapy (HRT). All HRT may have risks which must be understood by a provider before considering any HRT.*

## Assessing Progesterone Status

Progesterone (Pg) is categorized into four groups for women:

- 0-0.5ng/mL - The adrenal glands make most of the Pg after the ovaries quit. If levels are very low, adrenal and ovarian hormone production of Pg may both be low.
- 0.5-2.0ng/mL - The normal range for a woman who is not cycling/ovulating and has proper adrenal Pg production.
- 2.0-6.0ng/mL - Most likely represents one of the following scenarios:
  - A) A woman who has ovulated but makes insufficient Pg for a premenopausal woman.
  - B) A postmenopausal or anovulatory woman whose adrenal production of Pg is slightly higher than normal.
- >6.0ng/mL - Women with levels above 6.0ng/mL have likely recently ovulated. We consider >12.0ng/mL to be strong Pg production.

Note: The Pg assessment is based off of two urine metabolites (a - Pregnanediol and b - Pregnanediol) that are extrapolated to provide an individual "serum equivalent" number that has been shown to correlate to serum Pg measurements.

# Progesterone | Estrogen: Potential Root Causes of Abnormal Lab Levels

## Low Progesterone

- Poor follicle development/poor quality corpus luteum
- NSAIDS (may suppress ovulation)
- Mirena (or similar) IUD/coil may suppress ovulation

## High Estrogen

- Sample collection during ovulatory phase (wrong day)
- Overweight/obesity
- Peri-menopause (surges of estrogen)
- Diabetes
- PCOS
- Estrogen supplementation (ERT)
- Poor liver clearance
- Gut Dysbiosis
- Environmental estrogens (BPA)
- Alcohol
- Ovarian cysts
- Inflammation

## Low Estrogen and Progesterone

- Sample collection during follicular phase (wrong day)
- Age (peri-menopause and menopause)
- Irregular cycles/skipped cycles/anovulation
- Hysterectomy with ovaries removed
- Anorexia
- Extreme exercise or training
- Extreme stress resulting in skipped menses
- Under body weight
- Hypogonadism (ovaries fail)
- Hypopituitarism (pituitary not communicating)
- Decreased blood flow to the ovaries (ie.surgery or smoking)
- Breast feeding
- Elevated prolactin
- Hypothyroidism
- PCOS
- Fertility medications
- Opioid pain medications (in last 6 months)
- Hormonal birth control (pill, patch, ring, implant, injection)

# Progesterone | Estrogen - Premenopausal: Potential Treatments for Consideration

	Very Low E2 <0.7ng/mg		Modestly Low E2 0.7-1.8ng/mg		Within Range E2 1.8-4.5ng/mg		Elevated E2 >4.5ng/mg		
	No Symptoms	Low Symptoms	Low Symptoms	High Symptoms	Low Symptoms	High Symptoms	No Symptoms	High Symptoms	
Progesterone <2ng/mL (normal for postmeno) <sup>1</sup>	E2 results within or below the postmenopausal range may imply ovarian failure. Test LH + FSH (blood). Consider chaste tree, vit. B6, vit. E, carotenoids, HRT.		Consider chaste tree, vit. B6, vit E.		Consider chaste tree, vit. B6, Pg-HRT.		Confirm no EDCs, <sup>4</sup> aromatization <sup>2</sup> from T. Consider chaste tree, vit. B6, phase 1/2 support, calcium-d-glucarate, fiber. Consider Pg-HRT.		
	A	B	C	D	E	F	G		
	Evaluate cortisol. Consider phytoestrogens.		Consider HRT, phytoestrogens. <sup>3</sup> Evaluate cortisol.	Address EDCs. <sup>4</sup> Consider Pg-HRT, Phase 1/2 support, fiber. Rule out inflammation. Consider Cycle Mapping Test.	Evaluate cortisol. Consider vit. E, phytoestrogens. <sup>3</sup>	Address EDCs, <sup>4</sup> inflammation. Consider fiber.			
Progesterone 2-6ng/mL (below luteal) <sup>1</sup>	E2 results within or below the post menopausal range may imply ovarian failure. Consider chaste tree, vit. B6, vit. E, carotenoids, phytoestrogens, HRT. Consider Cycle Mapping test to see E2 fluctuation thru the cycle. Seek underlying cause of low E2 before treatment considerations.		Consider chaste tree, vit. B6, vit E, HRT.		Consider chaste tree, vit. B6, carotenoids, Pg-HRT. Consider Cycle Mapping Test.		Address EDCs <sup>4</sup> or aromatization <sup>2</sup> from T. Consider chaste tree, vit. B6, carotenoids, phase 1/2 support, calcium-d-glucarate, fiber. Address inflammation, especially with high E symptoms. Consider Pg-HRT.		
	H	I	J	K	L	M			
Progesterone >6ng/mL (normal luteal)	Consider Cycle Mapping test to confirm low levels. Adequate Pg implies ovulation which requires adequate E2.	Adequate Pg levels imply ovulation. Consider treatments listed above if symptoms persist. Seek underlying cause.	Consider vit. E, phytoestrogens. <sup>3</sup> Seek underlying cause.	Evaluate phase 1/2. High E symptoms could be due to inflammation. Consider Cycle Mapping test.	Consider other causes: Hot flashes (high cortisol, hyperthyroidism); vaginal dryness (low testosterone); acne (check androgens, gut health)	Address EDCs, <sup>4</sup> inflammation. Consider phase 1/2 support, fiber, chaste tree, vit B6, carotenoids. Consider HRT if Pg <12ng/mL.	Address EDCs <sup>4</sup> or aromatization <sup>2</sup> from T. Consider phase 1/2 support, calcium-d-glucarate, fiber.	Address EDCs <sup>4</sup> or aromatization <sup>2</sup> from T. Consider phase 1/2 support, calcium-d-glucarate, fiber. Consider Pg-HRT if Pg <12ng/mL.	Address EDCs <sup>4</sup> or aromatization <sup>2</sup> from T. Consider phase 1/2 support, calcium-d-glucarate, fiber.
If Poor Phase 1 Metabolism	Consider general support of phase 2 plus sulforaphane and glutathione. Supporting phase 1 with DIM or I3C is not advised as they will likely lower E2.*  <sup>*To support Phase 1 without lowering E2, consider sulforaphane, crucifers, carrots, rosmarinic acid (rosemary, holy basil, lemon balm).</sup>		Consider phase 2, (glutathione, NAC) support.		Consider DIM/I3C, brassica family, but if estrogen levels are low, DIM/I3C will likely decrease levels further.*	Strongly consider DIM/I3C, brassica family.	Consider DIM/I3C, brassica family, sulforaphane, glutathione support.	Strongly consider DIM/I3C, brassica family, sulforaphane, glutathione support.	
If Poor Methylation (Phase 2)	If estrogen metabolite levels are very low (<0.4), all metabolite ratios are less precise because the levels are very near or below the detection limit.		Support methylation. <sup>5</sup> Consider genetic testing (MTHFR, COMT, etc.).		Support methylation. <sup>5</sup> Consider genetic testing (MTHFR, COMT).		Support methylation. <sup>5</sup> Consider genetic testing (MTHFR, COMT). Poor methylation may be contributing to high E2 levels.		
	CC	DD	EE	FF					

1. For all low Pg results, be sure to confirm that the patient collected in the luteal phase, is not postmenopausal and not on hormonal BC or opioids.

2. Aromatase Inhibitors (reduce conversion of androgens to estrogen) include chrysin, damiana, and certain medications. High estrogen may be helped by inflammation reducing substances like NAC, turmeric, resveratrol, mangosteen, pomegranate, fish oil, etc.

3. Phytoestrogens include Dong quai, hops, isoflavones (daidzein, genistein), red clover, kudzu, pueraria mirifica, fennel, anise seed, black cohosh.

4. Endocrine Disrupting Chemicals (EDCs) - some of these compounds may be estrogenic and some (i.e. BPA, atrazine) can also increase levels of E2.

5. Methylation support may include magnesium, methyl-Vit B6/B12, TMG, choline, SAMe, methionine, folate (methylfolate).

**Disclaimer:** This form is a reference for providers and not to be considered medical advice or diagnostic for any specific case. Treatment decisions are always to be made at the discretion of a qualified provider.

# Progesterone | Estrogen - Postmenopausal: Potential Treatments for Consideration

	Very Low E2<0.2ng/mg	Expected E2, 0.2-0.7ng/mg		Above Expected E2, 0.7-1.8ng/mg		High E2>1.8ng/mg
		Low E2 Symptoms	High E2 Symptoms	Low E2 Symptoms	High E2 Symptoms	
Progesterone <0.5ng/mL (below post)	E2 and Pg both come primarily from adrenals which should be evaluated. With or without symptoms, ERT <sup>1</sup> may be considered if concerned about low estrogens risks (bone, heart, brain, gut health).	Consider giving phytoestrogens <sup>4</sup> and Pg-HRT. Evaluate adrenals.		Symptoms may not be E2 related. E2 may be fluctuating or exogenous. Consider giving Pg-HRT and evaluate adrenals.	Consider giving Pg-HRT to balance higher than expected estrogens. Consider "High E2" suggestions. Evaluate adrenals.	Identify the source of E2 (inflammation? ovarian? HRT?) and take efforts to reduce and address detox. <sup>3</sup> Consider Pg-HRT and evaluate adrenals.
		A Consider low dose ERT but balance with adequate Pg.	B Once Pg is balanced and symptoms reduced, consider low dose ERT.	C	D	E F
Progesterone 0.5-2ng/mL (normal post)	With or without symptoms, consider ERT if concerned about low estrogens risks (bone, heart, brain, gut health). Evaluate adrenal hormones and also balance any ERT with Pg-HRT.	Consider Pg-HRT and low dose ERT or phytoestrogens. <sup>4</sup> Consider phytoestrogens if avoiding ERT for symptom relief.	Consider Pg-HRT. If symptoms reduce consider low dose ERT or phytoestrogens. <sup>4</sup> Evaluate adrenals as symptoms may not be E2 related.	Consider Pg-HRT to balance higher than expected estrogens. Evaluate adrenals.	Identify the source of E2 (inflammation? ovarian? HRT?) and take efforts to reduce and address detox. <sup>3</sup> Consider Pg-HRT.	L
Progesterone >2.0ng/mL <sup>2</sup>	With or without symptoms, consider ERT if concerned about low estrogen risks. Evaluate adrenal hormones and also balance any ERT with Pg-HRT.	Consider low dose ERT or phytoestrogens. <sup>4</sup>	Symptoms may not be E2-related. Confirm patient is not on HRT or cycling.	Confirm patient is not menstruating or on HRT. If not, see above categories. Pg should be made by adrenals now, so check cortisol for elevations.	P	Patient has normal pre-menopausal levels. Evaluate actual menstrual status or possible HRT.
If Poor Phase 1 Metabolism	When estrogen levels are this low, all metabolite ratios are less accurate (near the detection limit). If ERT is given, consider retesting metabolites after 3 months. Metabolism favoring 16-OHE1 may help for bone health. DIM/I3C is not advised when estrogen levels are this low.  <i>*To support Phase 1 without lowering E2, consider sulforaphane, crucifers, carrots, rosmarinic acid (rosemary, holy basil, lemon balm)</i>	Consider phase 2, sulforaphane, glutathione support.		Consider DIM/I3C, brassica family, sulforaphane, glutathione support.	Strongly consider DIM/I3C, brassica family, sulforaphane, glutathione support.	Strongly consider DIM/I3C, brassica family, sulforaphane, glutathione support. Poor phase 1 metabolism may be contributing to high E2.
If Poor Methylation (Phase 2)		S DIM/I3C may induce estrogen deficiency if the patient is not on ERT.*	T Use DIM/I3C with caution (will lower E2).*	U	V	W
	R	Support methylation. <sup>5</sup> Consider genetic testing (MTHFR, COMT) for more specific treatment.		X	Y	Z Support methylation. <sup>5</sup> Consider genetic testing (MTHFR, COMT) for more specific treatment. Poor methylation may be contributing to high E2.

1. Estrogen Replacement Therapy (ERT) can be considered for women with low levels and related symptoms. ERT should be given with great care and after considering labs, symptoms and patient history. Common, effective routes of administration include transdermal, pellets and intravaginal. Oral and sublingual E2 can also be used but may include risks not associated with the other modes of supplementation. In many cases, balancing ERT with Pg-HRT (which is often oral) is recommended. See DUTCHtest.com for additional resources on ERT.

2. For Pg values higher than 6ng/mL, confirm the patient is not menstruating or taking exogenous hormones (progesterone or pregnenolone).

3. Aromatase inhibitors (reduce conversion of androgens to estrogen) include chrysin, damiana and certain medications. High estrogen may also be helped by inflammation-reducing substances like NAC, turmeric, resveretrol, mangosteen, pomegranate, fish oil, etc.

4. Phytoestrogens include Dong quai, hops, isoflavones (daidzein, genistein), red clover, kudzu, Pueraria mirifica, fennel, anise seed, and black cohosh.

5. Methylation support may include magnesium, methyl-Vit B6/B12, TMG, choline, SAMe, methionine, and folate (methylfolate).

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# DUTCH TESTING & (B)HRT GUIDE - WOMEN

*Disclaimer: This form is a reference for providers and not to be considered medical advice or an endorsement of any particular HRT therapy. Any HRT may involve risks, and it is the sole responsibility of the provider to consider these risks and make treatment decisions.*

Oral Progesterone	Estradiol Patch	Estradiol Cream/Gel	Testosterone or Estradiol Pellet	Vaginal Estrogen or Testosterone	Testosterone Cream/Gel	DHEA
<b>Why</b>						
Effective at balancing ERT, but clinical effects are due largely to metabolites formed in the gut. A good option when postmenopausal women struggle with sleep. A different ROA may be better for premenopausal women. 100-200mg has been shown to balance concurrent ERT.	Patches offer consistent hormone dosing over time and are very effective at managing hot flashes. Even low doses typically increase bone mineral density (BMD).	Proven to increase serum and urine levels as well as improve hot flashes and BMD. Transdermal E2 is attractive because it is easy to use and bypasses first pass metabolism. Estriol often given in doses 1 - 4 times higher than estradiol.	Pellets offer consistent hormone dosing over time for testosterone and estradiol. Research is limited on effects on hot flashes and BMD. Because serum/urine E2 levels match or exceed those seen in patches, E2 pellets are likely to help with hot flashes and BMD.	Low doses increase local tissue levels while higher doses also increase systemic levels. Placing in the top 1/3 of the vagina significantly increases uterine levels. Estriol often given in doses 1 - 4 times higher than estradiol.	Transdermal testosterone can be used to correct low T and improve sex drive and muscle mass.	Sublingual or oral DHEA will increase systemic levels and also contribute to downstream androgens (testosterone) and estrogens.
<i>ERT, especially with an intact uterus, should be balanced with adequate progesterone (vaginal or oral preferred).</i>						
<b>Common Dosing Strategies</b>						
<b>Low</b> 25 - 50 mg	<b>Low</b> 0.012 - 0.025 mg	<b>Low</b> 0.1 - 0.25 mg Estradiol 0.1 - 1.0 mg Estriol	<b>Low</b> <5 mg Estradiol 20 - 50 mg Testosterone	<b>Low</b> 0.01 mg Estradiol 0.25 mg Testosterone	<b>Low</b> 0.5 - 2.0 mg	<b>Low</b> 1 - 5 mg
<b>High</b> >200 mg	<b>High</b> 0.1 mg	<b>High</b> 1.0 - 2.5 mg Estradiol 2.0 - 5.0 mg Estriol	<b>High</b> >12 mg Estradiol >125 mg Testosterone	<b>High</b> 0.5 mg Estradiol 2 mg Testosterone	<b>High</b> 10 - 20 mg	<b>High</b> 25 - 50 mg
<b>Most Common</b> 100 - 200 mg	<b>Most Common</b> 0.05 mg	<b>Most Common</b> 0.25 - 0.5 mg Estradiol 0.25 - 2.5 mg Estriol	<b>Most Common</b> 5 mg Estradiol 100 mg Testosterone	<b>Most Common</b> 0.1 mg Estradiol 0.25 - 1.0 mg Estriol 0.25 - 1.0 mg Testosterone	<b>Most Common</b> 1 - 5 mg	<b>Most Common</b> 5 - 10 mg
Consider taking continuously or as an on/off cycle	Consider taking continuously or as an on/off cycle and changed 1 - 2 times per week	Consider taking daily continuously or as an on/off cycle	Inserted every 3 - 4 months	Taken daily, possibly with cycling	Taken daily, at waking or bedtime	Usually taken daily
<b>How to Monitor with DUTCH</b>						
DUTCH results only show which metabolites are preferred. Evaluate which pathway is dominant (alpha or beta). If patients push down the alpha pathway, a lower dose may be used. Those who prefer beta metabolism and aren't sleeping well might benefit from a higher dose.	<b>Monitoring Estrogen Replacement Therapy (ERT)</b>  Target values between the top of the postmenopausal range (0.7ng/mg for estradiol) and within the first third of the premenopausal range (about 2.5ng/mg).  The specific target for a patient depends on the patient's history and symptoms as well as the patient and provider's comfort level with the risks for too much (breast cancer, etc.) and too little (osteoporosis, etc.) estrogen.  It is recommended to closely monitor phase I metabolites to ensure that too many 4-OH metabolites are not formed. Methylation should also be evaluated and supported if inadequate. DUTCH OATs may also be helpful to ensure that a nutrient deficiency is not present. ERT may induce vitamin B6 deficiency. Proper metabolism requires B6, B12, and glutathione.  For testosterone pellets, premenopausal levels should be targeted and patient symptoms monitored. Evaluate 5a-reductase activity before dosing with testosterone to ensure there isn't excessive 5a metabolism.			Levels above the postmenopausal range imply systemic uptake. For localized (vaginal) effects only, results should not exceed the postmenopausal range. Expect higher E2 levels compared to E1 and downstream metabolites.  Progesterone metabolites underestimate systemic progesterone when taken vaginally.	It is optimal if levels of T (as well as metabolites) are in range. Less is needed if 5a metabolites are favored.  Also monitor patient symptoms for excessive T.	Monitor conversion to testosterone, E2, and metabolites of both. DHEA and testosterone metabolites may be artificially elevated if the patient doesn't skip the dose of DHEA the day of and day before the test (as described in the test instructions).  Transdermal progesterone, oral estrogen, and sublingual hormones, are not well monitored by DUTCH and are not represented on this form along with a few other lesser used HRT options.

# Testosterone - Female: Symptoms

Physiology - Female	
Testosterone (T) is made primarily from two locations. Some T is made throughout the body from the adrenal gland's DHEA and adrostenedione production. In pre-menopausal women, the ovaries also make some T.	
Low Testosterone	
<u>Symptoms</u>	<u>What are other causes of these symptoms (other than low testosterone)?</u>
Belly Fat	High estrogen, sleep disturbance, cortisol, blood sugar dysregulation, hypothyroidism
Bone Loss	Low estrogen, thyroid issues, nutrient deficiency, lack of exercise, hereditary, parathyroid issues, antacids, steroids, SSRIs, low Pg, high cortisol, multiple anovulatory cycles during adolescence
Low Energy	Low DHEA, low Pg, SNS excitation/stress/cortisol, blood sugar dysregulation, serotonin/GABA/dopamine issues, hypothyroidism, sleep disturbance
Low Sex Drive	Low DHEA, low Pg, SNS excitation/stress/cortisol, blood sugar dysregulation, serotonin/GABA/dopamine issues, sleep disturbance, high estrogen, blood sugar dysregulation, hypothyroidism
Low Muscle Mass	Thyroid issues, lack of exercise, nutrient deficiency, stress
Mood Issues/Brain Fog	Low DHEA, low Pg, low pregnenolone hypothyroidism, sleep disturbance, neurotransmitter issues, high estrogen
High Testosterone	
<u>Symptoms</u>	<u>What are other causes of these symptoms (other than high testosterone)?</u>
Acne	Gut dysbiosis, diet choices, stress, endocrine disruptors, nutrient deficiency, high estrogen
Aggression	High estrogen, neurotransmitter issues, blood sugar dysregulation, sleep dysregulation, stress
Body/Facial Hair Growth	Hereditary, endocrine disruptors
Thinning Scalp Hair/Hair Loss	Thyroid issues, iron deficiency, stress, endocrine disruptors, nutrient deficiency

# Testosterone - Female: Lab Assessments

For female patients, DHEA, T, and their metabolites are all considered. Evaluate patient results then proceed to the root cause and treatment considerations. The following descriptions may be helpful to consider treatment options for your patient's testosterone status.

## Low Testosterone

Low T may characterize patients for which any of the following are true:

- T is low and its 3 metabolites (5a-DHT, 5a/5b-androstanediol) are low or low normal.
- T is low normal and its metabolites are mostly low.
- Total DHEA production is low, and testosterone is low or low normal.
- T is within the lower part of the range, but low T symptoms persist.

## Normal Testosterone

Normal Testosterone may characterize patients for which any of the following are true:

- T and most of its metabolites are within range.
- T is low, most other metabolites are within range, and the patient has no related symptoms.
- T is high, most other metabolites are within range, and the patient has no related symptoms.

## High Testosterone

High T may characterize patients for which any of the following are true:

- T is high and its 3 metabolites (5a-DHT, 5a/5b-androstanediol) are high or high normal.
- T is high normal and its metabolites are elevated, and the patient presents with high T symptoms.
- Total DHEA production, T, and its metabolites are high or high normal, and the patient presents with high T symptoms.

## DHEA Consideration

About half of a premenopausal woman's testosterone comes from DHEA (via adrenal production) while the other half comes from ovarian production. In postmenopausal women, nearly all of the available testosterone is

derived from adrenal DHEA. Davis and colleagues (JAMA, 2005 Vol 294) reported that low serum T did not correlate to poor sexual function in women but DHEA-S levels did. They went on to discuss DHEA's ability to convert to T, act on receptors and be further metabolized, all intracellularly. Always consider the patient's testosterone reservoir (DHEA) and T levels as both may be relevant to the patient's T status.

## Testosterone - Female: Potential Root Causes of Abnormal Lab Levels

### Low Testosterone

- Low ovarian/adrenal output
- Low precursors (DHEA, androstenedione)
- Poor hypothalamic/pituitary communication
- Surgically removed ovaries
- Age
- Decreased blood flow to the glands
- Diabetes
- Elevated SHBG (decreased free T)
- Medications (glucocorticosteroids, opioids, accutane)
- Zinc deficiency

### High Testosterone

- HRT transference
- Hyper-adrenal output
- Insulin
- Non-classical congenital adrenal hyperplasia
- PCOS
- Low levels of SHBG (high free T)
- Supplementation (T, Clomid, HCG)

# Testosterone - Female: Potential Treatments for Consideration

	Low Testosterone		Normal Testosterone		High Testosterone	
	No Symptoms	Low T Symptoms	Low T Symptoms	High T Symptoms	No Symptoms	High T Symptoms
<b>General Considerations</b>	If DHEA is normal, cellular testosterone may be adequate. Evaluate adrenal and ovarian function.	Consider tribulus, maca, shatavari, zinc, fenugreek, eurycoma longifolia, DHEA <sup>4</sup> or TRT <sup>3</sup> , and aromatase inhibition <sup>2</sup> if E1 or E2 are high.	Consider tribulus, maca, shatavari, zinc, fenugreek, eurycoma longifolia.	Spearmint tea may lessen symptoms.	With no symptoms, possibly no action. Some patients tolerate moderately high testosterone, especially if 5a-Reductase is not favored. See below.	Consider paeonia, vitex, liver support, herbal anti-androgens. <sup>7</sup> Consider PCOS. Rule out TRT transfer.
<b>If 5a-Reductase High/Favored<sup>1</sup></b>  Metabolism favoring androsterone over etiocholanolone	Investigate potential insulin dysregulation.		Investigate potential insulin dysregulation.		Investigate potential insulin dysregulation and consider blocking 5a-Reductase <sup>5</sup> to relieve symptoms. Consider possible PCOS. PCOS can be caused by ovarian (insulin) or adrenal dysfunction.	
	5a-metabolism may increase androgenic impact of T.	Blocking 5a-Reductase may exacerbate low T symptoms.	Blocking 5a-Reductase may exacerbate low T symptoms.	Consider blocking 5a-Reductase <sup>5</sup> to relieve symptoms. Consider PCOS.		
<b>If DHEA Lower</b>  (See "Total DHEA Production" on DUTCH report)	With or without low androgen symptoms, these patients may need more androgens. Consider DHEA <sup>4</sup> and evaluate adrenal and ovarian function.		Consider DHEA <sup>4</sup> and evaluate adrenal function.	Consider DHEA <sup>4</sup> if 5a-Reductase is not high. Evaluate adrenal function.	Evaluate adrenal function. If the patient has high T, monitor symptoms carefully if giving DHEA. <sup>4</sup>	If 5a-Reductase is not high consider paeonia, vitex, liver support.
<b>If DHEA Higher</b>  (See "Total DHEA Production" on DUTCH report) <sup>7</sup>	With higher DHEA, cellular T may be adequate even though urine testosterone is low. Evaluate cortisol.	With low T symptoms, lowering DHEA may not be advised. Evaluate glucose/insulin and cortisol.	With low T symptoms, lowering DHEA may not be advised. Evaluate glucose/insulin and cortisol.	Evaluate adrenal function. Consider PCOS. Blood sugar support. <sup>6</sup>	Consider blood sugar support. <sup>6</sup> Evaluate adrenal function. Consider PCOS.	

1. If androgens are preferentially pushed down 5a instead of 5b pathways, high levels of 5a-DHT may be produced at the cellular level. Excessive 5a-DHT may result in high androgen symptoms even in the absence of high T. 5a-DHT is 3x more androgenic than T. 5a-Reductase is best assessed by evaluating the most abundant 5a/5b metabolites (androsterone/etiocholanolone).

2. Testosterone conversion to estrogen can be blocked by products that include chrysin, damiana, and certain medications.

3. Testosterone Replacement Therapy (TRT) may be considered to increase testosterone. Pellets and transdermal or vaginal creams are commonly used. Also consider using DHEA.

4. DHEA can be taken orally or sublingually (transdermal or vaginal also available). For women, 5-10mg is a common dose.

5. 5a-Reductase is blocked by saw palmetto, nettles, pygeum africanum, zinc, EGCG (green tea extract), reishi mushroom.

6. Inositol, berberine, magnesium, a-lipoic acid, fiber, etc. Use lab testing (HbA1c, insulin, etc.) as needed.

7. Spearmint tea, chaste tree, licorice, white peony, green tea, black cohosh, red reishi.

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# Testosterone - Male: Symptoms

## Physiology - Male

Testosterone (T) is made primarily from the testes upon signaling from the brain with LH (released from the pituitary). The testes make both T and epi-T. T is metabolized to 5a-DHT and two forms of androstanediol. The amount of T created from adrenal DHEA is minimal.

## Low Testosterone

<u>Symptoms</u>	<u>What are other causes of these symptoms (other than low testosterone)?</u>
Belly Fat	High estrogen, sleep disturbance, SNS excitation/stress/cortisol, blood sugar dysregulation, hypothyroidism
Bone Loss	Low estrogen, low Pg, thyroid issues, high cortisol, nutrient deficiency, lack of exercise, hereditary, parathyroid issues, antacids, steroids, SSRIs
Low Energy	Low DHEA, low Pg, SNS excitation/stress/cortisol, blood sugar dysregulation, serotonin/GABA/dopamine issues, hypothyroidism, sleep disturbance
Low Sex Drive	Low DHEA, high estrogen, low Pg, SNS excitation/stress/cortisol, blood sugar dysregulation, serotonin/GABA/dopamine issues, sleep disturbance, blood sugar dysregulation, hypothyroidism
Low Muscle Mass	Thyroid issues, lack of exercise, nutrient deficiency, stress
Mood Issues/Brain Fog	Low DHEA, hypothyroidism, low Pg, high estrogen, sleep disturbance, neurotransmitter issues
Gynecomastia	High estrogen, sleep disturbance
Erectile Dysfunction	High estrogen, low Pg, blood sugar dysregulation, hypothyroidism, sleep disturbance

## High Testosterone

<u>Symptoms</u>	<u>What are other causes of these symptoms (other than high testosterone)?</u>
Acne	Gut dysbiosis, diet choices, stress, endocrine disruptors, nutrient deficiency, high estrogen
Aggression	High estrogen, neurotransmitter imbalance, blood sugar dysregulation, sleep dysregulation, stress
Body/Facial Hair Growth	Hereditary, endocrine disruptors
Thinning Scalp Hair/Hair Loss	Thyroid issues, iron deficiency, stress, endocrine disruptors, nutrient deficiency
Prostate Problems	Prostate infection

# Testosterone - Male: Lab Assessments

Urinary testosterone (T) is of primary importance on the DUTCH test®. It is also important to monitor the three downstream metabolites (5a-DHT, 5a-androstanediol, 5b-androstanediol) as well as epi-testosterone.\* The three downstream metabolites should generally rise and fall along with T. Some patients may have unique metabolism patterns, so interpret with care.

## Low Testosterone

Low T may characterize a patient in the following scenarios, especially when low T symptoms persist:

- T is below the reference range (<25ng/mg).
- T is within the overall reference range of 25-115ng/mg but is below the age-dependent range for the patient.
- T is on the lower side of the range and symptoms of low T persist.

*Some low T scenarios may include suggestions for Testosterone Replacement Therapy (TRT). All TRT may have risks which must be understood by a provider before considering any TRT.*

## Normal Testosterone

Normal T describes patients comfortably within the reference range. Patients on the lower side of normal with low T symptoms may benefit from higher T. Patients with slightly elevated levels and no symptoms may not need any treatment.

## High Testosterone

Slightly elevated T may not be problematic for some men. See the treatment guide if high T symptoms exist.

**\*Epi-testosterone is a nonandrogenic testosterone analog used to confirm testicular androgen production.**

- If T values are less than half of epi-testosterone values, the urine results may be unreliable (confirm with a serum T test).
- If T and epi-testosterone results are both below 10ng/mg, there may be significant suppression of gonadal hormone production. In these cases, it may be prudent to test LH in serum and investigate causes of T suppression (opioids, anti-androgens, steroids, etc.)
- If T values are dramatically higher (>2-3 times) than epi-testosterone, the patient may be taking exogenous T therapy.

## Testosterone - Male: Potential Root Causes of Abnormal Lab Levels

### Low Testosterone

- Medications (performance steroids, glucocorticosteroids, opioids, Accutane, anti-androgen therapy)
- Recent testosterone supplementation
- Zinc deficiency
- Environmental exposure
- Regular THC use
- Alcohol
- Age
- Sleep disturbance
- Obesity
- Hypothyroidism
- Diabetes
- Increased aromatization
- Hyperprolactinemia
- Elevated SHBG
- Leptin and leptin receptor mutation
- Isolated or combined pituitary or hypothalamic disease
- Hypogonadism/removal of testicle
- Testicular infection
- Space occupying lesion to pituitary or hypothalamus
- Infarction affection pituitary or hypothalamus
- Decreased blood flow to the glands
- Autoimmune anti-Scc antibodies - Leydig cell specific
- Radiation to the groin area, chemo at-large
- Traumatic Brain Injury

### High Testosterone

- Low levels of SHBG (high free T)
- Supplementation (T, Clomid, HCG)
- Increased/healthy growth hormone levels (supplementation for growth hormone)
- Resistance training/HIIT
- Some young men may innocuously have slightly elevated T levels

# Testosterone - Male: Potential Treatments for Consideration

	Low Testosterone		Normal Testosterone		High Testosterone	
	No Symptoms	Low T Symptoms	Low T Symptoms	High T Symptoms	No Symptoms	High T Symptoms
<b>General Considerations</b>	Rule out hypothyroidism, high prolactin, diabetes, opioid/steroid use, alcohol, toxicant exposure.		Evaluate cortisol for elevations and the Sympathetic Nervous System for excitation. Consider treatments in box "B" for low T.	Address any inflammation or insulin dysregulation. See 5a-Reductase below as high T symptoms may be caused by 5a-DHT.	Slightly elevated T may not be problematic. If patient complains of low T symptoms, check cortisol or Sympathetic Nervous System excitation.	Address any inflammation. Consider liver detox. Possibly test LH/SHBG, thyroid, adrenals.
	Even without symptoms, consider testing TRT. <sup>4</sup>	Consider tribulus, maca, fenugreek, zinc, withania, mucuna, eurycoma longifolia, TRT. <sup>4</sup> Evaluate LH/SHBG in serum.				
If 5a-Reductase High/Favored <sup>1</sup> Metabolism favoring androsterone over etiocholanolone and 5a-androstanediol over 5b-androstanediol	Investigate potential insulin dysregulation. If 5b-Reductase is preferred, it may contribute to low T symptoms due to less androgenic 5a-DHT. Hypothyroidism may correlate with 5b-metabolism.	G	Investigate potential insulin dysregulation.	I	Investigate potential insulin dysregulation and consider blocking 5a-Reductase <sup>2</sup> for prostate health, particularly if high T symptoms exist.	J
If Estradiol is High	Inflammation, belly fat, high insulin, BPA, atrazine exposure can increase E2. Possibly block aromatase. <sup>3</sup> Optimize phase 1 metabolism and methylation of estrogens.	K	Review testosterone and estrogen balance.	H	Inflammation, belly fat, high insulin, BPA, atrazine exposure can increase E2. Possibly block aromatase. <sup>3</sup> Optimize phase 1 metabolism and methylation of estrogens.	M
If DHEA is Low (See "Total DHEA Production" in DUTCH Report)	Low DHEA may be worth addressing with DHEA, <sup>5</sup> but do not expect DHEA to convert significantly to testosterone. Monitor estrogen if giving DHEA. Monitor cortisol levels also.	N	Consider DHEA <sup>5</sup> supplementation but check overall adrenal production first. Monitor estrogen if giving DHEA.	O	With high T symptoms, giving DHEA may not be appropriate. Investigate overall adrenal health.	P
					Consider DHEA <sup>5</sup> supplementation but check overall adrenal production first. Monitor estrogen if giving DHEA.	Q
					With high T symptoms, giving DHEA may not be appropriate. Investigate overall adrenal health.	R

- If androgens are preferentially pushed down 5a instead of 5b pathways, high levels of 5a-DHT may be produced at the cellular level. Excessive 5a-DHT may result in high androgen symptoms even in the absence of high T. 5a-DHT may also lead to prostate problems (especially if estrogen is also high).
- 5a-Reductase is blocked by saw palmetto, nettles, pygeum africanum, zinc, EGCG, reishi mushroom, and medications like Finasteride.
- Testosterone conversion to estrogen can be blocked by products that include chrysin, damiana, and medications like Anastrozole.
- Low testosterone may be primary hypogonadism where the testicles do not produce adequate T (in these cases blood LH will be elevated) or secondary hypogonadism where the pituitary produces inadequate LH to signal the testes. In older men Testosterone Replacement Therapy (TRT) may be considered to increase testosterone. Injections, transdermal creams, and pellets are common TRT applications. Younger men may also consider HCG (analog to LH) or Clomiphene (acts on the brain to stimulate LH production).
- In men 10-50mg is a common dose of DHEA. Sublingual dosing may result in less estrogen conversion compared to oral.

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# DUTCH TESTING & (B) HRT GUIDE - MEN

*Disclaimer: This form is a reference for providers and not to be considered medical advice or an endorsement of any particular HRT therapy. Any HRT may involve risks, and it is the sole responsibility of the provider to consider these risks and make treatment decisions.*

Pellet	Injection	Transdermal	DHEA	HCG or Clomiphene
<b>WHY</b>				
Testosterone pellets offer consistent hormone dosing over time. Most pellet doses tend to suppress endogenous testosterone production. They can be given with aromatase inhibitors if estrogen production is a concern.	The most frequently used testosterone injections are testosterone cypionate (8 day half-life) and testosterone enanthate (4-5 day half-life). Injections provide robust testosterone levels for 1-2 weeks typically. Bi-weekly dosing (lower dosing) may offer improved steady state and less highs and lows.	Testosterone creams and gels are the most popular TRT formulation but can be challenging to dose and monitor effectively. Doses between 50 and 150mg are commonly used in studies in order to see improvements in muscle mass and other clinical parameters. Application is convenient, but patients must also be careful to avoid transference (to partners, children, or pets).	Even though testosterone is downstream from DHEA, very little testosterone is made from circulating DHEA. The testes make testosterone directly (from cholesterol), so do not give DHEA expecting significant increases in testosterone. Oral or sublingual DHEA is often used. The latter may absorb directly in the mouth and bypass gut/liver metabolism, which may result in less estrogen production.	Human chorionic gonadotropin (hCG) acts as an LH analog and stimulates the Leydig cells to produce testosterone. Clomiphene citrate, a selective estrogen receptor modulator (SERM) can also be used for secondary hypogonadism. By blocking negative feedback of estrogen receptors, it increases gonadotropin levels, indirectly increasing testosterone production. These two options are not advised for primary hypogonadism.
<b>Common Dosing Strategies</b>				
<b>Low</b> 400 mg  <b>High</b> 1600 - 2000 mg  <b>Most Common</b> 800 - 1200 mg  <i>Inserted every 4-6 months</i>	<b>Low</b> 25 - 100 mg  <b>High</b> >300 mg  <b>Most Common</b> 100 - 250 mg  <i>Self-administered every one to two weeks</i>	<b>Low</b> 25 - 75 mg  <b>High</b> 150 - 250 mg  <b>Most Common</b> 50 - 100 mg  <i>Typically applied daily</i>	<b>Low</b> 5 - 10 mg  <b>High</b> >100 mg  <b>Most Common</b> 10 - 25 mg  <i>Typically taken daily</i>	<b>HCG</b> 100 - 250 ug (2000 - 5000 IU) <i>Taken 2 - 3 times/week</i>  <b>Clomiphene</b> 25 mg <i>Taken every other day</i>
<b>How to Monitor with DUTCH</b>				
Urine testosterone levels are often supraphysiological in the days following an injection and in the first three months of pellet therapy. With 1200 mg testosterone pellets, results are expected to be 90-220ng/mg over this period (reference range 25-115ng/mg).  Monitor testosterone along with its metabolites to assess 5a-DHT production and evaluate potential need for blocking 5a-reductase. Patients on TRT should also be evaluated for aromatization of testosterone to estradiol by monitoring estradiol and its metabolites.	In men who are not on TRT, epi-testosterone is expected to be found in similar concentrations as testosterone. When gonadal production of hormones is suppressed by TRT, epi-testosterone may be a good indicator of this suppression. Typically levels below 10ng/mg indicate suppression (and especially if <5ng/mg). While correlating data has not been generated, these levels may parallel serum LH levels. Both LH and epi-testosterone are suppressed by most doses of injections and pellets.	Doses proven to increase muscle mass (25-100mg) in most recipients typically push DUTCH testosterone levels to levels matching the reference range for young, healthy men (50-115ng/mg). Monitoring 5a-DHT and its metabolite will assist in evaluating if 5a-blockers may be appropriate. Epi-testosterone levels will often be only partially suppressed (not below 10ng/mg), which implies that endogenous production (and likely pituitary LH secretion) is only partially suppressed. Monitor estrogen conversion and metabolism as well.	Overall DHEA levels can be monitored with the total of DHEA metabolites (DHEA-S, etiocholanolone, androsterone). Also monitor the downstream conversion to estrogens along with estrogen metabolites. Be aware that DHEA can form testosterone metabolites without necessarily making testosterone itself.	Providers may want to target young, healthy testosterone levels (50-115ng/mg) with these therapies. 50-150% increases are common in hypogonadal men. Metabolites of testosterone (including DHT production) should all be monitored along with estrogen production and metabolism. Estradiol production will often exceed physiological levels with hCG use.

# MONITORING (B)HRT WITH LAB TESTING

Tutorials available at [www.dutchtest.com/videos/hormone-tutorials](http://www.dutchtest.com/videos/hormone-tutorials)



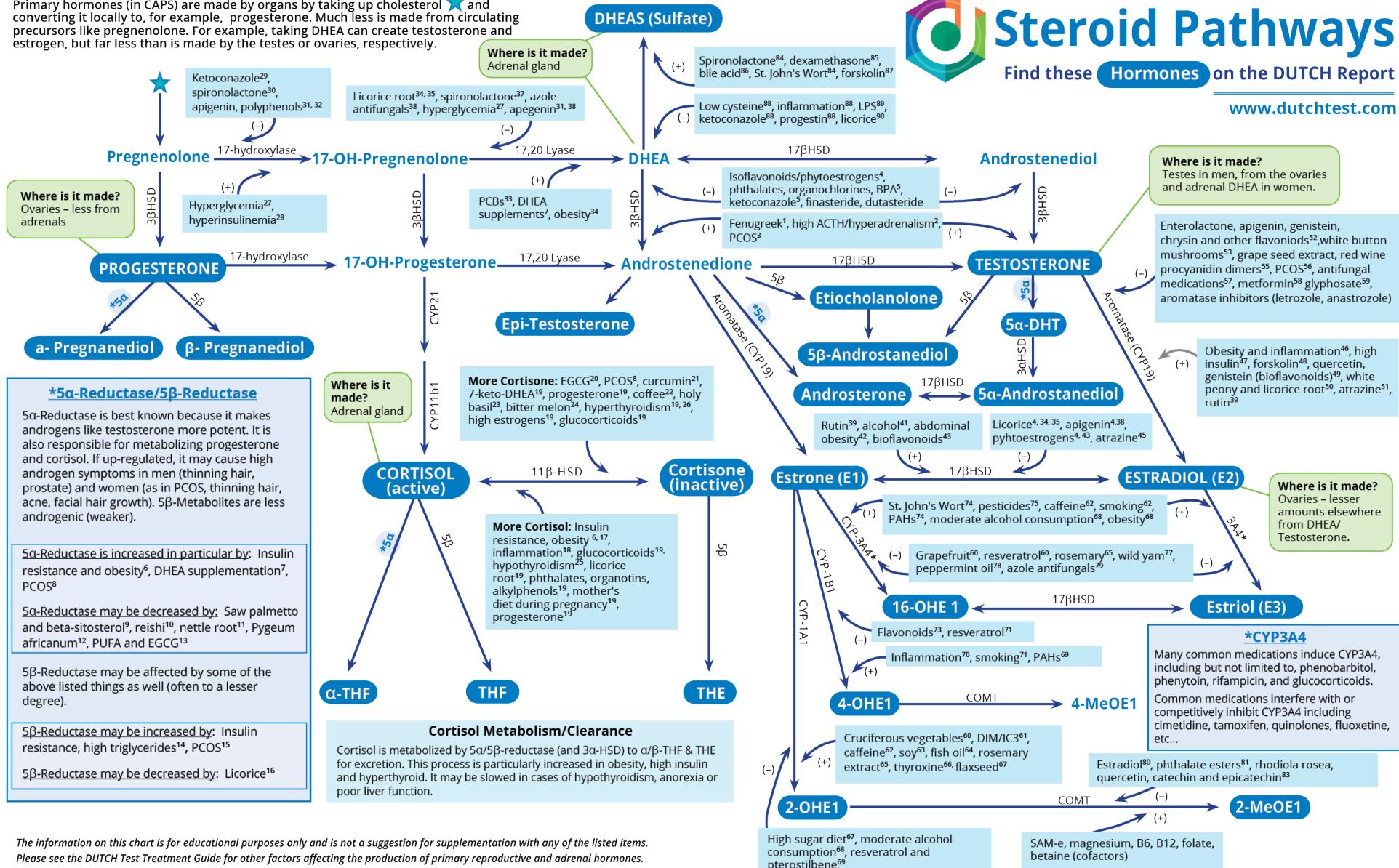
Oral Progesterone	Patch, Pellet, Injection	Transdermal Estrogen	Transdermal Testosterone	Transdermal Progesterone	Vaginal or Anal Mucosa	Oral Estrogen	Sublingual
✗ DUTCH	✓ DUTCH	✓ DUTCH	✓ DUTCH	✗ DUTCH	✓ DUTCH (E/T)	✗ DUTCH	✗ DUTCH
The DUTCH test provides useful feedback when using oral progesterone to aid sleep disturbance related to menopause. 5a (more active) and 5b (less active) metabolites are measured to individualize doses of oral progesterone. Much of the clinical impact is from the effects of the 5a-metabolites.	Values increase intuitively with dosing. For estrogen patches, see Transdermal Estrogen comments. Pellets and injections also increase levels intuitively, but the increase may exceed what is seen in serum testing. DUTCH allows for monitoring both the proper dosing of hormones as well as metabolic patterns.	Target values between the top of the postmenopausal range and the lower third of the premenopausal range correlate with patient clinical improvement (bone density, hot flash relief, etc.). Doses that push levels to the middle of the premenopausal range and beyond may be excessive. DUTCH is preferred over serum due to the inclusion of metabolites.	Levels generally parallel measurable clinical outcomes (increased lean body mass, decreased LH values in men). Epitestosterone values can also be used to assess gonadal suppression due to TRT (levels decrease as TRT increases and are <10 ng/mg with complete suppression).	Creams and gels cannot be effectively monitored with any lab testing. Values increase only slightly with dosing. Because of the uncertainty of tissue levels, take caution to use concurrently with estrogen therapy without endometrium surveillance (ultrasound or biopsy).	Special method removes potential contamination and monitoring is helpful with most hormones. Very low doses may impact local tissue without increasing lab values.  ✗ DUTCH (Pg)  Progesterone is measured indirectly in urine by measuring pregnanediol. This metabolite is underrepresented when taken vaginally.	Cannot be used to effectively monitor dosing due to 1st-pass metabolism. Most of the hormone in urine has not been in circulation as "free" hormone.  While dosing is not effectively monitored with DUTCH, metabolite patterns can be effectively assessed.	Lab testing is not effective. DUTCH is confounded by the hormone that is swallowed.  While dosing is not effectively monitored with DUTCH, metabolite patterns can be effectively assessed.
✗ SERUM	✓ SERUM	✓ SERUM	✓ SERUM	✗ SERUM	✓ SERUM	✓ SERUM	✗ SERUM
Results go up-and-down quickly. If taken at bedtime, levels return to baseline within a few hours. Results can also be inaccurate due to progesterone metabolites cross-reacting with immunoassay tests.	Serum testing is well suited for use with these types of therapies. Results increase with increased dosing in a fairly linear fashion.	Effective for monitoring estrogen creams and gels similarly to patches. Levels may have an up-and-down pattern throughout the day, unlike when using patches.	Results correlate to clinical symptoms. In men, lean body mass increases only when serum (and likely urine) results increase.	Values do not increase significantly with dosing.	While serum levels likely represent systemic uptake of hormone, interpret with care as you may not know if your value represents a peak or a trough.	Serum testing offers the best feedback on monitoring the actual dose of oral estradiol.	Serum testing is not effective. Results rise and fall too rapidly for useful testing. In many cases, results are back to baseline within a few hours.
✗ SALIVA	What about salivary testing?						
The literature to date reveals that salivary testing is clinically inaccurate for monitoring many situations, including transdermal hormone creams. Hormone injections, estrogen patches, and oral tablets along with vaginal hormones may be properly represented by salivary testing, although data is limited. For each of the situations in which salivary testing may parallel the clinical impact, DUTCH (for injections, patches, vaginal estrogen, and testosterone) or serum testing (for injections, patches, oral estradiol, and vaginal hormones) are better options. While salivary testing is the Gold Standard for free cortisol measurement, avoiding its use for monitoring HRT is advised.							

Primary hormones (in CAPS) are made by organs by taking up cholesterol  and converting it locally to, for example, progesterone. Much less is made from circulating precursors like pregnenolone. For example, taking DHEA can create testosterone and estrogen, but far less than is made by the testes or ovaries, respectively.

 Steroid Pathways | The Human Steroidome Database | STEROMD

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The information on this chart is for educational purposes only and is not a suggestion for supplementation with any of the listed items. Please see the DUTCH Test Treatment Guide for other factors affecting the production of primary reproductive and adrenal hormones.

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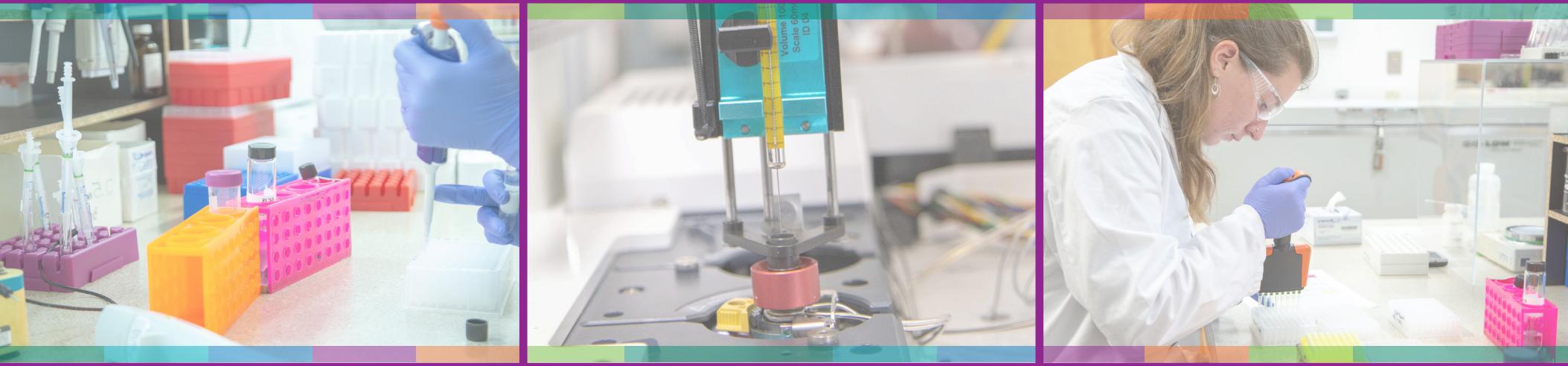
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