

### Salivary Analysis of Hormones

Numerous studies support the use of salivary hormone analysis to map out menstrual cycle hormone profiles.<sup>1-7</sup> A study by Gandara measured estradiol and progesterone in serum and saliva and rated menstrual cycles as normal or abnormal according to the results. There was good agreement between serum and saliva, with both sample types finding normal or near normal cycles in 78% of women studied. The author concluded that “whole saliva samples ... provide a noninvasive, feasible method of determining menstrual cycle profiles.”<sup>2</sup>

### Month-Long Hormone Assessment

The Month-Long Hormone Assessment requires the collection of eleven saliva samples over 33 days. Progesterone and estradiol levels are reported for each of the 11 samples and graphed chronologically, clearly illustrating how the

hormones interact throughout the cycle. In addition, equal amounts of saliva from each of the 11 samples are pooled and testosterone, DHEAS and cortisol are measured - providing a month-long ‘average’ of these key hormones.

Women with abnormal bleeding (heavy, sporadic, light), amenorrhea, fertility issues or cycle-specific symptoms such as migraine headaches, hot flushes, or mood disturbances may benefit from a Month-Long Assessment. Symptom information is requested for the sample days and by correlating the patient’s self-reported symptoms with hormone levels throughout the menstrual cycle, it is often possible to find an underlying hormone imbalance. Cases presented on the following pages demonstrate the value of the MLHA and correlating symptoms and hormone levels.

### Fertility issues

- ▶ Inadequate, early, or late progesterone surges in the luteal phase can affect ability to conceive.
- ▶ Menstrual cycle length may affect fertility. For example, a woman whose progesterone peaks on day 14, rather than between days 19 and 21, may have difficulty conceiving because ovulation will also be earlier.

### Abnormal bleeding

- ▶ Heavy bleeding is usually associated with high estradiol levels, but may also occur as a result of: low estradiol, a relative imbalance of estrogen and progesterone, anovulation or androgen excess. The Month-Long Hormone Assessment (MLHA) helps identify many of the causes of abnormal bleeding.

### Amenorrhea

- ▶ High androgens and/or anovulation are potential underlying causes of amenorrhea.
- ▶ Oral contraceptive use affects hormone production.

### Mood swings

- ▶ By tracking mood-related symptoms with hormone levels, hormone imbalances that contribute to mood issues may be identified.

### Cycle specific symptoms

- ▶ Certain symptoms may occur at specific times in the menstrual cycle. For example: hot flashes may occur late in the luteal phase when Pg is falling and E2 rises unexpectedly.

Clinical utility and ease of sample collection makes salivary hormone analysis ideal for a Month-Long Hormone Assessment. Samples can be kept in the freezer as collections proceed, and all eleven samples can be mailed together in the pre-paid mailer when collection is complete.



**Estradiol**  
**Progesterone**  
**Testosterone**  
**DHEAS**  
**Cortisol**

The MLHA provides the most comprehensive view of saliva hormone levels in menstruating women.



## Hormones

### Estradiol (11 points over 33 days)

- ▶ High estradiol levels may impair thyroid function, and/or contribute to erratic bleeding.
- ▶ Low estradiol levels may contribute to abnormal bleeding and difficulty conceiving.
- ▶ Estradiol is needed for the proper function of progesterone receptors, and maintenance of the right balance between estrogens and progesterone is crucial for hormone health.

### Progesterone (11 points over 33 days)

- ▶ Insufficient progesterone relative to estradiol can result in estrogen dominant symptoms like weight gain at hip, breast tenderness, anxiety, fluid retention and fibrocystic breasts.

### Cortisol (pooled average)

- ▶ Elevated cortisol can interfere with the action of progesterone and testosterone at gene regulatory sites. Consequently, women with normal progesterone and/or testosterone levels may exhibit signs of deficiency when cortisol levels are high. This is called a functional deficiency.
- ▶ High cortisol can induce the enzyme aromatase, which speeds the conversion of testosterone to estradiol. High cortisol may elevate estradiol levels, especially when DHEAS and/or testosterone are also elevated.

- ▶ Excess cortisol is catabolic for bone and also opposes the action of testosterone, which is anabolic for bone. Thus, significant bone loss may occur with elevated cortisol levels.
- ▶ Prolonged secretion of cortisol over time may impair the ability of the adrenal glands to make optimal amounts of cortisol.

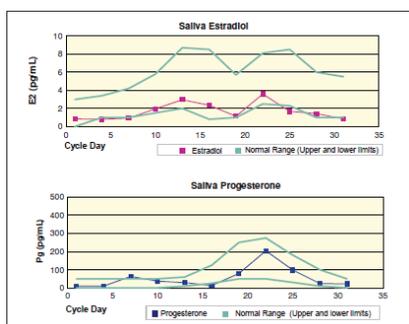
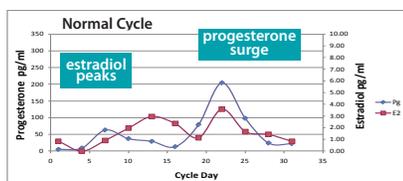
### Testosterone (pooled average)

- ▶ High testosterone correlates with insulin resistance and metabolic syndrome.
- ▶ Low testosterone may be responsible for symptoms like low sex drive, vaginal dryness and bone loss.

### DHEAS (pooled average)

- ▶ DHEA is stored in the blood mainly in its sulphate form, DHEAS.
- ▶ Cortisol and DHEA have opposite effects on immune function and insulin regulation.
- ▶ High cortisol levels require more DHEAS to be released to balance effects of cortisol. Thus, chronically elevated cortisol can result in a deficiency of DHEAS.
- ▶ Low DHEAS levels may be associated with hypothyroidism and chronic illnesses such as lupus and rheumatoid arthritis.

## Estradiol-Progesterone Graph



## Clinical Presentation

**Normal/Regular:** A regular menstrual cycle typically displays two distinct estradiol peaks. The first peak occurs at ovulation, and the second peak coincides with the mid-luteal progesterone surge.

A woman may have regular periods yet have an 'abnormal' menstrual cycle pattern. In the absence of issues like premenstrual syndrome, infertility or hormone-related symptoms, there is generally no need to map out the menstrual cycle hormones.

If menstrual cycle specific problems arise, investigation via a Month-Long Hormone Assessment is worthwhile.

## Possible Interventions

- Women with a normal cycle but experiencing symptoms may require further laboratory investigation.

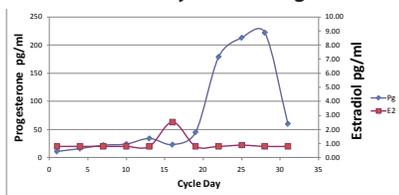
Choice of additional lab test(s) depends on patient symptoms.

Lab tests for consideration:

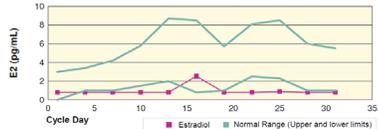
- Adrenal Function Panel
- Food Sensitivity Test
- Urine Elements
- Urine Steroids
- Urine Thyroid

## Estradiol-Progesterone Graph

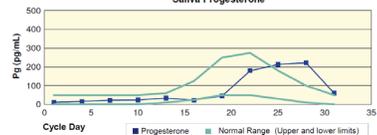
### Difficulty conceiving



### Saliva Estradiol



### Saliva Progesterone



## Clinical Presentation

38 year old, **regular menses**, difficulty conceiving.

- Symptoms include: feeling burned out, morning sluggishness, fatigue, sleep disturbances, feeling 'tired but wired'.

### Month-Long Hormone Assessment

- Progesterone peak is shifted right (late luteal phase). Ovulatory E2 surge is minimal and luteal E2 surge is absent.

Low estrogen and a delayed progesterone surge likely contribute to difficulty conceiving.

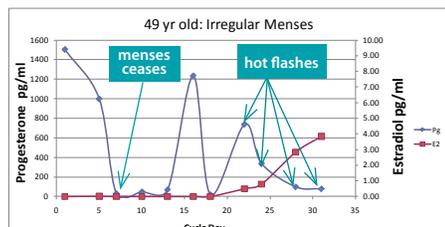
## Possible Interventions

- Literature shows the botanical *Vitex agnus-castus* normalizes progesterone in luteal phase and helps with infertility.

Lab tests for consideration:

- Adrenal Panel:** a flat diurnal cortisol profile may contribute to hormone imbalance and difficulty conceiving.
- Urnie Steroids:** may offer additional insights into hormone metabolism.
- Urine Thyroid:** insufficient thyroid hormone may impact ability to conceive.

### Wide fluctuations in Pg associated with perimenopause symptoms



49 year old, **irregular menses**, BMI <20

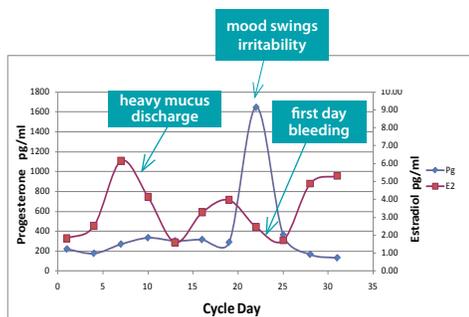
- Symptoms include: hot flashes, foggy thinking, memory lapses, decreased sex drive, fatigue.

### Month-Long Hormone Assessment

- Menses ceases when Pg levels crash.
- Anovulatory cycle.
- Erratic Pg output - two significant peaks.
- E2 not coordinated with Pg: hot flashes appear when Pg falling/E2 rising.

- Vitex agnus-castus* to normalize progesterone throughout cycle.
- Pg supplementation for 14 days per cycle.
- Low BMI may be contributing to erratic cycle. Modest weight gain might help.

### High progesterone associated with mood swings & irritability



46 year old, **regular menses**, BMI >30

- Symptoms include: feeling burned out, pressed for time, 'tired but wired', fatigue, anxiety.

### Month-Long Hormone Assessment

- Moodiness and irritability coincide with progesterone peak.
- Pg is ten times normal.

General complaints of foggy thinking and fatigue consistent with very high Pg levels.

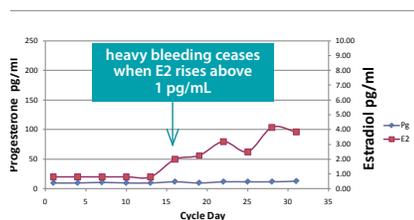
Typically associate irritability with low Pg, but opposite is true in this case. MLHA demonstrates value of knowing hormone levels as they relate to symptoms rather than just treating based on test results.

- Additional Pg is not recommended if cycle-specific symptoms worsen when Pg is high.
- Use botanical or homeopathic hormone balancing agents.
- Weight loss/decrease body fat to reduce estrogen stores.
- Improve estradiol elimination by increasing fiber.

Lab tests for consideration:

- Adrenal Panel:** a flat diurnal cortisol profile can lead to symptoms of fatigue and burn-out.

### Heavy bleeding stops with rise in E2



44 year old, **irregular menses**, normal BMI

- Primary complaint is heavy bleeding.

### Month-Long Hormone Assessment

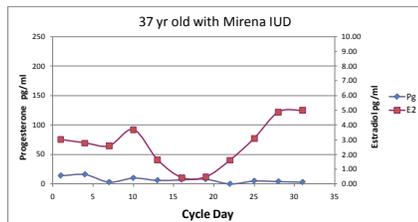
- Bleeding ceases when E2 rises above 1 pg/mL.

Usually associate heavy bleeding with high E2, but opposite is true in this case. MLHA demonstrates value of knowing hormone levels as they relate to symptoms rather than just treating based on test results.

- Cyclic progesterone may "resynchronize" Pg and E2, and induce ovulatory cycles.
- Phytoestrogens offer some estrogenic effects:
  - Flaxseed lignans
  - Soy isoflavones
  - Red clover isoflavones

## Estradiol-Progesterone Graph

### Levonorgestrel-containing IUD suppresses Pg



## Clinical Presentation

37 year old female, no menses, BMI >25

- Symptoms include: breast tenderness, water retention, sleep disturbances.

### Month-Long Hormone Assessment

- Anovulation
- Erratic E2 output
- E2/Pg imbalance

Profile shows imbalance between E2 and Pg. High estradiol relative to progesterone can lead to symptoms of breast tenderness, water retention and sleep disturbances.

## Possible Interventions

- Giving progesterone cyclically may ameliorate estrogen dominance symptoms.
- Giving cyclic progesterone in this circumstance is not known to impair contraceptive effect, but formal studies are lacking.

## Month-Long Hormone Assessment

### Frequently Asked Questions

#### What if a woman has a shorter than average menstrual cycle length?

For example, a woman with a 25 day cycle can collect every third day in the first half of her cycle, then every other day in the latter half of the cycle. In other words, she collects as follows: Days 1 (first day of bleeding), 4, 7, 10, 13, 16, 17, 19, 21, 23, and 25.

#### Is testing useful if a woman is using progesterone cream the last two weeks of her cycle?

If a woman is using progesterone cream, the results will reflect progesterone cream levels, not the endogenous progesterone level. Therefore, the progesterone levels reported will provide no useful information regarding ovarian production of progesterone.

#### Is the month-long assessment useful for post-menopausal women?

At this time, we have no data to suggest that the Month-Long Hormone Assessment is clinically useful for post-menopausal women.

#### What if patient forgets to collect one day?

Have patient collect the next day and adjust the remaining collection days. It is essential that we receive 11 tubes.

#### What if patient is on the birth control pill?

Generally, the use of synthetic hormones such as those in oral contraceptives suppress endogenous production resulting in lower levels of estradiol and progesterone. Thus, the typical profiles will not be seen in these cases. However, there is value in knowing the average level of each of the five hormones across a month.

## References

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